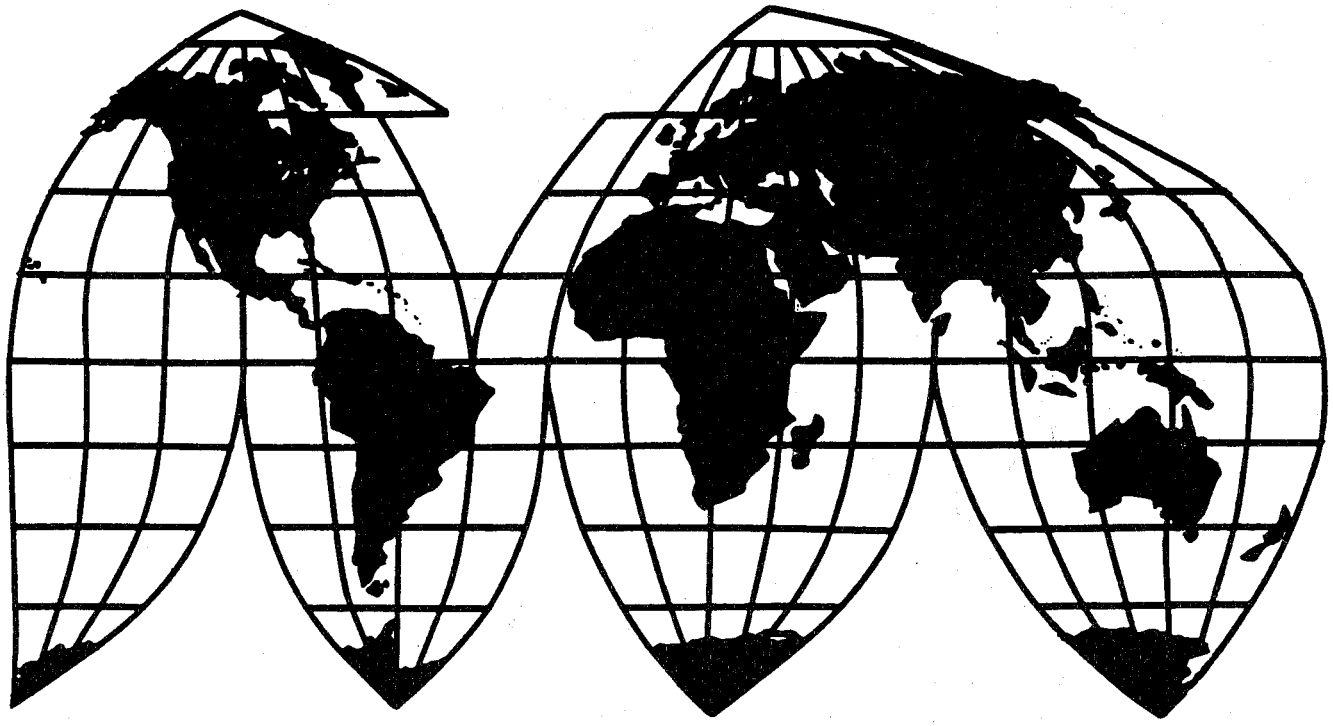
In the Matter of

Certain Salinomycin Biomass and Preparations Containing Same

Investigation No. 337-TA-370

Publication 2978 **July 1996**

U.S. International Trade Commission



Washington, DC 20436

U.S. International Trade Commission

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UNITED STATES INTERNATIONAL TRADE COMMISSION
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In the Matter of	Investigation No. 337-TA-370
CERTAIN SALINOMYCIN BIOMASS AND PREPARATIONS CONTAINING SAME	

NOTICE OF COMMISSION DECISION NOT TO REVIEW A FINAL INITIAL DETERMINATION TERMINATING THE INVESTIGATION BASED ON A FINDING OF NO VIOLATION OF SECTION 337

AGENCY: U.S. International Trade Commission.

ACTION: Notice.

SUMMARY: Notice is hereby given that the U.S. International Trade Commission has determined not to review the final initial determination (ID) issued on November 6, 1995, by the presiding administrative law judge (ALJ) in the above-captioned investigation, thereby terminating the investigation with a finding of no violation of section 337 of the Tariff Act of 1930.

FOR FURTHER INFORMATION CONTACT: Jean H. Jackson, Esq., Office of the General Counsel, U.S. International Trade Commission, 500 E Street, S.W., Washington, D.C. 20436, telephone 202-205-3104.

SUPPLEMENTARY INFORMATION: The Commission instituted this investigation, which concerns allegations of violations of section 337 of the Tariff Act of 1930 in the importation, sale for importation, and sale after importation of certain salinomycin biomass and preparations containing same on February 6, 1995. The Commission named the following firms as respondents: Hoechst Aktiengesellschaft, Hoechst Veterinar GmbH, and Hoechst-Roussel Agri-Vet Co.(collectively, Hoechst), and Merck & Co. Inc. (Merck).

An evidentiary hearing was held commencing June 5, 1995, and continuing through June 20, 1995, in which Kaken, Hoechst, and the Commission investigative attorney (IA) participated. On September 18, 1995, the ALJ issued an ID finding that Merck's activities did not violate section 337 and terminated Merck from the investigation. That ID became the Commission's final determination on October 10, 1995.

On November 6, 1995, the ALJ issued his final ID in which he found no violation of section 337. His decision was based on his finding that the patent at issue was invalid due to concealment of best mode and unenforceable due to inequitable conduct in its procurement. Petitions for review were filed by complainant Kaken and respondent Hoechst on November 21, 1995. Responses to the petitions were filed on December 1, 1995, by Kaken, Hoechst, and the IA.

This action is taken under the authority of section 337 of the Tariff Act of 1930, 19 U.S.C. § 1337, and section 210.42(h)(3) of the Commission's Rules of Practice and Procedure, 19 C.F.R. § 210.42(h)(3).

Copies of the nonconfidential version of the ID and all other nonconfidential documents filed in connection with this investigation are or will be available for inspection during official business hours (8:45 a.m. to 5:15 p.m.) in the Office of the Secretary, U.S. International Trade Commission, 500 E Street S.W., Washington, D.C. 20436, telephone 202-205-2000. Hearing-impaired persons are advised that information on this matter can be obtained by contacting the Commission's TDD terminal on 202-205-1810.

By order of the Commission.

Donna R. Koehnke

Donna R. Koehnke
Secretary

Issued: February 9, 1996

PUBLIC VERSION

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of	)	
	)	
CERTAIN SALINOMYCIN BIOMASS AND PREPARATIONS CONTAINING SAME	)	Investigation No. 337-TA-370
	)	

INITIAL DETERMINATION
Administrative Law Judge Sidney Harris

APPEARANCES:

For Complainant Kaken Pharmaceutical Company:

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Juan Cockburn, Esq.
Jeff Whieldon, Esq.

PUBLIC VERSION

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of	)	
	)	
CERTAIN SALINOMYCIN BIOMASS AND PREPARATIONS CONTAINING SAME	)	Investigation No. 337-TA-370
	)	
	)	

INITIAL DETERMINATION
Administrative Law Judge Sidney Harris

Pursuant to the Notice of Investigation, 60 Fed. Reg. 7069 (Monday, February 6, 1995), this is the Administrative Law Judge's Initial Determination in the Matter of Certain Salinomycin Biomass and Preparation Containing Same, U.S. International Trade Commission Investigation No. 337-TA-370. 19 C.F.R. § 210.42(a).

The Administrative Law Judge hereby determines that no violation of § 337 of the Tariff Act of 1930, as amended, has been found in the importation or sale of certain salinomycin biomass and preparations containing same by reason of alleged infringement of claim 2 of U.S. Letters Patent Re. 34,698.

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FINDINGS Of FACT

I. PROCEDURAL HISTORY

By publication in the Federal Register on February 6, 1995, the Commission gave notice of the institution of an investigation under section 337 of the Tariff Act of 1930, as amended (19 U.S.C. § 1337), pursuant to a complaint and motion for temporary relief filed by Kaken Pharmaceutical Company, Ltd., Tokyo 113, Japan ("Complainant") on December 23, 1994. A revised complaint and revised memorandum of points and authorities in support of the motion for temporary relief were filed on January 18, 1995. The complaint, as revised, alleges violations of section 337 in the importation into the United States, the sale for importation, and the sale within the United States after importation of certain salinomycin biomass and preparations containing same alleged to be manufactured abroad by a method covered by claim 2 of U.S. Letters Patent Re. 34,698 and alleged to incorporate "know-how" and improvements in breach of contract. The complaint further alleges that there exists an industry in the United States and that the domestic industry is being injured or threatened with injury by the imported accused products.

The complaint requests that the Commission institute an investigation and, after a full investigation, issue a permanent exclusion order and permanent cease and desist orders.

On January 30, 1995, the Commission ordered that an investigation be instituted to determine whether there is a violation of subsection (a)(1)(B) of section 337 in the importation into the United States, the sale for importation, or the sale within the United States after importation of certain salinomycin biomass and preparations containing same made abroad by a process covered by claim 2 of U.S. Letters Patent Re. 34,698, and whether there exists

an industry in the United States as required by subsection (a)(2) of section 337.

Pursuant to section 210.58 of the Commission's Final Rules of Practice and Procedure (59 Fed. Reg. 39020, 39062 (Aug. 1, 1994)), the motion for temporary relief under subsection (e) of section 337 of the Tariff Act of 1930, which was filed with the complaint, was provisionally accepted and referred to Administrative Law Judge Sidney Harris.

The Commission named Kaken Pharmaceutical, Ltd. as the Complainant, and the following companies as Respondents:

Hoechst Aktiengesellschaft Pharmaceutical
Frankfurt, Germany

Hoechst Veterinär Gesellschaft m.b.H
Munich, Germany

Hoechst-Roussel Agri-Vet Co.
Sommerville, New Jersey

Merck & Company, Inc.
White House Station, New Jersey

Teresa M.B. Martínez, Esq. and Juan Cockburn, Esq., Office of Unfair Import Investigations, was designated as the Commission Investigative Attorneys. Notice of Designation of Additional Commission Investigative Attorney (March 10, 1995).

On October 2, 1995, a Notice of Change of Commission Investigative Attorney was issued designating Juan Cockburn as the Commission investigative attorney instead of Teresa M.B. Martinez.

A preliminary conference in this investigation was conducted on February 8, 1995. Appearances were made on behalf of Complainant, all Respondents and the Office of Unfair Import Investigations ("OUII").

On February 6, 1995, Respondents moved to designate the temporary-relief phase of the investigation "more complicated." Motion No. 370-2. The motion was mooted in Order No. 3 on February 10, 1995.

On February 8, 1995, Complainant moved to withdraw its motion for a Temporary Exclusion Order in favor of an expedited hearing schedule. Motion Docket No. 370-3. On February 10, 1995, the Administrative Law Judge issued Order No. 3, granting Complainant's motion to withdraw its motion for Temporary Exclusion Order in favor of an expedited hearing schedule; setting procedural schedule; and issuing new ground rules.

On February 17, 1995, Merck moved for summary determination of no violation of 19 U.S.C. § 1337. Motion No. 370-4. The motion was denied. Order No. 9.

On May 3, 1995, the Hoechst Respondents moved for summary determination. Motion No. 370-16. This motion was denied. Order No. 16.

On May 26, 1995, Merck made a renewed summary determination of 19 U.S.C. § 1337. Motion No. 370-26. This motion was granted. Order No. 19.

All motions not previously ruled upon are hereby denied.

The hearing in the matter of Certain Salinomycin Biomass and Preparation Containing Same commenced on June 5, 1995 and concluded on June 20, 1995. All parties were represented at the hearing.

This Initial Determination is based on the entire record of this proceeding. Proposed findings not herein adopted, either in form or in substance, are rejected as not being supported by the evidence or as involving immaterial matters.

The findings of fact include references to supporting evidentiary items in the record. Such references are intended to serve as guides to the

depositions, exhibits, and testimony supporting the findings of fact; they do not necessarily represent complete summaries of the evidence supporting each finding. Some of the findings of fact are contained only in the opinion.

The following abbreviations are used in this Initial Determination:

CX - Complainant's Exhibit (followed by its number and the reference page(s)).

CPX - Complainant's Physical Exhibit

RX - Respondent's Exhibit (followed by its number and the reference page(s)).

RPX - Respondent's Physical Exhibit

FF - Finding of Fact

Dep. - Deposition

Tr. - Transcript

A. The Private Parties

1. Complainants

Kaken Pharmaceutical Co., Ltd. ("Complainant" or "Kaken") is a Japanese corporation with its corporate headquarters at 2-28-8 Honkomagome, Bunkyo-ku, Tokyo 113, Japan. Kaken is the owner of the '698 patent.

2. Respondents

Hoechst Aktiengesellschaft ("Hoechst" or "Hoechst AG") is an German corporation with a place of business at Bruningstrasse 50, 65929 Frankfurt am Main, Germany.

Hoechst Veterinär Gesellschaft m.b.H ("Hoechst") is a German corporation with a place of business at Rheingaustrasse 190, D-65203 Wiesbaden, Germany.

Hoechst-Roussel Agri-Vet Co. ("Hoechst") is a corporation organized under the laws of New Jersey with a principal place of business at Route 202-206 North, P.O. Box 2500, Sommerville, New Jersey 08876-1258.

Merck & Company, Inc. ("Merck") is a corporation organized under the laws of New Jersey with a principal place of business at 1 Merck Drive, P.O. Box 100, White House Station, New Jersey 08889-0100. This investigation was terminated as to Merck on the basis on a summary determination of no violation. Order No. 19 (unreviewed initial determination); Notice of Commission Decision Not to Review (Oct. 10, 1995).

II. CONSTRUCTION OF CLAIM 2 OF THE '698 PATENT

A. Introduction

A proper construction of the patent claim at issue to determine its scope is required for an analysis of infringement and validity allegations. Palumbo v. Don-Joy Co., 762 F.2d 969, 974 (Fed. Cir. 1985). Indeed, any determination on the issue of alleged patent infringement must result from a two-step process. First, a claim must be construed to determine its proper scope and meaning. Second, it must be determined whether the accused device or process is within the properly construed claim. Genetech, Inc. v. Wellcome Found. Ltd., 29 F.3d 1555, 1561 n.6 Fed. Cir. 1994 (citing Lemelson v. General Mills, Inc., 968 F.2d 1202, 1206 (Fed. Cir. 1992), cert. denied, 113 S.Ct. 976, 122 L.Ed.2d 131 (1993)). Claims must also be given the same meaning for infringement and validity analyses. White v. Dunbar, 119 U.S. 49, 51 (1886).

This investigation was instituted to determine, inter alia, whether Respondents infringe claim 2 of U.S. Letters Patent Re. 34,698. 60 Fed. Reg. 7069-70 (1995). Respondents assert that claim 2 of the '698 reissue patent is invalid. See, e.g., Respondents' Post-Hearing Br. at 2. Therefore, a determination of the proper meaning to be accorded claim 2 of the '698 reissue patent is necessary to resolve key issues in this investigation.

Claim 2 of the '698 reissue patent depends from claim 1, and thus incorporates all the limitations of claim 1 and further limits it. See 37 C.F.R. § 1.75(c).[1] Claims 1 and 2 of the '698 reissue patent are as follows:

> 1. A method of producing salinomycins, which comprises culturing a salinomycins-producing Streptomyces microorganism in a medium containing *12-25%* fatty acid or its precursor and ammonia or an ammonium salt and recovering the salinomycins from the culture.
>
> 2. The method of claim 1 wherein salinomycin is recovered together with the mycelial mass from the culture.

FF B 15.

The parties in this investigation have stipulated that the current Hoechst AG process for the fermentation of salinomycin uses [C] as the fatty acid precursor in its fermentation medium. FF[C]10. Furthermore, Respondents do not contest that in its manufacturing process Hoechst AG uses "ammonia or an ammonium salt." FF[C]9. The parties have also stipulated that in the current Hoechst AG process for fermentation of salinomycin, Hoechst AG recovers the salinomycin together with the mycelial mass from the culture. FF[C]8. In addition, the meaning of the claim limitations related to the terms "fatty acid or its precursor," "ammonia or an ammonium salt," and "mycelial mass" have not been put in issue by Respondents. Consequently, the meanings of most of the limitations of claims 1 and 2 of the '698 reissue patent are not contested.

Nevertheless, two central claim limitations are disputed by the parties, and they must be construed as a matter of law.

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[1] See also Wahpeton Canvas Co., Inc. v. Frontier, Inc., 870 F.2d 1546, 1552 n.9 (Fed. Cir. 1989)("One may infringe an independent claim and not infringe a claim dependent on that claim. The reverse is not true. One who does not infringe an independent claim cannot infringe a claim dependent on (and thus containing all the limitations of) that claim.").

The parties have stipulated that in the current Hoechst AG process for the fermentation of salinomycin, Hoechst AG cultures "a salinomycin-producing Streptomyces microorganism" for the production of salinomycin. FF[C]7. However, Complainant contends that the microorganism used in the fermentation culture is not part of the invention. Second, the parties dispute the meaning of the 12-25% range of fatty acid or its precursor limitation.

Following a discussion of the law applicable to proper claim construction, these claim limitations are construed.

B. General Law Applicable To Claim Construction

The construction of patent claims is a matter of law. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995).[2] All elements of a patent claim are material, with no single part of a claim being more important or "essential" than another. Id. at 988.

"Claims must be read in view of the specification, of which they are a part." Markman, 52 F.3d at 979, quoting Autogiro Co. v. United States, 384 F.2d 391, 197 (Ct. Cl. 1967). "The specification contains a written description of the invention that must enable one of ordinary skill in the art to make and use the invention." Markman, 52 F.3d at 979. The specification may serve as a sort of dictionary which explains the invention and may define terms used in the claims. Id. In fact, it has often been said that "a patentee is free to be his own lexicographer." Id. at 980, quoting Autogiro,

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[2] In Markman, the opinion for the majority of the Court stated that, notwithstanding the contrasting views expressed in the dissenting opinion, the terms "claim interpretation" and "claim construction...mean one and the same thing in patent law." 52 F.3d at 976 n.6. The Federal Circuit stated that for consistency it "would use the term construction when referring to the first step in an infringement analysis." Id.

384 F.2d at 397. However, "any special definition given to a word must be clearly defined in the specification." Markman, 52 F.3d at 980.

In considering the claims in view of the specification, it must be remembered that "[t]he written description part of the specification itself does not delimit the right to exclude. That is the function and purpose of the claims." Id.

To construe claim language, one "should also consider the patent's prosecution history, if it is in evidence." Id. Indeed, the prosecution history, or "file wrapper," "is of primary importance in understanding the claims." Id. As held by the Supreme Court:

> Th[e] construction of the patent is confirmed by the avowed understanding of the patentee, expressed by him, or on his [be]half, when his application for the original patent was pending . . . . [W]hen a patent bears on its face a particular construction, inasmuch as the specification and claim are in the words of the patentee . . . such a construction may be confirmed by what the patentee said when he was making his application.

Goodyear Dental Vulcanite Co. v. Davis, 102 U.S. 222, 227 (1880)(quoted in Markman, 52 F.3d at 980). Although the prosecution history should be used to understand the language of the claims, like the specification, it cannot enlarge, diminish or vary the claims. Markman, 52 F.3d at 980 (quoting Goodyear Dental Vulcanite, 102 U.S. at 227). The prosecution history "limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution." Southwall Technologies, Inc. v. Cardinal IG Co., 54 F.3d 1570, 1576 (Fed. Cir. 1995).

Extrinsic evidence may also be used to construe patent claims. Such evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. Extrinsic evidence may, for example,

help to explain scientific principles, technical terms, or the state of the art at the time of the invention. Id.

A "court may, in its discretion, receive extrinsic evidence in order 'to aid the court in coming to a correct conclusion' as to the 'true meaning of the language employed' in the patent." Id. (quoting Seymour v. Osborne, 78 U.S. (11 Wall.) 516, 546 (1871)). A "trial judge has sole discretion to decide whether or not he needs, or even just desires, an expert's assistance to understand a patent."

Extrinsic evidence is to be used to understand the patent, not to vary or contradict the terms of the claims.[3] Markman, 52 F.3d at 981. "When, after considering the extrinsic evidence, the court finally arrives at an understanding of the language as used in the patent and prosecution history, the court must then pronounce as a matter of law the meaning of that language." Id. The Federal Circuit "will not disturb that discretionary decision except in the clearest case." Seattle Box Co. v. Industrial Crating

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[3] Extrinsic evidence "may be necessary to inform the court about the language in which the patent is written. But this evidence is not for the purpose of clarifying ambiguity in claim terminology." Markman, 52 F.3d at 986. The Federal Circuit has held that:

> If the patent's claims are sufficiently unambiguous for the PTO, there should exist no factual ambiguity when those same claims are later construed by a court of law in an infringement action. See Intervet [America Corp. v. Kee-Vet Labs., Inc., 887 F.2d [1050,] 1053, 12 U.S.P.Q.2d [1474,] 476 [(Fed. Cir. 1989)] ("Ambiguity, undue breadth, vagueness, and triviality are matters that go to claim validity for failure to comply with 35 U.S.C. § 112-¶ 2, not to interpretation or construction.")(emphasis in original).

Id.

& Packing, Inc., 731 F.2d 818, 826 (Fed. Cir. 1984)(quoted in Markman, 52 F.3d at 981).[4]

C. "A Salinomycins-Producing Streptomyces Microorganism"

Complainant argues that "[t]he claimed invention does not relate to the use of any specific salinomycin producing microorganism, but, rather, the claimed invention relates to the use of the culture medium in connection with . . . any salinomycins-producing streptomyces." Complainant further contends that "[s]pecifically, the invention lay in the medium." Complainant's Post-Hearing Br. at 13-14.

Respondents take the position that the microorganism is recited in the claims and is just as much a part of the claimed invention as the media. Respondents' Post-Hearing Br. at 5 (footnote omitted).

The Commission investigative staff points out that the invention pertains to salinomycins, rather than all polyether antibiotics. OUII Br. at 5-6.

In the case of the '698 reissue patent, the claims, specification, prosecution history, and extrinsic evidence show that "a salinomycins-producing Streptomyces microorganism" is part of the claimed invention, and an element of independent claim 1.

As seen from the claims which are quoted above, independent claim 1 specifically claims a method of producing salinomycins "which comprises culturing a salinomycins-producing Streptomyces microorganism . . . ." Thus, there is an express recital in the claim that the method includes a

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[4] See also Winans v. New York & Eire R.R. Co., 62 U.S. (21 How.) 88, 101 (1859)("[P]rofessors or mechanics cannot be received to prove to the court or jury what is the proper or legal construction of any instrument of writing. A judge may obtain information from them, if he desire it, on matters which he does not clearly comprehend, but cannot be compelled to receive their opinions as matter of evidence.")(quoted in Markman, 52 F.3d at 981).

salinomycins-producing Streptomyces microorganism. As in any other patent claim, each of the claim elements specified in the claim is part of the claimed invention. Mannesmann Demag Corp. v. Engineered Metal Prods. Co., Inc., 793 F.2d 1279, 1282-83 (Fed. Cir. 1986). See 4 Donald S. Chisum, Patents § 18.03[4] (1995).

In support of the claim language, the specification of the '698 reissue patent teaches that the invention lies in the culturing of the microorganism, which is put into the culturing medium. The specification states as follows:

> The foregoing and other objects of the present invention have been attained by culturing a polyether type antibiotic-producing microorganism in a medium containing a fatty acid or its precursor and ammonia or an ammonium salt and urea.

FF B 3.

The specification refers specifically to the microorganism as part of the invention, as follows:

> The microorganism used in the present invention include [sic] generally polyether type antibiotics producing strains belonging to the genus of Streptomyces as well as the strains described in said literatures and their natural or artificial mutant.

FF B 4 (emphasis added).

The specification states further, as follows:

> The strains used in this invention include Streptomyces albus No. 80614 and its mutants artificially or naturally produced, as well as the other Streptomyces strains capable of producing salinomycins. However, some of the salinomycins can occasionally not be detected in the culture, depending on the strain and fermentation conditions.

FF B 5 (emphasis added).

Thus, the applicants clearly taught that the culturing of a particular kind of microorganism, namely streptomyces strains capable of providing salinomycins, is a distinct and necessary element of their claimed invention.

The Patent Examiner for the '698 reissue patent viewed the microorganism as essential to the claimed invention. During the reexamination proceedings, the Patent Examiner rejected the claims of the reissue application under 35 U.S.C. § 112, first paragraph, for lack of enablement. The basis for the section 112 rejection was stated as follows:

> Since the microorganism is essential to the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, the requirements of 35 USC § 112, first paragraph may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public.

FF B 6.

In response to the Examiner's rejection, counsel for Complainant Kaken (the assignee of the original and reissue patents) did not contest the Patent Examiner's assertion that the microorganism is essential to the claimed invention. Rather, he gave assurances that the microorganism was publicly available, and stated the position that the claims are not limited to the specific strain reflected in the Examples. FF B 7.

Additional evidence of the important role played by the microorganism in the claimed invention was adduced with respect to the high yield of salinomycin resulting from the claimed process. The patent specification states that an object of the invention is the production of "polyether type antibiotics in remarkably high yields with industrial advantages." FF B 8. Indeed, assertions of high yields were made at various points during prosecution of the reissue patent. FF B 9.

The evidence shows that high yields resulting from the claimed invention are due in part to the microorganism used in the fermentation process. The

team working on the invention that led to the original and the '698 reissue patent included one group that worked primarily on improvement of the microorganism strain, and one group that worked primarily on improvement of the culture medium. FF B 10. The improved strains give higher yields of salinomycin. As admitted by three of the named inventors and Complainant's expert witness on the issue of validity, the microorganism strain, and not just the culture medium, is essential to achieving high yields. FF B 11-14.

The Administrative Law Judge does not find that the evidence of record demonstrates that claim 1 reads on a particular microorganism strain, such as the 80614 strain, which is mentioned in the Patent Examples, SLS-K-7-68 strain, a highly successful Kaken strain that is discussed in detail later in this Initial Determination. The patent claims and other evidence clearly demonstrate that "a salinomycins-producing Streptomyces microorganism" is an element of independent claim 1, and consequently, the microorganism is material to the claimed invention. See Markman, 52 F.3d at 988.

D. The Requirement Of 12-25% Fatty Acid Or Its Precursor

Independent claim 1 of the '698 reissue patent and claim 2, which depends therefrom, require that the culturing of the microorganism take place in a medium "containing *12-25%* fatty acid or its precursor."

With respect to the 12-25% range of fatty acid or its precursor, complainant states as follows:

> [T]he skilled artisan would interpret the term "containing 12-25% fatty acid or its precursor" to include those situations in which the fermentation is begun with an oil content below 12% and oil is added to the fermentation medium so that the total amount of oil employed in the culture medium over the entire course of fermentation, including the amount initially present and the amount subsequently added, is greater than 12%, even if the total amount of oil added over the entire course of the fermentation exceeds 25%, because the total amount of oil added to the medium would have passed through the range of 12-25%. FF I 10; 11; 14.

* * *

> In summary, properly constructed Claim 2 of the '698 Patent reads on a method for producing salinomycin which comprises culturing a salinomycin-producing streptomyces microorganism in a medium in which the total amount of fatty acid or its precursor added thereto passes through the range of 12-25% and which contains ammonia or an ammonium salt and recovering salinomycin together with the mycelial mass. FF I 1-23.

Complainant's Post-Hearing Br. at 3-4.

Complainant and its technical expert witness on claim construction and infringement (Complainant had a separate expert witness on validity) views claim 1 of the '698 reissue patent as covering a "window" of 12-25% fatty acid or its precursor. FF B 20.

Respondents take a contrary position with respect to the 12-25% range. They contend that "the most plausible interpretation of Claims 1 and 2 . . . is that the 12-25% limitation refers to the total cumulative amount of oil added over the entire course of fermentation." Respondents' Post-Hearing Br. at 41. Respondents assert that Complainant's "expert admitted that such a 'passing through' argument eliminates any upper limit and makes the patent impossible to avoid at any oil level over 25% -- even 100%." Respondents contend that such an extension of the meaning of the patent claims is impermissible. Id.

The Commission investigative staff takes the position that "the appropriate construction to be given to the term '12-25%', based on the language of the specification and the prosecution history, is that the percentage range of fatty acid or its precursor refers to the total (or aggregate) amount of fatty acid or precursor that is added to the medium and

measured at the end of the process." OUII Post-Hearing Br. at 7 (emphasis in original).[5]

The evidence adduced at the hearing demonstrates that one of ordinary skill in the art as of May 1977, would understand the 12-25% limitation contained in claims 1 and 2 of the '698 reissue patent to refer to the total cumulative amount of fatty acid or its precursor put into the fermentation medium. The person of ordinary skill in the art would calculate the percentage by taking into account all the soybean oil (fatty acid precursor) used in the medium from the beginning of the fermentation process through the end of the process. See FF B 16. There is no credible evidence that the 12-25% range constitutes a "window" through which the amount of added oil passes.

The 12-25% range was added to independent claim 1 during the reissue proceeding. The original claim specifies no range of fatty acid or its precursor. However, the patent specification remained identical to the specification of the original patent. FF B 19.

Indeed, there is no teaching in the specification that the amount of oil "passes through" a range or a "window," or that the 12-25% range means anything other than the total amount of oil used during the fermentation

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[5] Respondents argue that Complainant has failed to satisfy the function/way/result test to prove infringement under the doctrine of equivalents, and that in any event, prosecution history estoppel prevents Complainant from applying an oil range above the 25% limit to the accused process. Respondents' Post-Hearing Br. at 41-43.

The Commission investigative staff takes the position that the 12-25% range covers the use of aggregate fatty acid above 25% which is not precluded by prosecution history estoppel. OUII Post-Hearing Br. at 11-14.

The issues relating to the doctrine of equivalents and prosecution history estoppel are discussed, infra, in the section on alleged infringement. See Southwall Technologies, 54 F.3d at 1578 ("The limit on the range of equivalents that may be accorded a claim due to prosection history estoppel is simply irrelevant to the interpretation of those claims.").

process. There is no evidence that the Examples in the specification demonstrate the use of fatty acid or its precursor passing through the 12-25% range. See FF B 23. In fact, the specification states plainly that "[t]he addition amount [of fatty acid] is generally about 1-25%, particularly about 12-20% based on the medium." See FF B 22. Thus, rather than describing a "window" or range through which the amount of added oil passes, the specification teaches one to add oil to the medium to arrive at a total amount of 12-25%. Nothing in the patent indicates that use of fatty acid precursor in amounts greater than 25% are included in the claim because the range of 12-25% was passed through.

The prosecution history of the '698 reissue patent supports this claim construction. In the Inaba Declaration, which was submitted during the reissue proceedings with data from comparative testing performed at Kaken, the calculation of the percentage of fatty acid or fatty acid precursor in the fermentation medium was based on the total cumulative amount of oil added to the medium throughout the entire process. FF B 25.

Reading the 12-25% range to refer to all oil used through the end of the fermentation process is further supported by the testimony of Respondents' technical expert witness, Dr. Hutchinson, who testified with respect to the understanding of one of ordinary skill in the art.[6] FF B 16, 18.

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[6] Dr. Hutchinson testified that alternative measurements of oil content may be expressed in terms of percentage similar to the range of percentages expressed in claim 1 of the '698 reissue patent. One could measure the amount of oil present at the beginning of the process. Instead, one could measure the amount of oil present at any time in the process. However, Dr. Hutchinson testified that although it would be reasonable to read the 12-25% range as referring to one of the alternative measurements, the preferred reading of the '698 reissue patent by one of ordinary skill in the art would be that the 12-25% range refers to the total amount of oil added during the process. FF B 18.

Furthermore, Dr. Hutchinson did not support the theory advanced by Complainant and its expert. Dr. Hutchinson termed that approach a "sliding scale" interpretation, and maintained that it does not relate to the claims which specify a clear upper limit of 25 percent for the process. Dr. Hutchinson testified that the interpretation advanced by Complainant's expert is unconventional, and not reasonable to him or to one of ordinary skill in the art. FF B 27.

Additional evidence concerning the construction of this claim limitation was adduced from current and former employees of Complainant Kaken. Mr. M. Hara (a former Kaken employee) and Mr. Yoneda (a current Kaken employee), who are two of the inventors named on the '698 reissue patent, admitted that the correct interpretation of the 12-25% fatty acid or fatty acid precursor range in independent claim 1 is the total amount of oil added together through the end of the process, i.e., the total amount of oil which was placed in the medium initially plus the amount of oil which was added along the way. FF B 24. This reading of the '698 reissue patent is in accordance with the understanding of Respondents' expert, Dr. Hutchinson. FF B 16.

Furthermore, with respect to its current commercial process for producing salinomycin, Kaken calculated the oil content by summing the total amount of oil added to the fermentation tank, including the initial charge and all subsequent additions during the process. FF B 26.

There is thus strong evidence in the record which supports the Administrative Law Judge's finding that the 12-25% range refers to the total amount of fatty acid or its precursor (such as oil) used throughout the fermentation process. The evidence of record contradicts the "passing through" construction proposed by Complainant Kaken.

III. CLAIM 2 OF THE '698 PATENT WOULD BE INFRINGED

A. General Law Applicable To The Issue Of Infringement

Complainant alleges that Respondents infringe claim 2 of the '698 patent literally or under the doctrine of equivalents. Complainant's Post-Hearing Br. at 5; OUII Post-Hearing Br. at 20. OUII takes the position that Respondents infringe claim 2 of the '698 patent under the doctrine of equivalents.

Literal infringement of the asserted claim occurs "[i]f accused matter falls clearly within the asserted claim . . . ." Graver Tank & Mfg. Co. v. Linde Co., 339 U.S. 605, 607 (1950); Southwall Technologies, 54 F.3d at 1575 ("To establish literal infringement, every limitation set forth in a claim must be found in an accused product, exactly.").

However, limiting patent enforcement exclusively to literal infringement "would place the inventor at the mercy of verbalism and would be subordinating substance to form." Graver Tank, 339 F.2d at 607. Thus, if the accused product or process does not literally infringe the patent at issue, it may infringe under the doctrine of equivalents. See In re Certain Doxorubicin and Preparations Containing Same, 20 U.S.P.Q.2d 1602, 1608 (United States Int'l Trade Comm'n 1991)("An allegation of infringement under the doctrine of equivalents presumes that literal infringement does not exist, i.e., that the asserted patent claims, properly interpreted, do not in terms cover the accused device or process.").

The Court of Appeals for the Federal Circuit in its recent decision in Hilton Davis Chem. Co. v. Warner-Jenkins Co., Inc., No. 93-1088 (Fed. Cir.

Aug. 8, 1995)(per curiam),[7] held that the doctrine of equivalents "applies if, and only if the differences between the claimed and accused products or processes are insubstantial."[8] Slip op. at 6, citing Graver Tank, 339 U.S. at 610.

In Hilton Davis, the Court stated that "[i]n applying the doctrine of equivalents, it is often enough to assess whether the claimed and accused products or processes include substantially the same function, way and result." Slip op. at 7. In many cases, the substantiality of the differences between the claimed and accused products or processes have been measured by reliance on that "so-called triple identity, or function-way-result, test ...." Id. However, the court held that "[i]t goes too far, however, to describe the function-way-result test as 'the' test for equivalency announced by Graver Tank." Id. at 8. An "important factor" to be considered in making the equivalence determination is "whether persons reasonably skilled in the

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[7] The opinion of the Federal Circuit in Hilton Davis was issued after the scheduled briefing in this matter was completed. It "restated the test for infringement under the doctrine of equivalents." Slip op. at 5. The parties in this investigation were requested to file supplemental briefs concerning alleged infringement under the doctrine of equivalents in view of the Hilton Davis opinion. Notice of Aug. 16, 1995. The parties were thereafter permitted to file comments on the supplemental briefs.

[8] The Federal Circuit has held similarly in other cases. For example in London v. Carson, Pirie, Scott & Co., 946 F.2d 1524, 1538 (Fed. Cir. 1991), the court held as follows:

> [W]here an infringer, instead of inventing around a patent by making a substantial change, merely makes an insubstantial change, essentially misappropriating or even "stealing" the patented invention, infringement may lie under the doctrine of equivalents.

In Perkin-Elmer, 822 F.2d at 1535, the Federal Circuit held that the doctrine of equivalents "is not designed to permit wholesale redrafting of a claim to cover non-equivalent devices, i.e., to permit a claim expansion that would encompass more than an insubstantial change."

art would have known of the interchangeability of an ingredient not contained in the patent with one that was." Id. at 9, quoting Graver Tank, 339 U.S. at 609.

The Hilton Davis court further stated that evidence of copying "is also relevant . . . not because the doctrine of equivalents rests on the subjective awareness or motivation of the accused infringer, but rather because copying suggests that the differences between the claimed and accused products or processes -- measured objectively -- are insubstantial." Slip op. at 10, citing Graver Tank, 339 U.S at 612. Evidence of "designing around" the patent claims is also relevant to the question of infringement under the doctrine of equivalent. Hilton Davis, slip op. at 11. When it is shown that a competitor became aware of a patent and attempted to design around its claims, the fact-finder may infer that the competitor, who is presumably one of skill in the art, designed substantial changes to avoid infringement. However, the strength of this inference may vary from case to case. For example, there have been cases where even independent development of a product or process led nonetheless to insubstantial differences with the claim of the patent-in-suit, and thus to a finding of infringement. Id. at 11-12.

Independent development is not irrelevant to the question of whether the doctrine of equivalents applies. In fact, the Federal Circuit in Hilton Davis stated that "the fact-finder must consider any evidence of independent development in a case where the patent owner alleges copying as probative of infringement under the doctrine of equivalents." Id. at 12-13.

In determining whether equivalence exists, an element by element comparison must be made. Pennwalt Corp. v. Durand-Wayland, Inc., 833 F.2d 931 (Fed. Cir. 1987), cert. denied, 485 U.S. 1009 (1988).

In all cases:

> [T]he vantage point of one of ordinary skill in the relevant art provides the perspective for assessing the substantiality of the differences. Valmont [Indus., Inc. v. Reinke Mfg. Co.], 983 F.2d [1039] at 1043 [(Fed. Cir. 1993)]. The test is objective, with proof of the substantiality of the differences resting in objective evidence rather than unexplained subjective conclusions, whether offered by an expert witness or otherwise.

Hilton Davis, slip op. at 9.

Given a properly construed claim, the decision whether or not the claim at issue is infringed, either literally or under the doctrine of equivalents, requires a factual determination. Southwall Technologies, 54 F.3d at 1575; Doxorubicin, 20 U.S.P.Q.2d at 1608. See Graver Tank, 339 U.S. at 609. The application of the doctrine of equivalents is a question of fact. Hilton Davis, slip op. at 14. The doctrine of equivalents is not a matter of equity to be applied at a court's discretion. Id. at 14-15.

Furthermore, a party alleging infringement has the burden of proving infringement by a preponderance of the evidence. Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 758 (Fed. Cir. 1984); Hughes Aircraft Co. v. United States, 717 F.2d 1351, 1361 (Fed. Cir. 1983).

B. The Hoechst AG Process

With respect to the accused Hoechst AG process, the parties have stipulated: 1) that Hoechst AG cultures a salinomycin-producing Streptomyces microorganism for the production of salinomycin; 2) that Hoechst AG uses

[C] in its fermentation as a fatty acid precursor; and 3) that Hoechst AG recovers the salinomycin together with the mycelial mass from the culture. FF[C]7, 8, 10. Respondents have also withdrawn their noninfringement arguments with respect to ammonia or ammonium salt. FF[C]9. Therefore, the only issue to be decided with respect to Complainant's

infringement allegations is whether the Hoechst AG process satisfies the claim limitation by which the fatty acid or its precursor is in the 12-25% range.

The [C] Hoechst AG commercial fermentation process for the production of salinomycin was put into commercial operation [C]

[9] [C]

[C]

The amount of fatty acid precursor [C] in Hoechst AG's current process for the production of salinomycin measured at the beginning of the fermentation process is [C] the amount of fatty acid precursor measured at any point in time during the process is always [C] [C] and the cumulative amount of fatty acid precursor measured at the end of the process is always greater than 25%.[10] FF[C]24.

In the [C] Hoechst AG commercial fermentation process for salinomycin, the total cumulative amount of fatty acid precursor [C] used over the course of fermentation [C]

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[9] A production process needs time to be introduced, and because not all fermenters were used in the new 1995 process, there was an overlap (or transition period) between the prior and new processes in 1994 and 1995. FF C 2.

[10] In the section of this Initial Determination containing numbered Findings of Fact on the issue of alleged infringement, there are additional findings concerning the oil levels contained in the Hoechst AG fermentation medium at various times during the process. In its reply brief, Complainant argues that "[c]ontrary to the position taken by the Commission Investigative Staff (Staff) and Respondents, there is no estoppel to prevent Claim 2 from covering a process starting with less than 12% oil." Complainant's Reply Br. at 3. However, Complainant does not assert that Respondents infringe claim 2 in such a manner, nor does it assert that Respondents infringe the '698 reissue patent by using less than 12% oil. See Complainant's Post-Hearing Br. at 3, 6-7; Complainant's Reply Br. at 3.

C. The Hoechst AG Process Does Not Literally Infringe Claim 2 Of The '698 Reissue Patent

Complainant argues that claim 2 of the '698 reissue patent is literally infringed by Hoechst AG's process because the total amount of [C] employed in the culture medium over the entire course of fermentation (including the amount initially present when the culture broth is inoculated and all the [C] subsequently added) passes through the 12-25% range. Complainant's Post-Hearing Br. at 5.

Respondents oppose any finding of infringement. The Commission investigative staff takes the position that infringement, while occurring under the doctrine of equivalents, does not occur through literal infringement.

In order to determine whether a fermentation process falls within the claimed range all the [C] added to the fermentation medium throughout the process must be combined. Furthermore, in view of the specification, the prosecution history and other evidence, the claim in suit is not a method wherein the amount of fatty acid or its precursor (e.g., soybean oil) "passes through" the 12-25% range. The 12-25% range refers only to the total amount of fatty acid or its precursor used in the process.

It is undisputed that the accused Hoechst AG process uses a total of more than 25% [C] It is also undisputed that the Hoechst AG process uses [C] as a fatty acid precursor. Thus, not every limitation set forth in claim 2 of the '698 reissue patent is found exactly in

the accused process because the Hoechst AG process uses more than 25% fatty acid precursor.[11]

Therefore, given the proper construction of claim 2, including the 12-25% range incorporated from claim 1, Respondents do not literally infringe claim 2 of the '698 reissue patent.

D. The Hoechst AG Process Would Infringe Claim 2 Of The '698 Reissue Patent Under The Doctrine Of Equivalents

Complainant argues that if the accused process does not infringe literally, then infringement should be found under the doctrine of equivalents. Complainant's Post-Hearing Br. at 5-8.

Respondents take the position that because of an amendment made during the reissue proceeding, infringement cannot be found under the doctrine of equivalents because Complainant is estopped from asserting the '698 reissue patent against a process such as the Hoechst AG process, which uses more than 25% fatty acid or its precursor [C] Respondents' Post-Hearing Br. at 40-44.

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[11] Subsequent to the hearing in this investigation, the Court of Appeal for the Federal Circuit issued its opinion in Exxon Chem. Patents, Inc. v. Lubrizol Corp., 93-1275, 94-1309 (Fed. Cir. Sept. 1, 1995). Complainant provided a copy of that opinion to the Administrative Law Judge, and took the position that the opinion supports a finding of literal infringement in this case. Letter of Steven B. Kelber, Esq., dated Sept. 18, 1995. Respondents also commented on the opinion. Letter of Basil J. Lewris, Esq., dated Sept. 19, 1995.

In Exxon Chemical, the Federal Circuit held that the claim at issue in that case was not "time-limited" and that literal infringement could be found "if Lubrizol's products at some time contained each of the claimed recipe ingredients in the amounts specifically claimed." Slip. op. at 9-10. However, the Federal Circuit made it clear that its holding was based on a review of the claims, the specification, and the prosecution history of the particular patent at issue in that case. The claim asserted in this case is quite distinct from that in Exxon Chemical. As discussed in detail above, a proper claim construction of the '698 reissue patent rejects Complainant's "passing through" or "window" theory.

The Commission investigative staff is of the view that file history estoppel does not apply with respect to the upper limit of the 12-25% range of fatty acid or its precursor, and that the accused Hoechst AG process is within the range of equivalents of claim 2 of the '698 reissue patent. OUII Post-Hearing Br. at 11-14, 20-22.

1. Complainant Is Not Estopped From Asserting Infringement Under The Doctrine Of Equivalents

The claims of the original '942 patent assigned to Kaken specified the use of a fatty acid or fatty acid precursor in the fermentation medium. However, the claims did not specify any particular amount of fatty acid or its precursor. FF[C]25-26.

On January 29, 1993, Complainant Kaken filed an application for reissue of the '942 patent. FF[C]27. Kaken sought to reissue its patent to distinguish its claims from the prior art patent to Berg et al. (U.S. Letters Patent 4,035,481), which describes culturing a Streptomyces in a medium that includes 0.46% soybean oil. FF[C]28. Thus, at the beginning of the reissue proceedings, a preliminary amendment to the claims of the '942 patent was requested, whereby independent claim 1 would be amended to add the limitation that the medium contain "at least 12%" fatty acid or its precursor. FF[C]29. Kaken stated that in contrast to the amount of oil added in Berg, "more substantial amounts, including the 12% by weight herein, confers on the process a dramatic increase in yield, that could not be predicted by those of skill in the art." FF[C]30.

In a June 30, 1993 Office Action in the reissue proceedings, the Patent Examiner rejected the claims under, inter alia, section 112 (second paragraph) for indefiniteness because they did not have an upper limit on the percentage of fatty acid or its precursor. FF[C]31-32. The Patent Examiner stated that

the claims were rejected "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention," and further that "[t]he specific percent of fatty acid to be added can not be determined since there is no upper limit stated within the claim." FF[C]37. The Patent Examiner believed that the specification would support an upper limit of 20%, and also expressed the concern that an amount higher than that might be toxic to the microorganism. FF[C]36.

On November 1, 1993, in response to the outstanding rejections, and as a result of discussions with the Patent Examiner and correspondence with Kaken's Japanese patent counsel, Kaken's patent attorney in the United States requested amendment of the claims to add the upper limit of 25% to the range of fatty acid or its precursor. FF[C]39. In the Remarks submitted with the amendment, which added the "12-25%" range to claim 1, it was noted that "[t]his upper limit of 25% is disclosed at column 2, line 30, the lower limit of 12% is disclosed at column 2, line 31." FF[C]40. It was further noted that the claims had been rejected on the ground that they introduced subject matter, and that the Examiner said the specification is limited to a fatty acid content of no greater than 20%. Kaken, through counsel, stated that "[t]his rejection has been met by insertion of a maximum amount of 25% (not 20%) as set forth in the specification, column 2, line 30. This amendment was later discussed with Examiner Robinson and appears adequate to meet the rejection, without more." FF[C]35, 41.

In the Remarks submitted with the November 1, 1993 Amendment adding the 25% upper limit it was also stated that the Examiner's rejection under 35 U.S.C. § 112, second paragraph, was "mooted by the amendment setting a limit on the amount of fatty acid content." The Remarks also stated that: (1) the

invention resides in the identification of a minimum limit, not the maximum limit; (2) the applicant has demonstrated that amounts in excess of 25% fatty acid are not toxic; (3) culturing at concentrations of 32% and 39% are also demonstrated (presumably in the Inaba Declaration); and (4) the upper limit is only of practical importance but not critical to patentability. FF[C]42.

After the amendment inserting an upper limit of 25% for fatty acid or its precursor, the arguments presented by Kaken's attorney, and the formal surrender of the original '942 patent, the Patent Examiner issued a Notice of Allowability for the '698 reissue patent. FF[C]43.

The primary issue to be resolved with respect to prosecution history estoppel is whether, as a matter of law, prosecution history estoppel may apply as a result of a claim amendment which was made to overcome a rejection under 35 U.S.C. § 112, second paragraph.

Whether one should apply prosecution history estoppel is a question of law. Southwall Technologies, 54 F.3d at 1579; Hoganas AB v. Dresser Indus., Inc., 9 F.3d 948, 952 (Fed. Cir. 1994). The Federal Circuit has explained that "the essence of prosecution history estoppel is that a patentee should not be able to obtain, through the doctrine of equivalents, coverage of subject matter that was relinquished during prosecution to procure issuance of the patent." Hoganas, 9 F.3d at 951-52. This rationale, considered alone, would indicate that an amendment to overcome a section 112 rejection could lead to an estoppel, if one could characterize such an amendment as genuinely having "relinquished" subject matter.

In other cases, the Federal Circuit has expressed the doctrine of equivalents in formulations which indicate that prosecution history estoppel arises only from amendments made to overcome rejections based on prior art.

For example, in Southwall Technologies, the court held that "the doctrine of prosecution history estoppel . . . limits expansion of the protection under the doctrine of equivalents when a claim has been distinguished over relevant prior art." 54 F.3d at 1578.[12]

An examination of important cases actually involving section 112 and prosecution history estoppel which have been decided by the Federal Circuit is useful.

In Caterpillar Tractor v. Berco, S.p.A., 714 F.2d 1110 (Fed. Cir. 1983), the Patent Examiner rejected as indefinite under 35 U.S.C. § 112 certain claims of a pending application filed by plaintiff Caterpillar. Caterpillar then filed a continuation-in-part application, containing new material which apparently remedied the deficiencies in the original application relating to section 112.[13] In the subsequent action for infringement, defendant Berco argued that file history estoppel should apply, but the Federal Circuit held to the contrary. 714 F.2d at 1115.

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[12] See also Southwall Technologies, 54 F.3d at 1583:

> The doctrine of prosecution history estoppel bars "a patentee from enforcing its claims against otherwise legally equivalent structures if those structures were excluded by claim limitations added in order to avoid the prior art."

Id. (emphasis added)(quoting Vaupel Textilmaschinen KG v. Meccanica Euro Italia S.p.A., 944 F.2d 870, 882 (Fed. Cir. 1991).

There are other cases which indicate that estoppel can also apply as a result of arguments submitted to obtain the patent. Haynes Int'l, Inc. v. Jessop Steel Co., 8 F.3d 1573, 1579 (Fed. Cir. 1993)(citing Townsend Eng'g Co. v. Hitec Co., 829 F.2d 1086, 1090 (Fed. Cir. 1987)); Hughes Aircraft, 717 F.2d at 1562 (citing Coleco Indus., Inc v. United States Int'l Trade Comm'n, 573 F.2d 1247, 197 USPQ 472, 480 (C.C.P.A. 1978)).

[13] There was an Examiner's amendment prior to issuance. However, the Federal Circuit described it as "not here relevant." Caterpillar Tractor, 714 F.2d at 1114.

Although no claim at issue in Caterpillar Tractor had been amended, unlike the '698 reissue patent, the decision was rendered specifically with respect to a desire by the patentee to invoke the doctrine of equivalents, and thus the reasoning of the Federal Circuit for rejecting estoppel is relevant:

> Claims 1 and 19 of the patent were first presented in the CIP. • * • [I]t is clear that Caterpillar did not present a claim defining the hinge section as having a thinner cross section than only one of the flanges and of course could not have cancelled or amended it to secure the patent. Nor did Caterpillar enter remarks in the file wrapper to the effect that the hinge section must have a cross section thinner than both of the flanges for the seal to work or for the claims to be patentable over the prior art. Nor would the prior art appear to dictate . . . such limitation. As above indicated, the rejection of interest was related to § 112, not to prior art. Thus, there is nothing in the file history to estop Caterpillar from relying on the doctrine of equivalents.

714 F.2d at 1115.

The Court thus linked the ability to assert prosecution history estoppel with an effort by the applicant to avoid prior art and not with an effort to remedy a section 112 rejection.

In Hi-Life Prods., Inc. v. American Nat'l Water-Mattress Corp., 842 F.2d 323 (Fed. Cir. 1988), the applicant accepted an amendment suggested by the Patent Examiner which apparently overcame an earlier rejection based on the prior art and contained an additional phrase, i.e, "disposed throughout," which helped to define the invention. It was the additional phrase that was reviewed by the Federal Circuit, and upon which the lower court found prosecution history estoppel to exist. In rejecting the view of the lower court, the Federal Circuit held, as follows:

> In this case, we cannot agree with the district court that these amendments preclude Hi-Life from asserting infringement under the doctrine of equivalents. Here, the patentee did not amend the claims to avoid cited prior art, but rather to better define a

> patentable invention. The limitation of disposing a lightweight material throughout an open cell foam was old in the non-waterbed art and did not in itself render the claims patentable. Accordingly, prosecution history estoppel was not created by the mere presence of the "disposed throughout" limitation in the claims.

842 F.2d at 326 (emphasis added).

Respondents point out that in Hi-Life, the amendment, which better defined the claims, was not preceded by a rejection by the Patent Examiner under 35 U.S.C. § 112, as in the case of the '698 reissue patent. Respondents' Reply Br. at 21 n.35. Nevertheless, the Federal Circuit's opinion makes it clear that an important basis for reversing the District Court's application of estoppel was that the portion of the amendment in question was not made to avoid prior art. Indeed, earlier in the Hi-Life opinion, the Federal Circuit formulated the doctrine of prosecution history estoppel as it has in other cases to reserve its application only to actions taken in response to prior art rejections, as follows:

> The doctrine of prosecution history estoppel precludes a patentee from asserting equivalents that would resurrect subject matter given up during prosecution to overcome rejections based on prior art.

842 F.2d at 325 (emphasis added).

In the recent case before the Court of Appeals for the Federal Circuit, Pall Corp. v. Micron Separations, Inc., 91-1393, -1394, -1409 (Fed. Cir. Sept. 26, 1995), it was argued that there was a lack of infringement under the doctrine of equivalents due to prosecution history estoppel. On the issue of whether an estoppel may arise in response to a rejection under 35 U.S.C. § 112, the Federal Circuit held as follows:

> Whether amendment or argument made in response to a rejection under § 112 produces an estoppel, as does amendment made to obtain allowance in view of cited references, is dependent on the particular facts. There is no all-encompassing rule that estoppel

> results from all claim changes, or all arguments, whatever their cause or purpose.
>
> As we have observed, a concession made or a position taken to establish patentability in view of prior art on which the examiner has relied, is a substantive position on the technology for which a patent is sought, and will generate an estoppel. In contrast, when claim changes or arguments are made in order to more particularly point out the applicant's invention, the purpose is to impart precision, not to overcome prior art. Such prosecution is not presumed to raise an estoppel, but is reviewed on its facts, with the guidance of precedent.

Slip. op. at 11-12 (citations omitted)(emphasis added).

In this case, independent claim 1 was amended merely to overcome an indefiniteness objection, and no arguments were made to narrow the claimed invention. See Moeller v. Ionetics, Inc., 794 F.2d 653, 659-60 (Fed. Cir. 1986)(prosecution history estoppel not applicable to amendment to point out the invention more particularly); Mannesmann Demag, 793 F.2d at 1285 (estoppel not necessarily created by an amendment designed only to remove a § 112 indefiniteness rejection).[14]

In the case of the amendment at issue in this investigation, the prosecution history does not demonstrate that any amount of oil in excess of 25% would necessarily be unpatentable (as would be the case if there were prior art covering an amount of oil above 25%). The lower limit of the range was inserted to distinguish from the prior art Berg patent. However, the insertion of the 25% upper limit merely distinctly points out the metes and bounds of the claim. This amendment does nothing to estop the appropriate

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[14] These cases were cited by the Federal Circuit in Pall, slip op. at 11-12, in which it was held that an estoppel did not result from the patentee's refiling of a claim to include a specific range of chemical properties, and later statements to the Patent Examiner which described the claimed range as "actually rather narrow" in response to a rejection under section 112. Id. at 9-13.

range of equivalents from attaching, as if the claim originally contained the 25% limitation.

Therefore, based on the opinions of the Federal Circuit cited herein, the Administrative Law Judge determines as a matter of law that Complainant is not estopped from asserting infringement under the doctrine of equivalents with respect to the use of fatty acids or fatty acid precursors in amounts greater than 25%.

2. Complainant Has Demonstrated That Under The Doctrine Of Equivalents The Amount Of Oil Used In The Hoechst AG Process Would Fall Within The Range Of Equivalents Due The '698 Reissue Patent

We must now determine whether Complainant has proved that the accused Hoechst AG process, which uses [C] falls within the range of equivalents to be accorded claim 2, which has an expressed upper limit of 25% fatty acid or its precursor.

In Texas Instruments, Inc. v. United States Int'l Trade Comm'n, 805 F.2d 1558, 1558 (Fed. Cir. 1986), the Federal Circuit stated that "[i]t has long been recognized that the range of permissible equivalents depends upon the extent and nature of the invention, and may be more generously interpreted for a basic invention than for a less dramatic technological advance." Similarly, the Supreme Court held in Continental Paper Bag Co. v. Eastern Paper Bag Co., 210 U.S. 405, 415 (1908), that "the range of equivalents depends upon and varies with the degree of invention."

In Hilton Davis, the Federal Circuit applied the doctrine of equivalents to a range of pH values stated in a patent claim, and recognized that prior Federal Circuit decisions "reaffirm[ed] that the Graver Tank objective criteria, as limited by prosecution history and prior art, confine the range of equivalents." Slip op. at 17-18.

Complainant argues that the invention of the '698 patent is pioneering, and is "thus entitled to a great range of equivalents." Complainant's Post-Hearing Br. at 8. However, the evidence of record does not support a finding that the '698 reissue patent effected such a great technological advance in the art that it warrants "pioneer" status. See Perkin-Elmer Corp. v. Westinghouse Elec. Corp., 822 F.2d 1528, 1532 (Fed. Cir. 1987); Hughes Aircraft, 717 F.2d at 1362.[15]

There is inadequate record evidence to show that the '698 reissue patent made the kind of difference in the daily operations of industry or in the general advancement of knowledge within the relevant art that one normally associates with a pioneer invention. The invention of the '698 reissue patent was a marked improvement in the field of antibiotics fermentation, especially with respect to salinomycin and other polyether antibiotics. The '698 reissue patent directed the field to the extensive use of oil in polyether fermentations. In that regard, the '698 reissue patent is a standard-setting innovation for those in the polyether antibiotic industry. FF[C]48-49.

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[15] See also In re Certain Window Shades, 230 U.S.P.Q. 183 (United States Int'l Trade Comm'n 1986), in which the Commission explained, as follows:

> The breadth of protection accorded a patent under the doctrine of equivalents is commensurate to the nature of the patent. Pioneer status (those reflecting a great technological advance) are given the broadest protection, while small improvements in a crowded field are afforded only a limited range of equivalents. The range of equivalents is determined in the context of the patent, prior art, and the circumstances of the case.

230 U.S.P.Q. at 191 n.26.

Therefore, the '698 reissue patent is entitled to a substantial range of equivalents.[16] See Hughes Aircraft, 717 F.2d at 1362.

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[16] In determining whether an accused product of process falls within the proper range of equivalents to which a patent claim is entitled, one would sometimes draw a different conclusion depending upon the precise point in time and development within the relevant art to which one refers, e.g., what was known in the art when the patent was applied for or issued versus later (possibly several years later) at the time of the alleged infringement.

Respondents have not attempted to exclude the test results which were made part of the Inaba declaration submitted during the reissue proceedings which show yields of salinomycin that are obtained with varying amounts of oil based on the date on which that evidence was made public and thus known in the art. However, Respondents opposed a finding of infringement in part because inventor Yoneda believed as of the 1977 priority filing date that large amounts of oil could be toxic to the microorganism. See Yoneda, Tr. 557-558. Complainant on the other hand sought to establish that under the proper interpretation of the patent law one should base the infringement determination on current information rather than what was believed at the time the priority application was filed. Complainant's Comments of Respondents' Supp. Mem. at 8, n.1. (citing Texas Instruments, 805 F.2d at 1563, and Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1581 (Fed. Cir.1984)). Thus, the question of when one assesses the equivalents of a claimed product or process has been raised in this investigation.

In Texas Instruments, cited by Complainant, the Federal Circuit unequivocally held as follows:

> It is not required that those skilled in the art knew, at the time the patent application was filed, of the asserted equivalent means of performing the claimed functions; that equivalence is determined as of the time infringement takes place.

805 F.2d at 1563.

Similarly, in Atlas Powder Co., the Federal Circuit held with respect to the question of equivalents, as follows:

> It is not a requirement of equivalence, however, that those skilled in the art know of the equivalence when the application is filed or the patent issues. That question is determined as of the time infringement takes place. In Hughes Aircraft Co. v. United States, 717 F.2d 1351, 1365, 219 USPQ 473, 483 (Fed.Cir.1983), this court held that devices changing the patented invention with advances developed subsequent to the patent could infringe under the doctrine of equivalents.

750 F.2d at 1581.

(continued...)

[16](...continued)

These holdings by the Federal Circuit conflict with earlier opinions of the Supreme Court in which it was held that equivalence must be assessed as of the date of the patent-in-suit and not at the time of alleged infringement. For example, in Gill v. Wells, 89 U.S. (22 Wall.) 1 (1874), the Court held, as follows:

> Old ingredients known at the date of letter-patent granted for an invention, consisting of a new combination of old ingredients, if also known at that date as a proper substitute for one or more of the ingredients of the invention secured by the letter-patent, are the equivalents of the corresponding ingredients of the patented combination. Such old ingredients, so known at the date of the letters-patent granted, are the equivalents of the ingredients of the patented combination, and no others, and it may be added that, and that only is what is meant by the rule that inventors of a new combination of old ingredients are as much entitled to claim equivalents as any other class of inventors.

89 U.S. at 15 (emphasis in original). The Court continued, as follows:

> Whether one device is or is not an equivalent for another is usually a question of fact, and often becomes a difficult issue to decide. * * * [T]he rule is that if the defendant omits entirely one of the ingredients of the plaintiff's combination, without substituting any other, he does not infringe, and if he substitutes another in the place of the one omitted, which is new or which performs a substantially different function, or even if it is old but was not known at the date of the plaintiff's patent as a proper substitute for the omitted ingredient, he does not infringe. By an equivalent in such a case it is meant that the ingredients substituted for the one withdrawn performs the same function as the other, and that it was well known at the date of the patent securing the invention as a proper substitute for the one omitted in the patented combination. Hence it follows that a party who merely substitutes another old ingredient for one of the ingredients of a patented combination is an infringer if the substitute performs the same function as the ingredient for which it was substituted, and was well known at the date of the patent as a proper substitute for the omitted ingredient; but the rule is otherwise if the ingredient substituted was a new one or performed substantially a different function, or was not known at the date of the plaintiff's patent as a proper substitute for the one omitted, as in that event he does not infringe.

89 U.S. at 28-29 (emphasis added)(citations omitted). Accord Gould v. Rees, 82 U.S. (15 Wall.) 187, 194 (1872)(When the defendant substitutes another ingredient -- even an old ingredient -- there is no infringement if it "performs a substantially different function, or was not known at the date of

(continued...)

In this investigation a preponderance of the evidence demonstrates that infringement would be found whether one takes into consideration only what was known in the art at the time of the reissue patent or only a short time later, at the time of infringement. The evidence is insufficient to show equivalence

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[16](...continued)
the plaintiff's patent as a proper substitute for the one omitted from his patented combination.")

In particular, the Supreme Court in Gill v. Wells, would not allow a substitute ingredient contained in a reissue specification to be regarded as an equivalent if it was not "well known as such an ingredient at the date of the original patent and as a substitute for the ingredient which was included in the patented combination." Gill v. Wells, 89 U.S. at 80.

The Inaba declaration and testing which informs one of skill in the art about the use of more than 25% oil in salinomycin fermentation is not contained in the patent specification, but was submitted later in connection with the reissue proceedings. Thus, the precise unfairness guarded against by the Supreme Court, i.e., basing infringement on an amended rather than an original specification, is not present here.

Lower courts have sought to differentiate their cases from the facts or the implied reasoning in Supreme Court cases such as Gill v. Wells and Gould v. Rees. Indeed, that process of differentiation by lower courts began in the last century and has continued into this decade. See, e.g., Micro Motion, Inc. v. Exac Corp, 16 U.S.P.Q.2d 1, 1007 (N.D. Cal. 1990)(purportedly "resolving the conflict" between the Supreme Court and the Federal Circuit in favor of the Federal Circuit); Edison Elec. Light Co. v. Boston Incandescent Lamp Co., 62 F. 397 (C.C.D. Mass. 1894)(different rule should apply at least to "pioneer" patents). Other courts have followed the Supreme Court, and determined equivalence as of the date the patent issued. See, e.g., Laser Alignment, Inc. v. Woodruff & Sons, Inc., 491 F.2d 866, 873 (7th Cir.), cert. denied, 419 U.S. 874 (1974).

The Supreme Court has never explicitly retreated from its rule that equivalence must be determined as of the date of a patent's issuance. In Hallibuton Oil Well Cementing Co. v. Walker, 329 U.S. 1 (1946), the Court stated, albeit as dicta, as follows:

> [T]he alleged infringer could have prevailed if the substituted device (1) performed a substantially different function; (2) was not known at the date of Walker's patent as a proper substitute for the resonator; or (3) had been actually invented after the date of the patent. Fuller v. Yentzer, [94 U.S. (4 Otto) 288] supra, at 296-97 [(1876)]; Gill v. Wells, supra, at 29.

329 U.S. at 13 (opinion of the Court by Justice Black).

if it is assessed at the time of issuance of the original patent. The showing of equivalence is strengthened, by the addition of the later information.

In determining whether or not the additional oil used in the accused process takes the process beyond the range of equivalents, the Administrative Law Judge refers to the "important factor" enunciated by the Supreme Court in Graver Tank, and recognized most recently by the Federal Circuit in Hilton Davis, which is "whether persons reasonably skilled in the art would have known of the interchangeability of an ingredient not contained in the patent with one that was." Hilton Davis, slip op. at 9, quoting Graver Tank, 339 U.S. at 609.

In this case, the basic "ingredient" at issue is [C] and the question is whether one skilled in the art would have known that [C] [C] with use of 12-25% oil, i.e., whether the [C] [C] is an "insubstantial substitution" in the claimed invention. Thomas & Betts Corp v. Litton Sys., Inc., 720 F.2d 1572, 1579 (Fed. Cir. 1983). Such a test for equivalency is designed to extend protection against infringement beyond the literal bounds of the patent claim. Id.

Prior to the issuance of the original '942 patent there were concerns about the use of large amounts of oil in the culturing of Streptomyces microorganisms. Furthermore, Complainant's own validity expert, Dr. Demain, pointed out during the hearing that in the fermentation technology it is generally not the case that if a little bit of oil is good, a lot of oil is better. FF[C]76.

Nevertheless, the invention by the Kaken project team represented a marked improvement over the prior art. The prior art used only small amounts of oil for fermentation of salinomycin, while Kaken's invention used much more

oil. See FF F 81, 118. Indeed, the disclosure of the invention directed those skilled in the art to the extensive use of oil in polyether fermentations. FF[C]54.

Upon the issuance of the '698 reissue patent, its prosecution history containing extensive data on tests performed with various amounts of oil became available to those skilled in the art. Complainant's expert testified that the difference between using a total of 25% oil rather than 32% oil in the fermentation to produce salinomycin is insignificant. His testimony was based on the test data contained in the prosecution history of the '698 reissue which shows that the differences between 25 and 32 percent soybean oil concentration mattered little in the final yield of the product.[17] FF[C]64. The prosecution history of the '698 reissue patent shows high yields of salinomycin with amounts of oil above 25%, and even with a tailing off of production, that high yield is maintained with as much as 39% oil. FF[C]53. In addition, the testing contained in the file history demonstrates that there is no toxicity associated with using amounts of oil greater than 25% at least up to 32% for the fermentation of salinomycin. FF[C]51.

Based on the teachings of the original patent and enhanced by the copious test data available to those skilled in the art which are contained in the reissue file history, it is clear that the use of [C]

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[17] While the original '942 patent and the '698 reissue patent showed that an increased amount of oil was beneficial, Dr. Demain testified that one would generally take note of a preferred range expressed in a patent and conclude that the use of oil higher than that level is detrimental. Thus, the preferred range contained in independent claim 1 of the '698 patent and indicated in the specification constitutes evidence against finding equivalence between 30% oil and the preferred 12-25%. See FF C 76. However, one would also know that the testing data contained in the '698 reissue prosecution history showed that dramatic results continued with the use of 32% or 39% oil.

[C] over the entire fermentation process (lasting at least dozens if not hundreds of hours)[18] is an "insubstantial change which, from the perspective of one of ordinary skill in the art, adds nothing of significance to the claimed invention." Valmont Indus., 984 F.2d at 1043. Consequently, whether assessed at the time of reissue or currently the accused Hoechst AG process would fall within the range of equivalents to which claim 2 of the '698 reissue patent is entitled.

3. The Evidence Does Not Show That Hoechst AG's Accused Process Satisfies The Function-Way-Result Test

Much of the evidence offered at the hearing was presented in the context of whether or not the accused Hoechst AG process satisfies the function-way-result test. This may have been due at least partly to the fact that the Hilton Davis opinion did not issue until after the hearing, and partly to the fact that under recent case law and Hilton Davis, the triple identity test remains an important tool for determining whether infringement under the doctrine of equivalents has occurred. The evidence of record does not show that the accused process satisfies the triple identity test. However, as held in Hilton Davis, while satisfaction of the triple identity test may show that there is an insubstantial difference between the claimed and accused products and processes, it is not the only test for infringement under the doctrine of equivalents. In any event, the Administrative Law Judge believes that an analysis under the triple identity test is appropriate for inclusion in this Initial Determination because the parties each took a

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[18] It is also significant that for a substantial portion of the fermentation time [C] the total amount of [C] added in the Hoechst AG process is [C] and at any given point the measurement of oil concentration is [C] FF C 57, 22.

position concerning it, and thus such an analysis addresses the evidence more completely.

Complainant Kaken presented evidence on the issue of alleged infringement primarily through one expert witness, Mr. Sybert. Mr. Sybert testified that Kaken test results he saw in the file history of the '698 reissue patent indicate there were "very good yields and very high yields, at least up to 32 percent and perhaps somewhat beyond. Tests were shown up to 39 percent at which there was some tailing off but not sharply which would be indicative of toxicity." FF[C]45. The function of both the claimed and accused processes is to produce salinomycin in high yield through the culturing of a microorganism with fatty acid or its precursor and ammonia or ammonium salt. The first prong of the triple identity test is met.

However, with respect to the 25% figure for oil, Mr. Sybert also testified as follows:

> In reviewing the file history, it appeared to me that there was a reasonable peak in the activity level without any sharp drop-off on either side. That plateau in activity level centered around the 25 percent range and, therefore, it would be one reason for selecting that number as part of the range. There possibly are other reasons relating to, as I saw in some of the documents, not wishing to adversely affect or dilute out the other nutrients.

FF[C]46 (emphasis added).[19]

Such testimony by Complainant's expert witness about a plateau in activity centered around 25% and the possibility of adverse effects, including dilution of other nutrients above 25%, as described in the prosecution history, raises important questions about whether the use of more than 25% oil

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[19] Mr. Sybert's testimony relating to a plateau of productivity around 25% total oil is confirmed by the Kaken test results attached to the Inaba declaration submitted during the reissue proceedings. FF C 45, 46, 53.

actually functions in the same way, or substantially the same way, as 12-25% oil.

Mr. Sybert testified that he understood fatty acids to provide a needed metabolic building block that the microorganism uses for the production of salinomycins during its growth and production phase. However, he further testified that he did not know the specific pathway followed, saying "within the many pathways that one can plot out, I don't know." FF[C]74-75. Mr. Sybert admitted he had no specific expertise as a microbial nutritionist whose area of study would include the cause-and-effect relationship of individual nutrients in the fermentation mixture.

It is not clear that the testimony of a microbial nutritionist would be necessary to prove the triple identity test. However, the fact remains that there is no explanation in the record as to why yield obtained with oil above 25%, continues to be high, but occurs above a certain "plateau."

The Administrative Law Judge notes that inventor M. Hara admitted that 16% was used in the preferred embodiment, and that there is no explanation as to why 16% as compared with 12% or 25% is better. See FF[C]79.

The fluctuations in yield above the claimed range (at least up to 39%) do not appear to be great or to change the fact that the microorganism uses the oil to produce dramatically high yields of salinomycin. Thus, the Administrative Law Judge does not find that the uses of various amounts of oil

[C] represent a substantial change in the claimed invention. Nevertheless, the record is very sparse with respect to how salinomycin is produced by the microorganism in a fermentation medium and why or how fatty acid or oil is used. There is no explanation in the record as to why the differences in yield above 25% oil occur and whether [C]

used in the accused process is used in substantially the same way as the oil in the 12-25% range. Therefore, based on the evidence of record the Administrative Law Judge cannot find that the added oil in the accused process functions in substantially the same way as the claimed process.

In addition, the testimony of Complainant's expert in the area of alleged infringement also calls into question whether [C] gives substantially the same result as the use of 12-25% oil. While Kaken told the Patent Examiner that the upper limit of 25% is one of "practical importance" and not meant critically to characterize the invention, Kaken also told the Patent Examiner and thereby included in the prosecution history negative information about oil levels above the claimed range.[20] Kaken stated, as follows:

> [A]n excess of fatty acid complicates retrieval, without securing any benefit. Note, for example, that maximum production obtained at 32% treatment is higher than the maximum production obtained at 39% and that further, maximum production as 25% may in fact be greater than the maximum production at 32%.

FF[C]47.

The retrieval of salinomycins (together with the mycelial mass) is a required element of claim 2 which is at issue in this investigation. If maximum production at 32% oil is higher than at 39%, and Kaken believes that maximum production at 25% is higher than at 32%, it is unclear where [C] and whether the results are substantially the same as with 25% oil. The representation to the Patent Examiner on the matter of

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[20] The Administrative Law Judge does not herein rely on the prosecution history to show estoppel. Rather, it is noted that the parties have relied on technical information contained in the prosecution history for evidence on the issue of alleged infringement.

retrieval that is complicated by the presence of excess fatty acid cannot be dismissed.

Therefore, due to questions raised primarily by evidence offered by Complainant, and a lack of evidence explaining the way in which the accused process functions, it cannot be found that the record supports a finding by a preponderance of the evidence that the accused process satisfies the triple identity test.

However, the Administrative Law Judge does not find that any of the questions raised concerning the triple identity test lessens the finding that Hoechst AG's simple increase in the use of [C] in its accused process, which continues to give high yields of salinomycin, represents anything other than an insubstantial change over the invention as set forth in the patent claim.

4. Complainant Has Not Demonstrated That Complainant Copied The Claimed Process

Complainant argues that Hoechst AG arrived at the accused process by copying Kaken. See, e.g., Complainant's Supp. Br. at 7-12; Complainant's Supp. Findings of Fact F I 124 - F I 142.

No one disputes the fact that Hoechst AG was aware of the '698 reissue patent at issue before it began salinomycin production with the accused process. Furthermore, Respondents do not appear to take issue with Complainant's arguments that for years Hoechst AG was a licensee of Kaken, and that Hoechst AG received microorganisms from Kaken as well as Kaken technical information. See Respondents' Supp. Reply Mem. at 3-7; Respondents' Comments on Complainant's Supp. Findings of Fact at 10-12. However, some of Complainant's arguments on this topic seem misplaced inasmuch as Complainant takes the position that the microorganism is not part of the claimed

invention. Hoechst AG uses a strain other than the deposited 80614 strain disclosed in the '698 reissue patent.

In any event, Respondents have not argued noninfringement based on any claim element other than the amount of oil (fatty acid precursor) used in the accused process. The primary deficiency in Complainant's position on copying is that its arguments do not clearly address the key issue which is whether Hoechst AG copied the claimed process with respect to the amount of oil used in its fermentation.

[C]

[C] While some depositions of Hoechst AG employees and other evidence pertaining to Hoechst AG were admitted into evidence, it was not requested that any witness be brought from Germany to testify at the hearing. Consequently, although Hoechst AG ultimately decided [C] to their process which is found herein to be an insubstantial change in the claimed process, the portions of the evidence cited by Complainant do not show that [C] occurred because at some point Hoechst AG merely copied the patented process.

E. Conclusion On The Infringement Issue

According to Respondents' argument on alleged infringement, which is not based on the microorganism or the use of ammonia or ammonium salt, the only material difference between the process of claim 2 of the '698 reissue patent and the accused process performed by Respondent Hoechst AG is that the accused process uses more oil than the amount of oil explicitly claimed in the patent, [C] is used by Hoechst AG instead of 12-25% as stated in the claim. A preponderance of the evidence shows that the patent at issue is

entitled to a substantial range of equivalents, and further that the increased oil used in the accused process represents only an insubstantial change to the invention as set forth in the claim. Therefore, it has been demonstrated that Respondents would infringe claim 2 of the '698 reissue patent under the doctrine of equivalents, if the patent were valid and enforceable.

IV. THE BEST MODE REQUIREMENT OF 35 U.S.C. § 112, FIRST PARAGRAPH

Respondents' view is that the '698 reissue patent and the '942 original patent are invalid under 35 U.S.C. § 112, first paragraph, for failure to disclose the best mode of carrying out the claimed invention. Complainant and the Commission investigative staff oppose a finding of invalidity on any grounds, including failure to comply with the best mode requirement.

A. General Law Applicable To The Best Mode Requirement

The first paragraph of section 112 of the Patent Act provides as follows:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112, ¶ 1 (emphasis added).

The Court of Appeals for the Federal Circuit has held that "[t]he purpose of the best mode requirement is to ensure that the public, in exchange for the rights given the inventor under the patent laws, obtains from the inventor a full disclosure of the preferred embodiment of the invention." Dana Corp. v. IPC Ltd. Partnership, 860 F.2d 415, 418 (Fed. Cir. 1988), cert. denied, 490 U.S. 1067 (1989).

The Federal Circuit set forth the best mode requirement, as follows:

> In short, a proper best mode analysis has two components. The first is whether, at the time the inventor filed his patent application, he knew of a mode of practicing his claimed invention that he considered to be better than any other. This part of the inquiry is wholly subjective, and resolves whether the inventor must disclose any facts in addition to those sufficient for enablement. If the inventor in fact contemplated such a preferred mode, the second part of the analysis compares what he knew with what he disclosed -- is the disclosure adequate to enable one skilled in the art to practice the best mode or, in other words, has the inventor "concealed" his preferred mode from the "public"? Assessing the adequacy of the disclosure, as opposed to its necessity, is largely an objective inquiry that depends upon the scope of the claimed invention and the level of skill in the art.

Chemcast Corp. v. Arco Indus. Corp., 913 F.2d 923, 927-28 (Fed. Cir. 1990)(emphasis in original).

Thus, the best mode inquiry has subjective and objective components. The best mode inquiry presents a "subjective, factual question" as to "the inventor's state of mind as of the time he filed his application" with respect to the best mode contemplated by him for carrying out his invention. Id. at 926. "[T]he level of skill in the art and the scope of the claimed invention [are] additional, objective metes and bounds of [the] best mode disclosure."[21] Id.

Although the inventor's state of mind as to the contemplated best mode must be determined, state of mind is not the focus of the inquiry as to whether or not the best mode was concealed in the patent application. A "concealment" of the best mode may occur accidentally or intentionally. Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1535 (Fed. Cir.), cert. denied, 484 U.S. 954 (1987). As the Federal Circuit recently held:

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[21] The Federal Circuit has held that "[n]otwithstanding the mixed nature of the best mode inquiry, and perhaps because of our routine focus on its subjective portion, we have consistently treated the question as a whole as factual." Chemcast Corp., 913 F.2d at 928.

> While in appropriate circumstances, a failure to disclose the best mode may be so egregious as to constitute inequitable conduct, Consolidated Aluminum [Corp. v. Foseco Int'l Ltd.], 910 F.2d 804, 15 USPQ2d 1481 [Fed. Cir. 1990] (intentionally withholding best mode and disclosing fictitious mode constituted inequitable conduct), specific intent to deceive is not a required element of a best mode defense.

Graco, Inc. v. Binks Mfg. Co., 35 U.S.P.Q. 1255, 1258 (Fed. Cir. 1995) (emphasis in original) (citing Spectra-Physics, 827 F.2d at 1535).

B. The Inventors Were Required To Disclose The Best Microorganism Strain Known To Them For Carrying Out The Claimed Invention

The parties are in disagreement concerning the fundamental issue of whether the Kaken inventors were required to disclose the microorganism strain if there was one that worked best and was known to them. Respondents rely in part on Acme Resin Corp v. Ashland Oil, Inc., 20 U.S.P.Q.2d 1305 (S.D. Ohio 1991), aff'd without opinion, 954 F.2d 735 (Fed. Cir.), cert. denied, 113 S.Ct. 189, 121 L.Ed.2d 133 (1992), which involved a patent for extending the "bench life" of binding components (used in making foundry cores and molds) by adding certain organic phosphorus compounds. The court found that the invention was the addition of the organic phosphorous compounds, and not the binding components which were known in the prior art. Nevertheless, a best mode violation was found because the inventor knew when he filed his patent application with which binding component the organic phosphorous compounds worked best; but did not disclose it.

In this case, Complainant takes the position that the invention lies in the culturing medium, and not the microorganism cultured in the medium. Although that position is rejected in this Initial Determination, even if that were the case, under Acme Resin a best mode violation nonetheless would be found. The inventors were well aware when they made their application for a patent and argued for patentability on the basis of "remarkably high yields"

of 60,000 μg/ml and higher (referred to in Example 3 of the specification) that those yields were not due solely to the medium but depended on which microorganism strain was cultured. FF D 38, 73-85. Despite numerous fermentation experiments conducted by the inventors, the only strain with which such high yields had ever been obtained was Kaken's SLS-K-7-68 strain. FF D 36, 77, 83. Use of the inventive culturing medium with other strains did not produce yields of such great magnitude. Thus, apart from the issue of whether the invention includes the microorganism strain, under the reasoning of Acme Resin, it was not enough for the inventors to disclose their medium while concealing the SLS-K-7-68 microorganism strain which the inventors knew worked best in the medium.

The circumstances in this case are, of course, stronger than those in Acme Resin because independent claim 1 of the '698 reissue patent shows the microorganism to be part of the invention. Furthermore, the binding components at issue in Acme Resin were readily available commercially, whereas the best microorganism strain at the time of the original patent application, Kaken's SLS-K-7-68, was not publicly available. FF E 16-18.[22]

Complainant relies in large part on Randomex, Inc. v. Scopus Corp., 849 F.2d 585 (Fed. Cir. 1988), see Complainant's Post-Hearing Br. at 13-14, in which the Federal Circuit gave guidance on the meaning of the best mode requirement by describing a hypothetical situation and stating in part, as follows:

> [I]f one should invent a new and improved internal combustion engine, the best mode requirement would require a patentee to divulge the fuel on which it would run best. This patentee, however, would not be required to disclose the formula for

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[22] To this day, neither this strain nor any of its descendants is publicly available.

> refining gasoline or any other petroleum product. Every requirement is met if the patentee truthfully stated that the engine ran smoothly and powerfully on Brand X super-premium lead free "or equal." Making engines and refining petroleum are different arts, and the person skilled in the art of making engines would probably buy the suggested gasoline. But if the hypothetical maker or user did not want to use the Brand X super-premium, he would then explore the "or equal" alternative of the patent disclosure.

849 F.2d at 590.

The Federal Circuit's hypothetical in Randomex helps illustrate the law applicable here, and shows that the Kaken inventors were required to disclose the SLS-K-7-68 strain. The invention in the hypothetical is an engine, and not the fuel; nevertheless the inventor is obligated to disclose from among all the available fuels and brands of fuel precisely which brand (or its equal) works the best. Thus, even if the microorganism were not part of the invention, the inventors would have been obligated to disclose which of the salinomycins-producing Streptomyces strains the inventors knew worked best in the claimed process.

Of course, there are significant factual differences between the hypothetical in Randomex and this case which further support the requirement that the microorganism strain be disclosed. For example, the microorganism is not the fuel of fermentation (which is more likely oil or the carbon contained therein); it is more like the engine itself. Furthermore, the best microorganism strain for use in the claimed invention could not merely be named as it was in the Randomex hypothetical as "Brand X," since it (or an equal) is not publicly available. The SLS-K-7-68 strain was a Kaken trade secret which, as discussed below, was the result of an extensive development program.

The evidence shows that one skilled in the pertinent art would in fact be experienced and/or educated in the formulation of culturing media as well as in the development of microorganism strains. The team whose work led to the claimed invention was composed both of individuals at Kaken who performed primarily strain improvement and those who performed primarily medium improvement. In addition, consultations took place among all team members with respect to microorganism fermentations; and the names of all individuals were listed as inventors on the original and reissue patents. FF B 2, 10, D 47-53; RX 5. It is clear that those skilled in the art of antibiotics fermentation would be accustomed to reviewing detailed information about the strain and the medium used in fermentations.[23] Therefore, if the SLS-K-7-68 strain could be duplicated, instructions should have been given in the patent specification disclosing how to do so. If the SLS-K-7-68 strain could not be duplicated, the inventors (through Kaken) should have put a sample in a depository that is accessible to the public. Both these practices are customary in the art and are often required under patent law.

Complainant also relies in part on Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1531 (Fed. Cir. 1991), in which the Federal Circuit held that "[t]he best mode inquiry is directed to what the applicant regards as the invention, which in turn is measured by the claims. Unclaimed subject matter is not subject to the disclosure requirements of § 112 . . . ." However, "a salinomycins-producing Streptomyces microorganism" as expressly recited in the text of claim 1 is part of the claimed invention. The culturing of a

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[23] The inventors knew that those of skill in the art would expect detailed information on the microorganism because their patent, in its Examples and elsewhere, refers the reader to the publicly deposited 80614 strain. The problem is, as discussed below, that the reference to the 80614 strain is inaccurate and serves to conceal the strain that genuinely worked the best.

salinomycins-producing Streptomyces microorganism is not incidental to the claimed invention. The microorganism strain is as much responsible for the high yield of salinomycin reported by the inventors as the medium itself. In fact, Patent Example 3 describes the preferred embodiment of the claimed invention, FF D 124, 199, 206, 214, and the high yield reported therein was at the time of application known by the inventors to occur only with the SLS-K-7-68 strain, See e.g., FF D 107, 125.

At the time they applied for their patent,[24] the inventors knew that there was one salinomycins-producing Streptomyces microorganism strain which worked better than all others they had used, i.e., Kaken's SLS-K-7-68 strain. Therefore, in order to satisfy the best mode requirement of section 112, the inventors were under an obligation to disclose the SLS-K-7-68 strain.

A detailed discussion follows which concerns the development of the SLS-K-7-68 strain, the inventors' knowledge that the SLS-K-7-68 strain was a distinct microorganism strain, the fact that SLS-K-7-68 strain was part of the preferred embodiment of the claimed invention, and the fact that the SLS-K-7-68 strain was not disclosed in the '698 reissue patent.

C. The SLS-K-7-68 Strain Was Developed Only After An Extensive Strain Improvement Program

The '698 reissue patent specification states that "[t]he strains used in this invention include Streptomyces albus No. 80614 and its mutant artificially or naturally produced, as well as other Streptomyces strains capable of producing salinomycins." FF B 5. It is undisputed that the SLS-K-7-68 strain was developed from the 80614 strain.

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[24] There is no dispute among the parties that the critical date in this regard is the 1977 foreign application priority date to which the '942 original and '698 reissue patents refer. See CX 1 (RX 5), '698 Reissue Patent.

Complainant Kaken argues in its brief that it took only four months to develop the SLS-K-7-68 strain, and in its proposed findings of fact that it took only one month. See, e.g., Complainant's Post-Hearing Br. at 18; Complainant's Proposed Findings of Fact at 38. Complainant contends in essence that one need only consider the final step in its strain improvement program to determine how long it took to obtain the SLS-K-7-68 strain.

The evidence of record shows that Complainant Kaken's position with respect to how one evaluates a strain improvement program, such as that carried out by Kaken in connection with the present invention, is completely at odds with the way in which such programs are in fact carried out by those in the art.

Kaken isolated the 80614 strain in 1968 from soil samples taken in Japan. Kaken deposited the 80614 strain at a Japanese depository with the designation FERM-P No. 419, and also at a depository in the United States with the designation ATCC 21838. The 80614 strain became publicly available prior to the issuance of the Kaken's product patent (U.S. Letters Patent 3,857,948). While the earliest test results from Kaken for the 80614 strain are no longer available, results from 1974 show low yields of salinomycin. FF D 36. More recent testing in 1994 and 1995 confirmed that there are low yields of salinomycin when the deposited 80614 strain is used in the claimed process. FF D 212-214.

Although documents pertaining to the beginning of the effort to improve the 80614 strain are no longer available, according to the named inventor who supervised the Kaken strain improvement program, Mr. Masayuki Hara, the work was begun by 1972. FF D 37. Documentary evidence from the period commencing in 1974 shows that Kaken obtained at least eight new strains from the 80614

strain by subjecting it to monospore isolation. FF D 56. In 1975, Kaken derived at least seven more strains from previously obtained descendants of the 80614 strain by various techniques, including ultraviolet radiation, heavy particle irradiation and monospore isolation. FF D 58. Kaken proceeded to test more than 2,500 isolates of these strains. In 1976, Kaken developed at least nine more new strains. Among all the aforementioned strains, the SLS-K-7-68 strain, which was developed in 1976, was far superior to all other strains because it produced substantially higher yields of salinomycin than any of the other strains. FF D 60-65.

An article by Complainant's expert witness, Dr. Demain, shows that strain improvement programs are usually measured from their beginnings. FF D 70. Dr. Hutchinson explained that strain improvement programs in the mid-1970s were not a routine process. FF D 233. Such programs were, and still are, lengthy, complex, circuitous, and labor-intensive, with results that are unpredictable. Different development teams, although given the same objective, would select different combinations and techniques. FF D 234.

Part of the unpredictability in a strain improvement program results from the seemingly random nature of genetic mutations.[25] Considerable judgment and skill are necessary in choosing successful paths in a strain improvement program. Certain techniques may lead to blind alleys while others, at least for a time, appear to be fruitful. FF D 234.

In the 1970s, strain improvement programs required an unavoidably long period of time (on the order of years or even decades), and the same is true

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[25] The process of strain improvement is somewhat analogous to the search for a needle in the haystack, except it is even more difficult because, unlike the needle, the microorganism continually changes throughout the search as a result of the mutations. FF D 249. Thus, some strain improvement programs are unsuccessful. FF D 250.

today. FF D 236. There is no guarantee that even after years of effort a strain improvement program will result in the discovery of an improved microorganism strain capable of antibiotic production at a commercially acceptable level. FF D 258.

Kaken's own search for an improved salinomycins-producing Streptomyces microorganism evidences the unpredictability of strain improvement programs. For example, the identical procedures which resulted in the discovery of the SLS-K-7-68 strain were used a year earlier with a related yet different microorganism strain, and produced a strain with far lower yields than produced by the SLS-K-7-68 strain. FF D 244.

The SLS-K-7-68 strain was first obtained by Mr. Kaoru Hara. The SLS-K-7-68 strain has yields in the claimed process of between 40,000 and 80,000 μg/ml. FF D 63, 108, 229. When Mr. Masayuki Hara referred at the hearing to Mr. Kaoru Hara's supposed ability to obtain a high-producing strain in a onetime trial, Mr. M. Hara testified that was a sort of a "world record." FF D 242. Mr. M. Hara felt that "luck was on" Kaken's scientists when Mr. Kaoru Hara developed the high-producing SLS-K-7-68 strain. FF D 247.

It appears that quite a bit of "luck" is involved in successfully finding an improved microorganism capable of producing high levels of antibiotic, as one experiences first-hand the low probabilities of deriving a suitable strain through monospore isolation and/or techniques that rely on artificial mutagens. FF D 246, 247. Certainly, the development of the SLS-K-7-68 strain had not been assured and was considered a remarkable improvement.

However, Mr. K. Hara's successful efforts were not a lucky one-shot deal, as Kaken would have it.[26] Mr. K. Hara's eventual development of the SLS-K-7-68 strain took place only after a long and laborious path originating with the 80614 strain. For example, Ms. Nakamura, a Kaken employee during the development of the claimed invention and a named co-inventor who worked primarily on strain improvement, used monospore isolation on the 80614 strain yet was unable to develop a strain with high productivity. FF D 226. In 1974-1975, Ms. Nakamura performed three sequential monospore isolations starting with original strain 6, isolating and testing a total of almost 900 isolates. The best strain she isolated after the final monospore isolation yielded only approximately 19,000 μg/ml. FF D 227. Again in 1974-1975, Ms. Nakamura attempted to improve yield by performing monospore isolation. She performed four sequential monospore isolations starting with original strain 6, isolating and testing a total of over 1,000 isolates. After the final monospore isolation, Ms. Nakamura concluded that the final isolates were not good in terms of yield and therefore did not retain them. FF D 228. Ms. Nakamura's actual experience demonstrates that performing monospore isolation on the 80614 strain will not necessarily result in a high-producing strain.

Similarly, artificial mutation techniques known in 1977 and even now do not guarantee isolation of a high-producing strain. There was in 1977, and is now, no guarantee of ever isolating a strain with the 50,000 to 80,000 μg/ml salinomycin yields that the SLS-K-7-68 strain exhibits because of the

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[26] Of course, if Kaken and inventor M. Hara are correct and inventor K. Hara's successful isolation of the SLS-K-7-68 strain was truly a "world record" due to the occurrence of "luck," then the requirement to disclose the SLS-K-7-68 strain and to make it publicly available was substantially increased because in that case Kaken and the inventors could not have reasonably relied on anyone else being lucky enough to achieve Mr. K. Hara's world record.

unpredictability of mutagenic techniques. FF D 229. In fact, when increases are seen in antibiotic production following treatment with a mutagen, they are typically small and occur infrequently. FF D 230. Mutagens most commonly decrease the level of antibiotic production. FF D 231.

Ms. Nakamura's efforts with mutation techniques demonstrate the unpredictability of those techniques. Starting with original strain 6, from 1974 to 1975, Ms. Nakamura used monospore isolation followed by ultraviolet irradiation to induce mutations for strain improvement. Well over 500 individual isolates were tested. The highest yielding isolates yielded only from 14,000 units to approximately 15,500 units. FF D 232. Ms. Nakamura's actual experience demonstrates that performing artificial mutation techniques on the 80614 strain or its descendants will not necessarily result in a high-producing strain. However, Mr. K. Hara obtained the SLS-K-7-68 strain after subjecting its parent strain the A2-54 strain, which was derived from the 80614 strain by microsphere isolation, to ultraviolet radiation. FF D 140, 154.

During the hearing, Complainant emphasized the fact that prior to obtaining the SLS-K-7-68 strain, Mr. K. Hara began a new path of research with the 80614. This decision on the part of Mr. K. Hara was typical of research undertaken when there was an apparent dead end in the potency of a particular strain that had been under development. The Kaken strain development program was characterized by work on a variety of strains that were removed by varying degrees from the deposited 80614 strain, and Kaken returned to the 80614 strain to develop new strains at various times in its program. FF D 36, 55, 227, 228. Mr. K. Hara's return to the 80614 cannot be considered apart from all the other research that he had available to him which showed previous

efforts to have been unsuccessful. In any event, the path of strain improvement did not proceed directly from the original 80614 strain to the SLS-K-7-68 strain. Rather, there were several isolates between the two, including the A2-54 parent strain of the SLS-K-7-68 strain. FF D 61-62.

Drs. Hutchinson and Demain agreed that a research team in 1977-1978 starting with the teachings of Kaken's patents in front of them would have taken about the same amount of time that it took Kaken, and possibly even longer, to go from the wild-type 80614 strain to a strain capable of commercial levels of antibiotic production. FF D 223.

Complainant argues, "[t]hat duplication of the '698 examples may involve some man hours of labor without inventive effort does not detract, in any way, from its routine nature, and does not make the effort required 'undue experimentation.'" Complainant's Post-Hearing Br. at 16, citing Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). However, in Hybritech, the Federal Circuit rejected a best mode argument based only on "testimony by various Hybritech employees that sophisticated, competent people perform the screening and that the screening proces is labor-intensive and time-consuming." 802 F.2d at 1385.

In this case, Kaken's strain improvement program required more than the mere screening of samples for a microorganism. Kaken's program involved thousands of monospore isolations, fermentations, and the application of various artificial mutagens in the effort to find a previously undiscovered strain and/or to create a superior microorganism strain. Kaken's efforts were inventive; they were not routine; and they were also conducted without any guarantee of success. The evidence shows that there is no guarantee that

anyone skilled in the pertinent art could take a Patent Example, such as the preferred embodiment contained in Example 3, obtain a sample of the 80614 deposit and then proceed to duplicate the Example, including the specified yield of salinomycin, regardless of the amount of time given to perform this task.

Respondents' expert witness, Dr. Hutchinson, testified that one cannot ignore the blind alleys and unsuccessful attempts made during a strain improvement program. He observed quite aptly that the person who says that the development of the SLS-K-7-68 strain took only four months is like the person who says that it took him only a short time to walk out of a maze because he is counting only his final path, while ignoring all the previous, unsuccessful paths he had already eliminated by the time he finally walked out of the maze. FF D 234, 69.

It is clear that Kaken conducted an extensive strain improvement program to derive the SLS-K-7-68 strain. Although Complainant argues that the SLS-K-7-68 strain was developed in one to four months, the record in this investigation demonstrates that it was developed as part of an extensive Kaken strain improvement program which lasted at least four years and finally came to fruition. The final months of effort cannot be separated from the years of failure, progress and learning previously obtained in the experimentation and development beginning with the 80614 strain.

D. The Inventors Considered The SLS-K-7-68 Strain To Be The Best For Carrying Out Their Invention

Complainant states that "[w]ith respect to strain, there was simply not a 'best mode' or best way of carrying out the invention." Complainant's Post-Hearing Br. at 10. Complainant argues that the '698 reissue patent contains the information necessary to carry out the best mode of practicing the

invention, including "the specific improved medium that Kaken disclosed, in its know-how documents, to its licensees." Id. However, Kaken's own documents, including those know-how documents, clearly show that at the time of the priority applications, the inventors recognized that the SLS-K-7-68 strain was necessary to carry out their invention in the best way known to them at the time.

The contemporaneous documentary evidence demonstrates that from the outset, it was recognized by Mr. K. Hara in his June and July 1976 reports that the SLS-K-7-68 strain, which he obtained and believed to be a mutant, gave significantly higher yields than previous strains, including the parent strain (A2-54). FF D 93, 110, 114.

Kaken, its counsel and some of its witnesses made various attempts during the hearing and in papers filed in this investigation to criticize Mr. K. Hara, who is now deceased and cannot defend or further explain his work and his observations. They have said that he made inept conclusions, was ignorant of various important characteristics of microorganisms, and that he was poorly educated. Kaken and some of its witnesses now say that they never agreed with some of Mr. K. Hara's observations about the SLS-K-7-68 strain, that they believe the SLS-K-7-68 is not a mutant strain, that it is unstable, and that they did not believe that it was the best mode of carrying out the invention of the '698 reissue patent.

However, there is no documentary evidence showing that anyone at Kaken, including the other inventors, ever stated disagreement with Mr. K. Hara or criticized his work until this litigation. There is no explanation as to why Mr. K. Hara, if he was so poorly educated and so often mistaken, was given such important responsibilities for strain development, or why he managed to

succeed so well in his important task of strain improvement -- unless his success was supposedly due merely to what his former superior called "luck." Furthermore, there is no explanation for why, if his views were incompetent, they were echoed by his superiors. In fact, there is abundant evidence that the named inventors and Kaken recognized the superiority of the SLS-K-7-68 strain, and recognized the strain as being quite out of the ordinary, indeed a superior mutant.

The monthly report of Mr. M. Hara (the late Mr. K. Hara's supervisor) for August 1976 stated that the SLS-K-7-68 strain had a potency of "1.7 times the average value." FF D 167. Later in October 1976, Mr. M. Hara again noted that the SLS-K-7-68 strain has "high potential" and "rapid oil consumption." FF D 96. In the same month of October 1976, approximately five months after the SLS-K-7-68 strain was developed, Kaken referred to the strain as a "superior mutant," when reporting to its licensees. This report was based on information provided from Mr. M. Hara's group. FF D 96. While such a description of the SLS-K-7-68 strain may have been made first by Mr. K. Hara, it was read, adopted and forwarded by co-inventor Mr. M. Hara to others at Kaken.

On June 1, 1977, one day after the filing of the Japanese priority application, a Kaken know-how report provided to Kaken's licensees stated, as follows:

> The isolation of mutants for salinomycin production were continued to obtain "Improved" strains. Ultraviolet-ray, X-ray, [gamma]-ray radiations, and N.T.G., $NaNo_2$ treatments were used for the mutagenic techniques. The selection of mutants among the survivors were made by the morphorogical [sic, morphological] changes, methionine auxotrophs, speed of consumption [sic, consumption] of oil and salinomycin producing ability, <u>but the mutants superior to SLS-K-7-68 have not been obtained as yet</u>.

FF D 77 (emphasis added).

It has been admitted by Kaken in this investigation that at least one of the inventors knew of the information contained in this report before June 1, 1977. FF D 82. Furthermore, Mr. M. Hara admitted in his hearing testimony that the information contained in this report came from his group. It was based on testing performed by another named co-inventor, Mr. Yoneda. FF D 78. The testing was done after consultation among all the named inventors. FF B 10.

In addition to the internal Kaken documents and the reports given to Kaken licensees, the articles written by various inventors demonstrate their acceptance of the SLS-K-7-68 strain as superior to others.

An article published in 1980 by two named inventors, Dr. Miyazaki and Mr. M. Hara, contains information known to them before the filing of the priority patent application. FF D 86. Their article, including Fig. 6 contained therein, illustrates the fact that the improvement in yield obtained by the use of the SLS-K-7-68 strain exceeded the combined improvement of merely adding oil and ammonium salt. The article states that the "improved SLS-K strain" produced a 1.5-fold conversion efficiency increase, a "dramatic increase in production."[27] FF D 86, 88.

In 1982, the same two inventors related the past efforts at Kaken as follows:

> One of the great dreams of industrial fermentation is the promise of productivity gains by the use of improved strains .

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[27] The 1980 Miyazaki and M. Hara article was published in Japanese. There was testimony and colloquy during the hearing concerning the proper translation of the Japanese phrase rendered as "a dramatic increase in production." It was determined that such a translation is acceptable, and further that in English one might say that the authors wished to convey the concept that the productivity was improved by "leaps and bounds." FF D 88.

> . . . [W]e obtained daughter strains that were significantly different from the parent. We thereby developed a strain called SLS-K which, when cultured in the oil medium to be described below, is 1.5 times more efficient at converting soybean oil into salinomycin. This resulted in a dramatic increase in production.

FF D 149 (emphasis added).

In a 1983 Kaken article, prepared in part by Mr. M. Hara, it is stated:

> As a result, on several occasions, we obtained new strains, in which positive differences against the parent strain were recognized. Particularly, one strain which we named SLS-K, displays a better utilizability of an oil medium. The conversion rate of soybean oil to salinomycin increased widely as much as 1.5 times compared with conventional strains, thus contributing much to the improvement of productivity.

FF D 97.

Complainant argues that the Kaken documents cannot be used to show what the inventors thought, citing Glaxo, Inc. v. Novopharm, Ltd., 52 F.3d 1043 (Fed. Cir. 1995). Complainant's Post-Hearing Br. at 11-12. In Glaxo, the best mode issue rested on whether knowledge could be imputed to the inventor, or held against the corporate assignee of the patent under principles of agency law. The Federal Circuit held that the knowledge of the corporation, or of various persons working for the corporation, could not be imputed to the inventor when the inventor himself did know and was not told what the others knew. No best mode violation was found. The circumstances in this case are completely different.

At Kaken, information about the research leading to the claimed invention, including K. Hara's work on the strain improvement and the collective work of jar fermentation experiments, originated at the laboratory level and traveled up the chain of command to the corporate level. The statements made by Kaken to its licensees did not originate with corporate executives, or with patent agents and anonymous scientists as in Glaxo. Kaken

made its statements about the superiority of the SLS-K-7-68 strain based on information received from the inventors. FF D 74, 78, 79. Furthermore, the statements made by the inventors in their articles were their own. FF D 91. In addition, there is no contemporaneous or documentary evidence to show that any contrary or additional views were held by any named inventor. There is no evidence to show dissent among the inventors or that 18 years ago they disagreed in any respect with Mr. K. Hara. See FF D 75, 80. The current statements made by some of the inventors now in the midst of litigation, are contrary to the documentary evidence and are not deemed to be credible by the Administrative Law Judge.[28] The evidence shows instead that there were cooperative efforts and shared observations of the dramatic results obtained with the SLS-K-7-68 strain, which, after approval by Mr. M. Hara, were forwarded to the corporate level and adopted by Kaken.

In order to support their position that the inventors did not consider the SLS-K-7-68 strain to be part of the best mode, Complainant and the Commission investigative staff argue that the SLS-K-7-68 strain cannot be essential to the best mode of carrying out the claimed invention of the '698 reissue patent because the strain was not stable and therefore could not have been viewed as the best strain. However, the evidence of record demonstrates that the instabilities of the SLS-K-7-68 strain have been greatly exaggerated. More importantly, whatever the instabilities of the SLS-K-7-68 strain may be, they did not prevent the inventors from considering the strain to be the best

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[28] Post-hoc testimony has on other occasions been found to be inadequate to establish an inventor's subjective state-of-mind as it existed years earlier. See, e.g., Sinskey v. Pharmacia Ophthalmics, Inc., 982 F.2d 494, 499 (Fed. Cir. 1992), cert. denied, 113 S.Ct. 2346, 124 L.Ed.2d 256 (1993).

for use as a part of the claimed invention at the time they made their priority application. See FF D 125.

The SLS-K-7-68 strain was used for the experimentation that led to each of the Examples 1 through 4 contained in the original and reissue patents, including Example 3 in which the yield of 60,000 μg/ml is reported and which three of the inventors admit is representative of the best mode for practicing their invention. FF D 124; RX 5.

Kaken records show that soon after the SLS-K-7-68 was developed, co-inventor Yoneda abandoned work on all other strains and focused entirely on the SLS-K-7-68 strain in his efforts to optimize the fermentation conditions and obtain a commercial product. FF D 121, 122. Similarly, Kaken chose to put only examples (15 of them) using the SLS-K-7-68 strain in its June, 1977 know-how report to licensees. FF D 125. These decisions would not have been made if the SLS-K-7-68 strain had been considered too unstable -- or anything other than the best strain available at the time. Indeed, Complainant admitted during the discovery phase of this investigation that as of June 1, 1977, the best microorganism strain that Kaken had for use in the method of claims 1 and 2 of the original '942 and the '698 reissue patent was the SLS-K-7-68 strain.[29]

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[29] Respondents' Request for Admission No. 47 reads as follows:

> As of June 1, 1977, Kaken had not developed a microorganism strain that was superior to the SLS-K-7-68 strain when used in the methods described in claim 1 and 2 of the '698 reissue patent and the '942 patent.

Respondents' Request for Admission No. 48 reads as follows:

> As of May 31, 1978, Kaken had not developed a microorganism strain that was superior to the SLS-K-7-68 strain when used in the methods described in claims 1 and 2 of the '698 reissue

(continued...)

There is clear and convincing evidence that the inventors knew that the SLS-K-7-68 strain was best for use in their claimed invention as of the time they made their priority filing, and were therefore required to disclose it in order to satisfy the requirements of section 112, first paragraph.

E. The Original And The '698 Reissue Patents Conceal The Best Mode SLS-K-7-68 Strain

The only strain explicitly disclosed in the '698 reissue patent is the 80614 strain. FF D 203-204.

Complainant argues that the strain was nevertheless disclosed because the 80614 strain is the SLS-K-7-68 strain. The Commission investigative staff takes the position that the disclosure made in the specification was adequate for one of ordinary skill in the art. Respondents take the position that the '698 reissue patent does not disclose the SLS-K-7-68 strain, as required. Respondents argue that the '698 reissue patent conceals the SLS-K-7-68 strain because Complainant Kaken wanted to maintain the strain as a trade secret.

In Chemcast Corp., the Federal Circuit held that on the best mode issue one must asses the adequacy of the disclosure in terms of the level of skill in the art. 913 F.2d at 927-28. By that standard, it is clear the disclosure of the '698 reissue patent is inadequate to disclose the best mode for carrying out the invention.

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[29](...continued)
patent and the '942 patent.

Complainant Kaken's response to both Requests for Admission is as follows:

> It is admitted that the best strain had been selected using conventional techniques from the strains deposited as FERM P-419 and had been identified as SLS-K-7-68.

RX 673, Kaken's Resp. to Respondents Hoechst's First Set of Requests for Admission Nos. 1-55, at 19-20 (emphasis added).

Dr. Hutchinson testified that one skilled in the art would read the '698 reissue patent to indicate that the deposited 80614 strain was used in the Patent Examples, including Example 3 which is the preferred embodiment. FF D 21-28, 219. Complainant's expert, Dr. Demain, admitted that there is nothing in the Examples or elsewhere in the patent specification to indicate that anything other than the 80614 patent was used in the Examples. FF D 210. He admitted that there was no disclosure in the '698 reissue patent of any details for producing the SLS-K-7-68 strain. Dr. Demain made these admissions while fully recognizing that the specification makes the statement, which has been often relied upon by Complainant, that the "80614 and its mutants artificially or naturally produced" may be used. FF D 221. That statement in the specification provides no information concerning the existence of the SLS-K-7-68 strain or how the strain may be obtained.

Compounding the fact that the '698 reissue patent provides no indication of the SLS-K-7-68 strain's existence, or the fact that it worked best in the claimed process, is the fact that the SLS-K-7-68 strain was not deposited by Kaken so that those skilled in the art would not have access to it. See FF E 16. Thus, it was not the intention of Kaken and the inventors that one could request a sample of the SLS-K-7-68 strain from a public depository.

A large amount of evidence was adduced at the hearing to show that the SLS-K-7-68 strain is simply not the same as the 80614. Complainant's argument that it is, is unsupportable.

In the July 1976 research report by Mr. K. Hara, he stated early on in his involvement with the SLS-K-7-68 strain that "it is considered that the 7-68 strains are mutant." FF D 140. A September 1976 research report by Mr. K. Hara called the SLS-K-7-68 strain a "mutant strain . . . obtained by UV

radiation." FF D 95. The report stated that "the wild type characteristic has been lost."[30] FF D 95, 142. Similarly, the October 15, 1976 know-how report that Kaken sent to Hoechst under a license agreement stated that the "superior mutant, SLS-K7-68 [sic] was obtained by UV irradiation." FF D 147. In other know-how reports, and articles by some of the inventors, which have already been discussed the SLS-K-7-68 strain was labelled a mutant and the strain's dramatic and differentiating characteristics were recognized. See FF D 88, 97, 125.

A considerable amount of trial time and the parties' briefing has been devoted to the question of whether the SLS-K-7-68 strain is a mutant. Complainant argues that Respondents' best mode defense requires that the SLS-K-7-68 be a mutant.[31] Complainant's Post-Hearing Br. at 15. Certainly, if the strain is a mutant, the responsibility was far greater upon the inventors to tell those of ordinary skill in the art of the fact that Kaken had developed it and to provide them with a way of obtaining it. Indeed, no party has taken the position that a mutant of the 80614 is the same as the 80614 wild-type strain.

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[30] Another inventor, Dr. Miyazaki (who did not testify at the hearing), testified in his deposition that he "saw a clear difference between the SLS-K strains and the parent strains," including the 80614 strain. FF D 90.

[31] Complainant argues that although Hoechst had access to certain Kaken documents and worked with Kaken strains, Hoechst did not tell the FDA that the Hoechst production strain K-9-46 (derived from the SLS-K-7-68 strain) is a mutant of the deposited strain. Complainant's Post-Hearing Br. at 1, 12. Complainant did not call Hoechst witnesses to testify at the hearing on this subject. However, the deposition testimony of Hoechst's Dr. Rathscheck shows that in 1982 when the submission was made to the FDA, Hoechst did not attach importance to the question of whether it was accurate to state that its K-9-46 production strain was stored as ATCC 21838. FF D 1. The evidence of record does not make it clear how Hoechst handled its original FDA submission. During this investigation, Hoechst corrected its FDA submission with regard to its production strain to state that it is a mutant and not the ATCC 21838 strain as deposited. FF D 2.

However, as recognized by Respondents, Respondents' Reply Br. at 5, it is not necessary that the SLS-K-7-68 be shown to be a mutant in order for the '698 reissue patent to be invalid for failure to disclose the best mode. The evidence of record is such that the effect of using the SLS-K-7-68 strain had never been duplicated with any other strain, and further that the strain was obtained after an extensive development program which, even if replicated, might never produce the same results. The SLS-K-7-68 strain resulted only after thousands of monospore isolations and mutangenic treatments had been performed. Even if an equal number of monospore isolations were conducted, there would be no guarantee that one would obtain the SLS-K-7-68 or its equal. FF D 241, 245, 248, 251, 252.

In any event, the evidence of record overwhelmingly supports a finding that the SLS-K-7-68 strain was in fact derived by a genetic mutation in its parent strain (the A2-54 strain), which is a descendant of, yet not the same as, the 80614 strain. Some of the strongest evidence for this proposition has already been discussed, i.e., statements made at the time of the strains' development by the inventor who first isolated it (Mr. K. Hara) and statements of Kaken which were based on reports from Mr. M. Hara's group of inventors. However, there is additional evidence that the SLS-K-7-68 strain is a mutant.

Dr. Hutchinson testified at the hearing that a strain which has even one reproducibly different property from a parent strain is a mutant strain. FF A 22, 25, 26, D 159-161. The SLS-K-7-68 strain regularly exhibits many different properties from those of the parent strain, including a significantly higher ability to convert oil into salinomycin, a different pH,

and a different variation coefficient.[32] FF D 171, 172, 178. Dr. Hutchinson testified that the combination of all of these differences clearly demonstrates that the SLS-K-7-68 strain is a mutant strain. FF D 180.

Dr. Demain, Kaken's expert, refused to call the SLS-K-7-68 a mutant at the hearing. He did, however, admit that a strain which has a repeatedly different property from its parent strain is, by definition, a mutant strain.[33] FF 159, 181. Dr. Demain indicated that a difference in yield of about 10 to 15% between a strain and its parent strain would be indicative of the strain being a mutant strain. FF D 165. Kaken's testing of the SLS-K-7-68 strain in various media show that its yield is higher than that of the parent A2-54 strain by at least 18%, thereby satisfying the definition of a mutant given by Dr. Demain. FF D 111. Dr. Demain also admitted that a 1.5 fold increase in the ability of an organism to convert oil into salinomycin would be sufficient to demonstrate that the organism was a mutant strain. FF D 168, 184. The inventors' articles, discussed above, demonstrate such an improvement in efficiency for the SLS-K strain. Therefore, by Dr. Demain's criteria, the SLS-K-7-68 strain is properly classified as a mutant strain.

Dr. Demain further admitted that if a strain were the result of an ultraviolet irradiation treatment, he would assume that the mutation was caused by the ultraviolet irradiation rather than by a spontaneous mutation. FF D 162, 186. Kaken's records clearly show that Mr. K. Hara exposed the

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[32] Respondents take the position that the SLS-K-7-68 strain also has a different color than the 80614 strain. However, the evidence on this point was not clear. FF D 178, 179.

[33] Dr. Demain also admitted during cross-examination that the SLS-K-7-68 strain is different from the deposited 80614 strain, and that the Miyazaki article (RX 87) also indicates that the strains are different. Demain, Tr. 2170-2173.

parent strain to ultraviolet radiation before obtaining the SLS-K-7-68. FF D 139, 140, 142, 147. Thus, there is further evidence not only that the SLS-K-7-68 strain is a mutant, but that mutation was caused by artificial means.

Inasmuch as the SLS-K-7-68 strain differs so much from the 80614 strain, enough in fact to show that it is a mutant and an identical genetic mutation is difficult if not impossible to reproduce, Respondents state that the inventors were under an obligation to deposit the SLS-K-7-68 strain so that it would be publicly available.

The evidence summarized above shows that one skilled in the art could not readily develop the undisclosed best strain which took Kaken more than four years to find. Under such circumstances one cannot rely on the level of skill in the art to argue that a skilled person could simply develop the SLS-K-7-68 strain for himself, starting with the 80614 strain as deposited.[34] The unpredictability associated with the efforts to develop the SLS-K-7-68 strain required a public deposit of that strain in order to satisfy the best mode requirement.

The Commission investigative staff states that a deposit of the microorganism strain is not required citing Amgen, Inc. v. Chugai Pharmaceuticals Co., 927 F.2d 1200 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991) and Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991), in which a deposit of certain biological material was held

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[34] In general, patent applicants cannot rely only on what is known in the prior art to erase the need to disclose the best mode in their specification. Dana Corp., 860 F.2d at 419. In this case, no identification of the SLS-K-7-68 strain was made, and one of ordinary skill in the art was given only misleading information to work with.

to be unnecessary in order to satisfy the best mode requirement. OUII Br. at 34.

In Amgen, the patent covered a "host cell" which produced the desired therapeutic agent called EPO. A best mode defense alleged that the patentee did not disclose the host cell known to him at the time of application which produced EPO at a greater rate than other cells. The district court found that one of ordinary skill in the art could not duplicate the patentee's best mode without a deposit of the host cells in a public depository. The Federal Circuit reversed this portion of the lower court's findings. 927 F.2d at 1209.

The Federal Circuit based its decision on the fact that the evidence adduced during the trial showed that the invention as it relates to the best mode host cells could in fact be practiced by one skilled in the art following one of the patent's Examples. The court drew a distinction between the host cells in question and other biological materials obtained from nature and which therefore may be incapable of being practiced without access to the organism. The Federal Circuit held that "[i]f the cells can be prepared without undue experimentation from known materials, based on the description in the patent specification, a deposit is not required." The Federal Circuit, in response to arguments that an exact duplication could not be made, held that "[w]hat is required is an adequate disclosure of the best mode, not a guarantee that every aspect of the specification be precisely and universally reproducible." Id. at 1212.

In this case, the SLS-K-7-68 strain cannot be obtained by following instructions contained in the patent specification, since there is no disclosure of the existence of the SLS-K-7-68 strain, or how it was obtained

or that the strain was used to obtain the highest titers of salinomycin. If instructions had been given in the specification of the techniques utilized by the inventors to obtain this strain, there is still no guarantee that one of ordinary skill in the art could obtain a microorganism strain that even approximates the SLS-K-7-68 strain with respect to the production of salinomycin. In contrast to the facts in Amgen, in this case it cannot be said that the microorganism can be prepared without undue experimentation from known materials, based on the description in the patent specification. The nature of the SLS-K-7-68 strain is more closely analogous to that of a unique biological material obtained from nature and which may be incapable of reproduction without access to a deposited sample.

In Scripps, the charge was not one of concealment or undisclosed techniques. Rather, the best mode defense was based on the argument that because the process for screening monoclonal antibodies to obtain a particular antibody was so laborious, a deposit should have been made available to the public of the required antibody necessary to practice the best mode of the claimed invention. 927 F.2d at 1579. The Federal Circuit confirmed its earlier holding in Hybritech, to the effect that the need for a labor-intensive and time-consuming antibody screening process does not amount to concealment of the best mode. A deposit of the antibody necessary for the best mode was not required. Id. at 1579-80.

In this case, one of ordinary skill in the art is not merely confronted with the necessity to perform a laborious or time-consuming process. One is faced with the challenge of improving the 80614 strain as deposited so as to arrive at the SLS-K-7-68 strain or its equal, without any guidance from the

specification or any assurance of success even if one engages in one's own strain improvement program.

Respondents rely on In re Lundak, 773 F.2d 1216, 1218 (Fed. Cir. 1985), in which the Federal Circuit reviewed the development of the case law and the PTO regulation (formerly a Rule of the Patent Office) requiring the public deposit of biological materials in certain cases to satisfy the enablement requirement of section 112, first paragraph.[35] The court held in part, as follows:

> When an invention relates to a new biological material, the material may not be reproducible even when detailed procedures and a complete taxonomic description are included in the specification. Thus the then Patent Office established the requirement that physical samples of such materials be made available to the public, as a condition of the patent grant.

773 F.2d at 1218. Accord Amgen, 927 F.2d at 1210-11.

The same concern applies in this instance in which the inventors have revealed their best mode as having dramatically high yields of 60,000μg/ml, yet one could not practice the best mode in 1977 without the use of the SLS-K-7-68 strain. As discussed in detail above, there is no assurance, even

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[35] In rejecting the Preliminary Amendment, the Patent Examiner took the position during the reissue proceedings that the microorganism is essential to the claimed invention and that the particular strain used in the Patent Examples must be available in a public depository in order for the application to satisfy the enablement requirement of section 112 and for the patent to issue. FF E 35. Patent counsel for the applicants responded that the 80614 strain had been publicly deposited.

While Respondents have charged that such a response was a violation of the duty of candor owed to the PTO because the research leading to the Examples had in fact been performed with the SLS-K-7-68 strain instead of the 80614, the enablement requirement of section 112, first paragraph, has not been put in issue in this investigation. It appears that even with the 80614 strain, one could achieve higher yields using the medium disclosed in the '698 reissue patent than one could obtain with media taught in the prior art. See FF D 103-107. The issue here is not enablement, but rather, whether one could have practiced the best mode, with yields of 60,000 μg/ml or higher, without the SLS-K-7-68 strain.

with a detailed description of the monospore isolation techniques and mutagenic techniques used to obtain the SLS-K-7-68 strain, that one of ordinary skill (or even exceptional skill) in the art could obtain the SLS-K-7-68 in the same or less time than it took Kaken, or indeed ever. See FF D 252. Thus, a public deposit of the SLS-K-7-68 strain was necessary for one of ordinary skill in the art to practice the preferred embodiment.

Of course in this case, the inventors did not reveal the existence of the SLS-K-7-68 strain in their patent specification. They falsely stated that the 80614 strain was used in the Examples (including the preferred embodiment Example 3), and gave absolutely no details of how the SLS-K-7-68 strain was obtained.[36]

All of the crucial facts concerning the SLS-K-7-68 strain, including the scope and details of the Kaken strain development program and the characteristics of the SLS-K-7-68 strain, were well known to the inventors before they filed their patent application. Although it is not necessary to prove why the inventors failed to comply with the best mode requirement in order for Respondents' affirmative defense to have merit, the record adduced on the question of whether Kaken treated the SLS-K-7-68 strain as a trade secret contains clear indications of why the SLS-K-7-68 strain was not disclosed which further highlights the fact that it was not made available to the public.

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[36] Dr. Demain testified that in his patents, if he uses a mutant, he makes a public deposit of the microorganism or at least gives detailed information on how one could obtain the microorganism. He also testified that if he says in a patent that he used a particular microorganism, then that is the microorganism he used. For example, if he says that a deposited microorganism was used, then he used that microorganism as deposited. FF D 205.

There is generally a competitive advantage throughout the antibiotics fermentation industry in retaining production strains as trade secrets. FF E 2. Dr. Miyazaki stated that Kaken did not reveal high yielding production strains to the public. Mr. Inaba, a Kaken scientist, testified that Kaken considered these production strains to be trade secrets and that they were not made publicly available. Mr. Kobayashi, Kaken's Director of New Product Development in the mid-1970's, also testified that Kaken considered its production strains to be a trade secret. Even Kaken's President, Mr. Wakiyama, testified that it was Kaken's policy to maintain as a secret the production strains it uses to make antibiotics. FF E 7. Kaken obtained its production strains from the SLS-K-7-68 strain. FF D 2; RX 806C. Thus, Kaken chose to maintain the SLS-K-7-68 strain as a trade secret rather than to make it available to the public in exchange for the rights granted through the PTO. FF E 16-18.

In the cases relied on by Complainant, Hayes Microcomputer Prods., Inc. Patent Litig., 982 F.2d 1527 (Fed. Cir. 1992) and Christianson v. Colt Indus. Operating Corp., 870 F.2d 1292 (7th Cir. 1989), cert. denied 493 U.S. 822 (1989), the patentees did not disclose in their patent specifications the details for making their companies' products.[37] However, whether or not the information in question was a trade secret is irrelevant to the best mode issue. In neither case was it shown that the information was necessary to

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[37] Complainant further argues that "Miyazaki and Hara did not identify the strain actually used in their articles because it was so easy to obtain!" Complainant's Post-Hearing Br. at 19 (emphasis in original). However, the evidence of record clearly contradicts the argument that the SLS-K-7-68 strain was easy to obtain. Furthermore, it is clear that at the time the Miyazaki and Hara article was written, Kaken regarded the SLS-K-7-68 strain to be a trade secret. FF E 5, 16. That is the more plausible reason why the strain was not disclosed in the patent, or in subsequent writings by the inventors.

practice the best mode of the claimed invention. In contrast, the concealed SLS-K-7-68 strain was known by the inventors to be necessary to the best mode for carrying out their invention. Therefore, there is a best mode violation in this case for although the case law shows that trade secrets are not necessarily part of the best mode, there is no exemption from the best mode requirement due to the fact that the inventors (or their companies) consider information to be a trade secret.

F. Conclusion

The record demonstrates by clear and convincing evidence that the '698 reissue patent is invalid for failing to comply with the best mode requirement of 35 U.S.C. § 112, first paragraph. The inventors failed to disclose the best microorganism strain known to them, as of the effective filing date of the original patent application, for carrying out the claimed invention.

V. THE '698 REISSUE PATENT IS UNENFORCEABLE DUE TO INEQUITABLE CONDUCT

A. Background And General Law Applicable To The Issue Of Inequitable Conduct

Respondents argue that the '698 patent is invalid due to acts of inequitable conduct committed by the applicants and Kaken as well as by the patent attorney who prosecuted the reissue application before the PTO. Complainant Kaken and OUII take the position that the '698 patent is enforceable.

A patent is unenforceable if the patentee failed to disclose material information to the PTO, or submitted false material information, with an intent to deceive. Both materiality and intent to deceive must be proven by clear and convincing evidence. Kingsdown Medical Consultants, Ltd. v.

Hollister, Inc., 863 F.2d 867, 872 (Fed. Cir. 1988), cert. denied, 490 U.S. 1067 (1989).

The general rule concerning materiality is that information is material if there is a substantial likelihood that a reasonable patent examiner would consider it important in deciding whether to allow the application to issue as a patent. However, a patentee has no obligation to disclose a reference that is cumulative or less pertinent than those already before the examiner. Halliburton Co. v. Schlumberger Technology Corp., 925 F.2d 1435, 1439-40 (Fed. Cir. 1991).

The PTO's Rules impose a duty to disclose information material to patentability, and define materiality as follows:

> (b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and
> (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or
>
> (2) It refutes, or is inconsistent with, a position the applicant takes in:
> (i) Opposing an argument of unpatentability relied on by the Office, or
> (ii) Asserting an argument of patentability.

19 C.F.R. § 1.56 (1994) (RX 743).

In cases of inequitable conduct before the PTO, "direct proof of wrongful intent is rarely available, but may be inferred, from clear and convincing evidence of the surrounding circumstances." LaBounty Mfg. v. United States Int'l Trade Comm'n, 958 F.2d 1066, 1076 (Fed. Cir. 1982). The conduct at issue must be viewed in light of all the evidence, including evidence of good faith. Kingsdown, 863 F.2d at 876.

The actions of an applicant's attorney are chargeable to the applicant. FMC Corp. v. Manitowoc Co., Inc., 835 F.2d 1141 (Fed. Cir. 1987).[38]

B. Concealment Of The Best Mode SLS-K-7-68 Microorganism Strain

The Federal Circuit has recognized that although a finding of intent to deceive is not necessary to find a failure to comply with the best mode requirement, in some circumstances a failure to disclose is so egregious that it constitutes inequitable conduct. Graco, Inc., 35 U.S.P.Q. at 1258. For example, in Consolidated Aluminum, the Federal Circuit affirmed a finding of inequitable conduct, holding that intentional concealment of the best mode under the mask of a fictitious mode constitutes an intent to deceive the PTO.[39] 910 F.2d at 809.

As shown above, the SLS-K-7-68 microorganism strain is crucial to the high yields disclosed in the specification, particularly the 60,000 μg/ml of salinomycin stated in Example 3, and is part of the best mode for carrying out the claimed invention. Indeed, inasmuch as disclosure of the best mode is statutorily required it is inherently material to a patent prosecution.

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[38] Similarly, when a corporate assignee assumes responsibility for providing information during the prosecution of a patent, and then commits acts which constitute inequitable conduct, the patent will be found to be unenforceable. See, e.g., Consolidated Aluminum Corp. v. Foseco Int'l Ltd., 910 F.2d 804 (Fed. Cir. 1990).

[39] In the Consolidated Aluminum case, the Federal Circuit also found that acts of inequitable conduct committed during the prosecution of one patent permeated the prosecution of other related patents-in-suit, and thus rendered them unenforceable. 910 F.2d at 809-812. Accord Keystone Driller Co. v. General Excavator Co., 290 U.S. 240 (1933). The '698 patent is a reissue of the '942 original patent, and furthermore the original specification, including the Examples, was copied in its entirety. Consequently, there is no question that acts of inequitable conduct committed in connection with the '942 original patent affect the '698 reissue patent, and no party has argued to the contrary.

Consolidated Aluminum, 910 F.2d at 808-09; Dana Corp. v. NOK, Inc., 882 F.2d 505 (Fed. Cir. 1989).

Kaken has admitted that the SLS-K-7-68 strain was the strain actually used to carry out the work reported in all the Patent Examples, including the '942 original and the '698 reissue patent. FF E 19. The applicants and Kaken knew since before the application was made for the original patent, which shares the same specification as the reissue patent, that the SLS-K-7-68 was a mutant strain obtained after an extensive strain improvement program. FF D 73-85. Nevertheless, the patent falsely states that the 80614 strain was used.

A contrast of the draft Japanese priority applications, with the '942 original patent specification shows the inventors' initial intent to reveal their use of a mutant, and Kaken's deliberate refusal since the early stages of the patent application process to disclose the use of any improved strain.

Mr. Shibuya, a Kaken employee, had primary responsibility for writing the Japanese applications upon which the '942 original and '698 reissue patents rely for their priority filing dates. Two of the named inventors, Kaken employees Mr. M. Hara and Dr. Miyazaki, helped prepare the Japanese patent applications. They wrote drafts of Embodiments for the Japanese applications which correspond to Patent Examples 1, 2 and 3 of the United States patents. The draft Examples list three strains, i.e., the 80614 strain, the strain "divided" from the 80614, and the "improved mutant strain." FF D 84-85, E 25-26. Indeed, while preparing the Examples, Mr. Hara was aware of the information provided by his group which led Kaken to state in its June 1, 1977 know-how report that Kaken had not yet obtained mutants superior to the SLS-K-7-68 strain. FF E 27. Consequently, it is only natural that an

inventor working on the draft Examples should refer to the use of a mutant strain. Nevertheless, Mr. Kobayashi, Kaken's Director of New Product Development in the mid-1970s, deleted the reference to the mutant strain from the patent application.[40] FF E 30.

As submitted to the PTO, the Patent Examples, including Patent Example 3 which reports a dramatically high yield, falsely state that the 80614 strain was used to obtain salinomycin. Although the Patent Examples form a major portion of the specification for the '942 original and '698 reissue patents, they contain no indication that a mutant or any strain other than the 80614 strain was used.

There is no credible evidence that anyone at Kaken, including the inventors who signed the application, believed that yields as high as 60,000 μg/ml could be obtained with the 80614 strain, or that the 80614 strain was used in the Examples. Mr. Hara, Dr. Miyazaki and anyone else at Kaken who knew about the development program that led to the claimed process also knew that strains superior to the SLS-K-7-68 had not been developed when the Examples were submitted to the PTO. The Patent Examples insofar as they purported to use the 80614 strain were fictitious. That undoubtedly was known by the inventors and others at Kaken involved in the patent prosecution.

Kaken filed its reissue application with claims 1-4 on January 29, 1993.[41] If the falsehoods in the original specification had been innocent errors, Kaken could have corrected the United States specification to reveal

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[40] Mr. Shibuya testified only that he does not know why the reference was deleted at the time the applications were filed. FF E 31.

[41] Along with the reissue application, Kaken submitted the Inaba Declaration, which reported tests performed with Kaken production strains 91-2-57 and US-26-71. FF E 34.

that an improved mutant strain derived from the 80614 is necessary to practice the best mode. Kaken took no action to correct the specification, and thus the misrepresentation to the PTO was compounded.

The PTO issued an Office Action on June 30, 1993, which rejected claims 1-4 of the reissue application under 35 U.S.C. § 112, first paragraph, because, among other things, "the microorganism is essential to the claimed invention" and "[t]he strains of Streptomyces albus used within the Examples of the specification have not been properly deposited."[42] FF E 35. This rejection was received by Mr. Kelber of the Oblon firm, which prosecuted the original reissue applications.

In September 1993, Mr. Kelber wrote to Kaken's Japanese patent attorney, Mr. Shimada. Mr. Kelber asked whether the 80614 strain had been deposited "or is otherwise available to those of skill in the art . . . ." FF E 36. The September 1993 response of Mr. Shimada stated that the 80614 strain was deposited as ATCC 21,838.[43] FF 37.

On November 1, 1993, Mr. Kelber responded to the Patent Examiner's June 30, 1993 Office Action. He merely repeated the information obtained from Mr. Shimada to the effect that the 80614 strain was widely available. FF E

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[42] The purpose for which the Examiner raised the issue of the microorganism strain, i.e. the enablement requirement, is irrelevant in this case to the question of whether inequitable conduct was committed. It does not matter why the Examiner requested information about the strain used in the Examples. Either the 80614 strain was used or it was not. Thus, a false statement to the effect that the 80614 strain was in fact used necessarily affected the entire prosecution.

[43] Mr. Kelber also inquired of Mr. Shimada whether the two production strains used in the Inaba Declaration examples were publicly available. FF E 36. Mr. Shimada responded that those strains "are mutants of Streptomyces albus 80,614, and they are not deposited and thus not publicly available." FF E 37. That information was not specifically requested by the Patent Examiner, nor was it forwarded to her. FF E 38.

39-40. However, at his deposition, Mr. Kelber admitted that as of his November 1, 1993 response, he knew that the deposited 80614 strain was not used in Example 3, as follows:

> Q. As of November 1, 1993, your response to the office action as of that date you had known or you knew that the strain used in example 3 of the patent was not the 80614 strain as deposited, correct?
>
> A. That's correct.

FF E 41.

In fact, the evidence shows that Mr. Kelber knew in 1993 that Example 3 was performed using the concealed SLS-K-7-68 strain. FF E 42. Nevertheless, Mr. Kelber's response to the Examiner, who had stated her position that the microorganism strain is "essential" to the claimed invention, did not correct the falsehoods in the reissue application about the supposed use of the 80614 strain in the Patent Examples. The Examiner had no reason to doubt the information in the original patent and reissue application concerning the 80614 strain, and she obviously believed it. Mr. Kelber's response lacked any disclosure that the 80614 strain was not used in the Patent Examples, and that the SLS-K-7-68 strain was used instead. Mr. Kelber thus advanced the fraud that Kaken had been perpetrating since the original application, which was to have the Examiner and everyone else focus on the 80614 strain as deposited yet remain ignorant of the existence and use of improved strains, especially the SLS-K-7-68 strain. Mr. Kelber's November 1, 1993 response to the PTO was therefore an express misrepresentation.

Mr. Kelber changed his testimony at the hearing with respect to the question of when he became aware that a strain other than the 80614 was used as a basis for the Patent Examples. FF E 63, 70. He testified at the hearing

that he became aware of the use of the SLS-K-7-68 microorganism strain during April 1994 meetings at Kaken in Japan. FF E 67, 70.

Mr. Kelber testified at the hearing that he became aware between his deposition and the beginning of June 1995 that his deposition testimony was not accurate. FF E 64. He testified that his recollection regarding when he learned about the strain used in Example 3 changed after he reviewed the transcript of his deposition, his records of the litigation, the papers that were reviewed, the reissue file, and the papers contained in it. FF E 65.

In some cases a deposition is taken when the witness's recollection of past events needs refreshing, and a subsequent review of documents may result in more accurate testimony from the witness at trial. Yet such a scenario is not consistent with the events in this situation. Mr. Kelber had been litigating this case for at least 4½ months prior to his deposition, and had been involved in preparation for the case for a substantial period of time in advance of that. By the time of Mr. Kelber's deposition, the best mode and inequitable conduct issues had already been raised by Respondents, and he had already worked on his prehearing brief. FF E 66. With respect to the serious issue of whether he knew that the SLS-K-7-68 strain was used by Kaken in the Patent Examples when he responded to the Patent Examiner's rejection, there is every reason to believe that Mr. Kelber's deposition testimony was made in a considered manner and was based on his extensive and then current work with the evidence and facts of this case.

Even if Mr. Kelber's hearing testimony to the effect that he became aware of the SLS-K-7-68 strain in April 1994 were to be credited, it would nonetheless establish inequitable conduct. The '698 reissue patent did not issue until August 16, 1994, and the reissue prosecution therefore continued

well past April 1994. FF E 67. At the very least Mr. Kelber admitted at the hearing that when he learned in April 1994 that Example 3 was actually performed with a strain that was not deposited, he did not provide that information to the Examiner. FF E 68-69. He did, however, contact the PTO on Kaken's behalf to request that issuance of the reissue patent be expedited so that Kaken could commence litigation against Respondents. See Petition to Expedite Issuance and Advance the Printing Date and Declaration of Steven B. Kelber dated March 18, 1994 (RX 901 at 273-77). FF E 284.

There is also ample evidence that Mr. Kelber knew of the importance the SLS-K-7-68 strain had to the patent prosecution. Mr. Kelber knew during the reissue prosecution that the SLS-K-7-68 strain was not identical to the deposited 80614 strain. FF E 44. He also knew during the reissue prosecution that ultraviolet irradiation was used in the process of obtaining the SLS-K-7-68 strain, FF E 45, and that the use of ultraviolet irradiation increased the probability of mutation occurring, FF E 46-47. As discussed above, whether or not the SLS-K-7-68 strain was a mutant, it was so far removed from the 80614 strain both in performance and in the amount of research and development that went into obtaining it, that Kaken had a duty to disclose it to the PTO.

Mr. Kelber also knew during the reissue prosecution that at least one of the inventors considered the SLS-K-7-68 strain to be a mutant. FF E 48. In fact, he received a 1976 Kaken technical report during the reissue prosecution which indicates that "[t]he superior mutant, SLS-K7-68 [sic], was obtained by UV irradiation." FF E 51. He was also provided with a June 1, 1977 Kaken technical report before the conclusion of the reissue prosecution which

indicates that "mutants superior to SLS-K-7-68 have not been obtained as yet." FF E 52.

Mr. Kelber knew during the reissue prosecution, at least by April 1994, of the reference in the 1982 Miyazaki et al. article (RX 56) that the authors believed that the SLS-K-7-68 strain was significantly different from the parent strain. FF E 53. Mr. Kelber knew during the reissue prosecution of publications by inventors dated after 1977 in which at least two of the inventors characterized the SLS-K strain as an improved strain that resulted in a dramatic increase in yield. FF E 54. Mr. Kelber knew during the reissue prosecution that the SLS-K-7-68 strain was not deposited in any public depository. He also knew during the reissue prosecution that the SLS-K-7-68 strain was developed prior to the time the first Japanese foreign priority application to the '942 patent was filed. FF E 58. Nevertheless, Mr. Kelber did not disclose any of the documents concerning the SLS-K-7-68 microorganism strain to the PTO. FF E 59, 73-77.

Whether he acquired the information about the SLS-K-7-68 strain in 1993 as he testified in his deposition, or in 1994 as he testified at trial, Mr. Kelber did not tell the PTO that the SLS-K-7-68 strain was used in the work reported in the specification, including Example 3. FF E 69. He was well aware of the superior qualities attributed by Kaken to the secret SLS-K-7-68 microorganism strain, whether or not he believed it to be a mutant. He knew that the Examples were not carried out using the 80614 strain as deposited and which he identified to the Patent Examiner as having been used in connection with the Examples.

Therefore, based upon the entire record in this investigation, there is clear and convincing evidence that Kaken and Kaken's patent attorney knowingly

withheld material information from the PTO and made material misrepresentations to the PTO during the prosecution of the '698 reissue patent, and thus the patent is unenforceable.

C. Material Prior Art Was Purposefully Withheld From The Prosecution Of The '698 Reissue Patent

During the prosecution of the European counterpart patent application, the European Patent Office cited a reference labeled "NL-A-75 08629," corresponding to U.S. Patent No. 3,992,263 to Dietrich et al. (RX 115) ("the Dietrich patent") in a search report issued in 1978. FF E 163. The search report listed the Dietrich patent as falling within category "Y" meaning that it was "particularly relevant." FF E 165.

The Dietrich patent discloses the use of a Streptomyces and up to 16% oil as a carbon source and an ammonium salt in the fermentation of the antibiotic moenomycin. The use of 16% oil is within the range of fatty acid precursor claimed by the '698 reissue patent, which also claims the use of an ammonium salt. FF E 164, 242. The most significant difference between the claimed invention and the Dietrich patent is that the Dietrich patent does not seek to obtain salinomycin. However, Mr. Kelber's own search for prior art encompasses non-polyether antibiotics, such as moenomycin. The European Patent Office found the Dietrich patent particularly relevant to fermentation for salinomycin in the counterpart application.[44] Furthermore, there was a period when both Kaken and Mr. Kelber believed the Dietrich patent worthy of

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[44] Since at least 1982, it has been the general practice of Mr. Shimada's T.S. International to send immediately to Kaken's United States patent attorneys, the Oblon firm, prior art cited by the European Patent Office in foreign counterparts to the United States patent applications because of the duty of disclosure in the PTO. FF E 172 . It is also the policy of the Oblon firm that relevant prior art includes prior art cited in foreign search reports, such as the European Patent Office search report. FF E 180.

submission to the PTO in connection with the '698 reissue prosecution.[45] FF E 174, 177, 187-188. The Dietrich patent was material to the prosecution of the '698 reissue patent, and both Kaken and its patent counsel in the United States knew of that materiality.

In addition, the U.S. Patent Examiner provided a Statement of Reasons for Allowance as follows:

> The following is an Examiner's Statement of Reasons for Allowance: the amended claims narrow the scope of the invention to recite a method wherein the fermentation medium contains 12-25% fatty acid or its precursor. The limitation of 12-25% fatty acid or its precursor limits the claim so that the art neither anticipates nor makes obvious the claimed invention, because the art of record teaches similar processes using substantially less fatty acid and fails to provide any reasons or motivation to increase the concentration of the fatty acid in the fermentation medium.

FF E 239.

Although the materiality is not determined by a strict "but for" standard, Merck & Co., Inc. v. Danbury Pharmacal, Inc., 873 F.2d 1418, 1421 (Fed. Cir. 1989), the Dietrich patent might well have provided the precise motivation to increase the concentration of the fatty acid, or its precursor, in the fermentation medium which the Patent Examiner felt was lacking in the record before the PTO. FF E 240.

Mr. Kudo was the person at Kaken primarily responsible for the prosecution of the original and reissue patents. FF E 162. In late 1991 or early 1992, before the filing of the reissue application for the '698 patent, Mr. Kudo sent the Dietrich patent (as well as other prior art references that Hoechst had provided to Kaken) to T.S. International, which then sent the

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[45] The Administrative Law Judge does not find that the Dietrich patent renders the '698 reissue patent invalid. However, materiality does not depend on whether the claimed subject matter is patentable over the withheld prior art. Driscoll v. Ceballo, 731 F.2d 878, 884 (Fed. Cir. 1984).

prior art references to the Oblon firm for citation to the PTO. FF E 173. Therefore, by late 1991 or early 1992, the Dietrich patent and the other references were provided to the Oblon firm, and Mr. Kudo expected the Oblon firm to cite those references to the PTO when the reissue application was filed. FF E 174. In addition, Mr. Kelber at the Oblon firm was aware in early 1992 of a letter from Mr. Shibuya to Mr. Shimada that referred both to meetings between Kaken and Hoechst and certain prior art, including the Dietrich patent, that had been provided by Hoechst to Kaken. FF E 175. Thus, by January 1992, roughly a year before he filed the reissue application, Mr. Kelber already had the Dietrich patent. FF E 176.

Mr. Kelber alleged that the Dietrich patent was not filed with the reissue application because of an accident in file construction that occurred at his offices. FF E 244. Mr. Kelber admitted that were it not for the accident in file construction at the Oblon firm, he would have submitted the Dietrich patent when he originally filed the reissue application in January 1993. FF E 245.

The evidence shows that this oversight, if that is what it was, was never corrected. In fact, as discussed in more detail below, when Kaken and its patent attorney were faced with the decision whether or not to make the effort to disclose the Dietrich patent and other prior art for purposes of the reissue prosecution, they decided upon a course of action in which they physically sent the documents to the PTO yet knew that the documents would not be considered by the Patent Examiner during the reissue prosecution.

The nondisclosure of the Dietrich patent cannot be ascribed in its entirety to a clerical mistake; nor was the Dietrich patent the only material

prior art in the possession of Kaken and its counsel which was withheld from the PTO.

At Mr. Kudo's instructions, another reference forwarded to the Oblon firm in a February 28, 1994 letter from T.S. International for submission to the PTO was D. Boeck et al., "Narasin, A New Polyether Antibiotic: Discovery and Fermentation Studies," 18 Developments In Industrial Microbiology, 471-485 (1976) ("the Boeck article"). FF E 206. The Boeck article reports on 4-methylsalinomycin (also known as narasin), which is within the term "salinomycins" used in the claims of the '698 reissue patent. FF E 207. As of February 28, 1994, Kaken wanted to submit the Boeck article to the PTO in a manner so that the Examiner would substantively consider that reference. FF E 208.

Although, the Boeck article does not teach the use of large amounts of oil, FF F 28, it is especially material in view of Kaken's decision to submit the Inaba Declaration to show that salinomycins-producing microorganisms do not give high yields with even small amounts of oil, such as that taught in the prior art Berg reference. Mr. Inaba intended his testing using 0.5 percent soybean oil as the sole carbon source in Report 1 of the Inaba Declaration to be representative of Example 21 of the Berg patent, or at least the amount of oil used in Berg. The Berg patent, like the Boeck article, discloses production of 4-methylsalinomycin. FF E 214 . However, Example 21 of the Berg patent contained approximately 10% of a carbon source in the fermentation medium; specifically, 8% dextrin, 1.5% blackstrap molasses, and .46% soybean oil. FF E 215. The use of 0.5% of soybean oil is far too small an amount as a sole carbon source to permit a significant amount of antibiotic production. FF E 216. As admitted by Mr. Inaba, because the carbon source is

analogous to food for the microorganism, the test said to be representative of the Berg patent effectively starved the microorganism, resulting in low antibiotic yields. Mr. Inaba failed to tell the U.S. Patent Examiner that the microorganism was starved. FF E 217. The Boeck article teaches that omitting carbohydrates from a fermentation medium containing 2% oil results in a reduced yield of 4-methylsalinomycin. FF E 218. The Examiner was neither apprised by Kaken that in the test run alleged to be representative of Example 21 of the Berg patent, the microorganism was starved. Nor was the examiner provided with the Boeck article (as a result of its untimely submission by Kaken) when he evaluated Kaken's alleged "unexpected" results in the Inaba Declaration.

The Boeck article also should have been submitted to the Patent Examiner to be considered during prosecution of the '698 reissue patent because of what it teaches about the kinds of oils to be used with a salinomycins-producing microorganism. Numerous fatty acids and fatty acid precursors are described in the specification as within the scope of the '698 patent claims. However, Kaken witnesses admitted at the hearing that some of them do not produce good yields of salinomycin. FF E 220-221. Moreover, the Boeck article teaches that many of them actually inhibit the production of 4-methylsalinomycin. FF E 222.

For testing in his declaration, Mr. Inaba was instructed, in effect, to use only high-yielding oils. FF 225. If other fatty acids or fatty acid precursors had been used in the Inaba Declaration, the testing which was supposed to be representative of the claimed invention, far lower antibiotic yields would have resulted. FF 227. Given the Boeck article, such a result would have been expected.

If the Examiner had the Boeck article, it would have been clear that some of the fatty acids and fatty acid precursors listed by Kaken in the specification were inoperative for the purposes of the claimed invention. It also would have shown that the testing data supplied in connection with the Inaba Declaration would not be universal with respect to all fatty acids or fatty acid precursors, and thus would raise problems with the claim language.

The Oblon firm did not cite the Dietrich patent or the Boeck article to the PTO when the reissue application and first Information Disclosure Statement were filed. FF E 181, 228.

Mr. Kudo did not realize that the Oblon firm had not cited the Dietrich patent and other prior art to the PTO until after a January 12, 1994 Notice of Allowance of the reissue application. FF E 183. After issuance of the January 12, 1994 Notice and at Mr. Kudo's instructions, T.S. International sent a letter to the Oblon firm, dated February 28, 1994, that instructed the Oblon firm to submit additional prior art references to the PTO either by filing a file wrapper continuation application or by requesting reexamination after permitting the reissue application to issue as a reissue patent. FF E 184.

Thus, as of February 28, 1994, Kaken wanted to submit a number of prior art references, including the Dietrich patent, to the PTO in a manner so that the Examiner would consider the references. FF E 185. Kaken initially contemplated that the PTO would substantively consider these references, and Kaken's attorneys provided advice as to the best way to achieve such review. FF E 186. Mr. Shimada also desired to have the references in his February 28, 1994 letter put before the PTO so they could be substantively considered. FF E 187.

In his March 4, 1994 letter, sent to Mr. Shimada for transmittal to Kaken, Mr. Kelber recommended procedures for submitting the prior art that would have ensured its substantive review by the PTO. FF E 188.

The first option mentioned in the letter was to let the reissue application issue and then file for a reexamination proceeding to put the art before the PTO. FF E 190. However, Kaken never filed for reexamination. FF E 191. The second option described in Mr. Kelber's letter was not to let the reissue application issue. Instead Kaken could file a file wrapper continuation application so the PTO would have time to consider substantively the prior art. FF E 192. The third option was, while the reissue application was pending, to fail to submit a supplemental declaration which had been required by the U.S. Patent Examiner, which would cause him to issue a rejection and the art could then be placed before the Examiner. FF E 193. All of the options described by Mr. Kelber in his letter of March 4, 1994 to Mr. Shimada regarding submission of the prior art to the PTO would have resulted in the Examiner substantively considering the prior art. FF E 194. Mr. Kelber's letter to Mr. Shimada recommended pursuing the third option. FF E 195.

On March 8, 1994, Mr. Shimada responded to Mr. Kelber's letter by instructing him to proceed with the third option so that the art could be considered by the PTO. FF E 197. Thus, Kaken initially chose an option, recommended by Mr. Kelber, to have the prior art references substantively considered by letting the Examiner issue a rejection. FF E 198. By mid-March of 1994, however, Kaken had changed its plan and instead took action to ensure that the reissue patent would be issued as soon as possible. FF E 199.

In early March 1994, Kaken became aware that Hoechst had received FDA approval to sell salinomycin in the United States. This became a matter of urgent concern to Dr. Hori (Director, R & D Agrochemicals and Animal Health of Kaken). FF E 262. March of 1994 was a very sensitive time in Kaken's negotiations concerning a supply agreement with American Home Products ("AHP") because Kaken was committed to an expensive plant expansion and needed a Supply Agreement. FF E 263. AHP contacted Kaken and urged Kaken to take quick legal action against Hoechst. FF E 264.

Mr. Becze, a consultant in the United States for Kaken, sent a facsimile message to Kaken on March 2, 1994, suggesting that a prompt patent infringement action be filed against Hoechst, indicating as follows:

[C]
[C]
[C]
[C]
[C]
[C]

FF E 265-266.

As a result of this letter (RX 736C), Kaken tried to arrange a meeting with its patent attorneys as soon as possible. FF E 267. A meeting on March 15-16, 1994 which was held in the United States resulted from the FDA approval of Hoechst's salinomycin product. Dr. Hori made notes of the March 15, 1994 meeting that form part of RX 893C. The major subject of the meeting on March 15, 1994 was how to proceed with reissue of Kaken's patent. FF E 268-270. There was a discussion of how long it would take to obtain a reissued patent if the existing application were refiled. Refiling was decided to involve too long a time period, because Kaken needed to have a reissued patent as soon as possible to sue Hoechst. FF E 271.

Kaken's attorneys at the March 15, 1994 meeting told Kaken it was not a good idea to send a warning letter to Hoechst at that time because the '942 patent was invalid and the reissue patent application had not yet issued. FF E 272. Kaken was also told that it was in a position of obtaining a reissue patent in one week if Kaken didn't worry about the prior art references. FF E 275.

At the March 15, 1994 meeting, the statement "it is only inequitable conduct" was discussed in connection with the idea of submitting the prior art to the Patent Examiner in a way that the Examiner would not actually review it. FF E 295. Dr. Hcri understood from the March 15, 1994 meeting that there was "essentially no risk" in submitting the prior art to the U.S. PTO in a manner such that the Examiner would not review it. He understood from the March 15, 1994 discussion that 90% of U.S. litigation gets settled, and that Mr. Oblon's policy is to settle litigation. FF E 296-297.

The desire of obtaining quick allowance to sue Hoechst was discussed at the March 16, 1994 meeting.[46] Specifically, Mr. Corcoran expressed the interest of AHP, the licensee at the time, in obtaining quick issuance. Mr. James Heinle from Hoffmann LaRoche made a presentation at the end of the meeting regarding their desire to obtain quick issuance of the patent. FF E 276.

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[46] On March 16, 1995, the meeting was attended by Mr. Eguchi (Executive Managing Director of Kaken), Dr. Hori, Mr. Ikemoto (General Manager, Patent Division of Kaken), Mr. Kudo (Staff Patent Attorney of Kaken), Mr. Kelber, Mr. Becze (President, Princeton Regulatory Associates, Consultant to Kaken) who sent Kaken the facsimile of March 2, 1994, Mr. Corcoran (Vice President, Specialty Pharmaceuticals of American Home Products Corporation), Mr. Alice (Corporate Licensing Counsel of American Home Products Corporation), an interpreter, and Mr. James Heinle (Hoffmann LaRoche). FF E 269.

Mr. Kelber's recommendations in his March 4, 1994 letter concerning the submission of the prior art changed when Kaken informed him at the meetings of the need to secure prompt issuance of the reissue patent. FF E 277. Kaken wanted the reissue patent to issue quickly so it could bring an action. The decision in March 1994 to submit the prior art in a manner in which it would not be considered by the U.S. Patent Examiner was ultimately made by Kaken at a board meeting attended by Mr. Kudo. FF E 280-281.

In Mr. Shimada's letter of March 17, 1994 to Mr. Kelber, he instructed Mr. Kelber to change plans and file the supplemental declaration so that the patent could issue as soon as possible. FF E 282.

Kaken, through Mr. Kelber, then submitted the prior art references with the Supplemental Reissue Declaration in an attempt to limit the impact of charges of inequitable conduct that Kaken expected to be leveled by Hoechst. FF E 285. Mr. Kelber also submitted a declaration to the PTO to secure expeditious issuance of the case. FF E 284. However, Mr. Kelber knew that two of the references submitted in the Information Disclosure Statement were cited as "particularly relevant" in a search report issued by the European Patent Office in 1978 in a European application that corresponded to the '698 reissue patent, including the Dietrich patent. FF E 286.

In the March 18, 1994, Statement of Relevancy filed with the untimely submitted prior art after the Notice of Allowance, Kaken represented to the PTO that the references were not material, but that they were being submitted "in the interest of completeness." Yet, in Mr. Kelber's letter of March 17, 1994, to Mr. Shimada, Mr. Kelber indicated that the art discussed in the meeting on March 16 was being submitted "only to diffuse any possible charge of inequitable conduct that might arise." FF E 292.

The Statement of Relevancy indicates that the references cited in the Information Disclosure Statement have been provided by a number of sources, primarily third parties. The Statement of Relevancy did not, however, indicate that, in fact, the third parties thought the references invalidated the '698 reissue patent. FF E 293.

When Mr. Kelber submitted the prior art references to the PTO, he and Kaken had "the foreknowledge that they . . . [would] not be considered in the ordinary course of events." FF E 289. Kaken chose to follow a procedure that Kaken and its attorneys knew would result in the PTO refusing to consider the prior art Kaken had not yet cited. Eleven prior art references were submitted as part of the Information Disclosure Statement filed on March 18, 1993. The Patent Examiner, as expected, refused to consider these prior art references because the Information Disclosure Statement failed to comply with the rules set forth in 37 C.F.R. § 1.97. FF E 291.

The evidence adduced in this investigation clearly and convincingly demonstrates that Kaken and its counsel decided not to submit prior art references, including the Dietrich patent and the Boeck article which they had previously intended to submit, because they wanted an expedited issuance of the patent-in-suit. There is no credible evidence that only in the eleventh hour did Kaken and its counsel change their beliefs and determine that the references were all non-material to the patent prosecution. Their attempt to minimize charges of inequitable conduct by physically sending the references to the Examiner yet not disclosing them in a way which would allow the Examiner to consider them during the patent prosecution compounds the evidence that Kaken and its counsel knew that nondisclosure of the prior art was wrong.

The Administrative Law Judge finds by clear and convincing evidence that the '698 reissue patent is unenforceable due to inequitable conduct committed by the withholding of information material to its prosecution at the PTO.

D. The Totality Of Circumstances Demonstrates A Lack Of Respect For The Duty Of Candor Owed The PTO

In this case the totality of the evidence shows clearly and convincingly intentional acts of inequitable conduct. Furthermore, there is a lack of any credible evidence of good faith. In fact, there is strong evidence of other factors that motivated those concerned with the patent prosecutions to withhold or misrepresent material information.

There is evidence which puts the concealment of the SLS-K-7-68 strain into context. The evidence shows that strains such as the SLS-K-7-68 strain have great commercial value, and that concealing the SLS-K-7-68 strain would be economically advantageous to a company such as Kaken. FF E 1-6. Thus, Kaken did not generally disclose such strains, and that policy may have provided a motivation for the acts of inequitable conduct proven in this investigation. Furthermore, Kaken used its best strains and best oil to produce high yields, but did not reveal that the strains used were not available to the public. FF E 37-38, 144, 225.

Additionally, at the time of the reissue prosecution in 1994, Kaken wanted to get its reissue patent as quickly as possible in order to file a complaint with the Commission against the companies which comprise the Hoechst Respondents in this investigation with the goal of preventing them from entering the United States market[47] with salinomycin and its preparations. In

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[47] The term "market" as used here refers to sales of anticoccidials, including those containing salinomycin. As used in this sense, the term does not necessarily denote a relevant market as defined for a patent misuse analysis.

1994, after it was decided to file a complaint at the Commission against the Hoechst Respondents to prevent them from entering the United States market, a "countermeasures" project team was formed at Kaken for the sole purpose of winning this case. Members of the team included Mr. Inaba, Dr. Hori, Mr. Kudo, a Mr. Nakamura, and others at Kaken. FF E 259.

Kaken's desire to initiate this case as quickly as possible and to win it undoubtedly fueled Kaken's actions which show a lack of respect for the duty of candor and of the obligation of disclosure owed to the PTO during the ex parte reissue prosecution.

Kaken's disregard of PTO procedures was evidenced at the outset by the Reissue Declaration that formally began the entire process at the PTO. Mr. Wakiyama, the president of Kaken, signed the English language declaration found in the prosecution history of the reissue patent. Mr. Wakiyama does not read or understand the English language and no one read him his declaration in Japanese before he signed it. Before executing his declaration, Mr. Wakiyama did not read it. FF E 258. Thus, he signed his declaration without genuinely attesting to its accuracy and in contravention of the PTO's rules which require one to sign a declaration in one's own language with an English translation. See 37 C.F.R. § 1.69 (1994) (RX 743); Witherspoon, Tr. 1827-1832. There is no evidence that Mr. Wakiyama asked about what he was signing, and no evidence that anyone explained the details of the declaration to him. The PTO rules notwithstanding, that is not a forthright and appropriate procedure for the signing of any legal document to be submitted to the United States government, and one does not have to be a patent lawyer to understand this.

In addition, during the reissue prosecution, Kaken did not follow proper procedure in its submission of test data, and more importantly simply failed to tell the Examiner facts that were clearly material to the tests. In contrasting the claimed invention with the amount of oil used in the Berg reference, Kaken removed additional carbon or food sources from the medium with the small amount of oil used by Berg. Thus, Kaken essentially starved the microorganism and thus was assured the test example representing the prior art would not produce good yields of salinomycin. There may be nothing wrong in showing the Patent Examiner that a small amount of oil such as the small amount used in Berg will not, in and of itself, be sufficient to produce a high yield of salinomycin. However, that is not what Kaken did. Kaken explained what it was doing in terms of replicating the Berg patent. The Inaba Declaration states in part, as follows:

> In each of the tests 1-4, substantial improvements in yield are obtained where the fatty acid or its precursor content in the medium is at least 12%, as contrasted with prior art process of U.S. Patent 4,035,481 [to Berg et al.], using less than 1% fatty acid or its precursor. Thus, independent of microorganism strain, the source of fatty acid or its precursor, ammonium substance employed, culturing Streptomyces microorganisms capable of producing salinomycin in a medium containing at least 12% fatty acid or its precursor gives rise to startling and unobvious improvements in yield of the salinomycin obtained. This advantage is of extreme importance in making available, on a commercial scale.

Declaration of Inaba at 3, RX 901 at 28 (emphasis added).

Kaken's statements were a misrepresentation of what the experiments accomplished. The fact that the Examiner might have read the tests in adequate detail and compared them to the Berg patent to realize what had truly happened does not change the fact that Kaken presented the data in a misleading way.

Furthermore, Kaken added an ingredient in the testing which it regards as a trade secret, cobalt sulfate, to the fermentation media without telling the Examiner that it had done so or even listing the ingredient in the testing data so that the Examiner had any chance of discovering its use. FF E 149-150.

Kaken maintains that the [C] was added merely to compensate for the fact that it is missing in the water of the location in which the experiments were performed. However, [C] also has an active effect which stimulates the production of salinomycin in the microorganism used in the experiments. In fact, the evidence shows that because the starved microorganism in Kaken's experiment was not producing salinomycin at a high level, the [C] benefitted only the other culture with adequate oil and therefore exaggerated the difference between the cultures. FF E 151-152.

Regardless of the effect of the cobalt, the Examiner should have been told about its use and have been the one to determine its effects. Although it is not clear that Kaken withheld the information about the cobalt sulfate to deceive the Examiner, Kaken's behavior shows a disregard for the duties it owed the PTO during the ex parte prosecution of the '698 reissue patent.

It is against the backdrop of a general disregard for the need to be forthcoming with the Patent Examiner that the specific acts of inequitable conduct occurred.

E. Conclusion

Based upon strong evidence of specific acts of concealment and deception by the applicants, assignee Kaken and their patent attorney in connection with the '942 original and '698 reissue patents, the Administrative Law Judge finds

by clear and convincing evidence that the '698 reissue patent is unenforceable due to inequitable conduct before the PTO.

VI. CLAIM 2 OF THE '698 REISSUE PATENT IS NOT OBVIOUS

A. Background And Law Generally Applicable To The Issue Of Obviousness

Respondents argue that all claims of the '698 reissue patent, including claim 2 asserted against them in this investigation, are invalid for obviousness.

Complainant Kaken and OUII take the position that claim 2 of the '698 reissue patent is not obvious.

Section 103 of the Patent Act provides in pertinent part as follows:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 103 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains.

35 U.S.C. § 103. Thus, the claims of a patent are invalid if the differences between them and the pertinent prior art would have been obvious to one of ordinary skill in that art.[48] Graham v. John Deere Co., 383 U.S. 1, 37 (1966).

However, a patent is presumed to be valid, pursuant to 35 U.S.C. § 282, and the presumption of validity can be overcome only by clear and convincing evidence. Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861, 872 (Fed. Cir. 1985).

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[48] The Federal Circuit has held that "[t]he person of ordinary skill is a hypothetical person who is presumed to be aware of all pertinent prior art." Custom Accessories, Inc. v. Jeffery-Allan Indus., Inc., 807 F.2d 955, 962 (Fed. Cir. 1986).

The Federal Circuit has held that although an Examiner's decision on an original or reissue application is never binding on a court, it is evidence that the court must consider in determining whether the party asserting invalidity has met its statutory burden by clear and convincing evidence. Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1555 (Fed. Cir. 1985)(citing American Hoist and Derrick Co. v. Sowa and Sons, Inc., 725 F.2d 1350, 1359-60 (Fed. Cir.), cert. denied, 469 U.S. 821 (1984)). However, when an attacker produces prior art or other evidence not considered by the Examiner, there is no reason to defer to the Examiner so far as the effect of the new evidence is concerned. American Hoist and Derrick Co., 725 F.2d at 1359. Accord Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1139 (Fed. Cir. 1985).

Although the ultimate question on the issue of patent validity is one of law, a determination on the question of obviousness requires several factual determinations. Graham, 383 U.S. at 17. The Supreme Court held that:

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquires may have relevancy.

Id.

When prior art references require selective combination to render an invention obvious, the combination must not be based on the hindsight gained from the invention itself. Instead, "[s]omething in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination." Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F.2d 1044, 1050 (Fed.

Cir.), cert. denied, 488 U.S. 825 (1988). Prior art references need not explicitly suggest combining teachings. The knowledge generally available to one of ordinary skill in the art may lead one to combine the relevant teachings. In re Nilssen, 851 F.2d 1401, 1403-04 (Fed. Cir. 1988). "Obviousness does not require absolute predictability of success." In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988). Rather, "all that is required is a reasonable expectation of success." Id. at 904.

B. Level Of Ordinary Skill In The Art

A person of ordinary skill in the art as of 1977 would have had a Bachelor's Degree and at least two years of experience in antibiotic fermentation and biosynthesis. One would nevertheless have ordinary skill in the art if one had more experience to compensate for a lack of formal education, or vice versa. FF F 1.

C. Scope And Content Of The Prior Art; Differences Between The Prior Art And The Claimed Invention

The Federal Circuit has set forth the following general test to determine whether the subject matter of a reference should be considered prior art to the claimed invention:

> First, we decide if the reference is within the field of the inventor's endeavor. If it is not, we proceed to determine whether the reference is reasonably pertinent to the particular problem with which the inventor was involved.

In re Deminski, 796 F.2d 436, 442 (Fed. Cir. 1986). See also Orthopedic Equip. Co., Inc. v. United States, 702 F.2d 1005, 1009 (Fed. Cir. 1983)("In determining the relevant prior art of the claims in suit one looks to the nature of the problem confronting the inventor.")

The inventors named in the '698 reissue patent endeavored to improve a method of producing polyether-type antibiotics on an industrial scale by

culturing a Streptomyces microorganism. In particular, the inventors were concerned with obtaining salinomycin by culturing a Streptomyces albus. RX 5, '698 Reissue Patent at col. 1, lines 1-65; FF D 16, F 83, 93. Respondents rely on several pieces of art which they allege show, either alone or in combination, that the '698 reissue patent is invalid for obviousness. Each of these is within the field of endeavor of the inventors or is reasonably pertinent to the problem facing the inventors. Some references, such as those dealing specifically with the culturing of salinomycins-producing microorganisms or microorganisms which produce other polyether antibiotics, are clearly of help to one of ordinary skill in the art, faced with the same problem as the inventors. FF F 2-3. There are many species of Streptomyces. The various species differ in their preferred carbon sources for production of their secondary metabolites (including salinomycins). Therefore, one can obtain only a limited amount of guidance by comparing the results obtained with various Streptomyces. FF F 6.

Each piece of art relied on by Respondents has some relevance to the fermentation of antibiotics and would be considered by the hypothetical person of ordinary skill who has knowledge of all relevant prior art. One of ordinary skill in the art would not look only to polyether antibiotics when reading prior art to solve the problem faced by the inventors of the '698 reissue patent. One would need a broad perspective based on more than polyether references. FF F 7.

After identifying the scope and content of the prior art, as required under Graham, 383 U.S. at 37, the differences between the prior art and the claim at issue must be determined. The focus should be on the differences

between the hypothetical combinations of prior art and the claimed invention as a whole. In re Kaslow, 707 F.2d 1366, 1374 (Fed. Cir. 1983).

Respondents argue that Kaken has never properly rebutted the prima facie case of obviousness created by U.S. Letters Patent 4,035,481 to Berg et al. ("the Berg patent" or "Berg"), which caused Kaken to file for a reissue of its original patent and which was before the Patent Examiner during the reissue prosecution. There is no dispute that the Berg patent is relevant prior art to the '698 reissue patent.

The Berg patent teaches the use of a small amount of oil, such as soybean oil, along with other carbon sources, to culture a Streptomyces microorganism that produces polyether antibiotics, specifically 4-methyl salinomycin which is also called narasin. FF F 9-11. In Example 21, Berg teaches the use of 9.96% carbon sources, specifically: tapioca dextrin (tapioca starch) at 8.0%, black strap molasses at 1.5%, and a fatty acid precursor (refined soybean oil) in the amount of 0.46%. FF F 15. Furthermore, Berg teaches the use of ammonia or an ammonium salt. FF F 13.

However, Berg does not teach the use of amounts of oil in anywhere near the amounts taught by the claimed invention. Nor does Berg teach the use of oil as the main carbon source for the salinomycins-producing Streptomyces microorganism. Berg teaches only that a small amount of oil, while not essential, can enhance production. FF F 16.

As discussed elsewhere in this Initial Determination on the issue of inequitable conduct, during the reissue prosecution when Kaken addressed the Berg patent before the PTO, Kaken did not accurately represent to the Patent Examiner the background of its testing based on Berg Example 21. However, Kaken's failure to present Berg accurately to the Examiner does not alter the

fact that while Berg's teachings about oil are positive, they are nonetheless circumspect in that they only cover small amounts of oil and use oil to enhance the production of antibiotics rather than to feed the microorganism largely or entirely on fatty acid or fatty acid precursor.

Respondents argue that additional art (or combinations thereof) never considered by the Patent Examiner make obvious to a person of ordinary skill in the art the use of high concentrations of oil to enhance salinomycin yields. Respondents' Post-Hearing Br. at 35. The additional art relied on by Respondents is identified and discussed below.

• An article by Boeck et al., Narasin, A New Polyether Antibiotic: Discovery and Fermentation Studies, in Developments in Industrial Microbiology, 471-485 (1977), ("the Boeck article" or "Boeck"), also reports on narasin. It contains teachings that indicate against the use of large amounts of oil.

Boeck teaches that when using 2 percent oil, there is a reduced yield of antibiotic as compared to the use of starch. The teachings of Boeck may indicate to one of ordinary skill in the art that the use of oil, for example in the amount of six percent, would inhibit the culture, although this is qualified in that Boeck indicates that there simply was not enough carbon source for the microorganism. Based on the results reported in Table 6 of the article, one would conclude that for the production of narasin, oil is certainly poor as a carbon source in comparison to carbohydrates. FF F 24-25.

The Boeck article shows in Table 7 that while small additions in the amount of fatty acid precursor (soybean oil), of the magnitude taught in Berg, give mild increases in antibiotic titer, increases of as much as 2 percent do

not substantially improve antibiotic titer. FF F 27. In at least half of the cases investigated by Boeck, the addition of as much as two percent soybean oil resulted in a decrease in antibiotic titer. FF F 29. Boeck's reports of reduced titer with the use of oils can fairly be said to teach away from the claimed invention of the '698 reissue patent. FF F 24, 29.

The Boeck article is at best inconclusive as to what would happen if one relied on a higher percentage of oil as a carbon source for a microorganism which produced a polyether antibiotic. FF F 24.

• U.S. Patent 3,992,263 to Dietrich et al. ("the Dietrich patent" or "Dietrich") discloses the use of fats, including oil, in concentrations of from 0.1% up to 16% as a carbon source, and an ammonium salt, in the fermentation of Streptomyces which produce the antibiotic moenomycin. FF F 32. Although Dietrich involves a Streptomyces, moenomycin is not similar in chemical structure to salinomycin. FF F 36-37. Furthermore, Dietrich contains teachings which would also discourage one from using high amounts of oil to obtain an increase in antibiotic titer. FF F 33-35.

Although the Dietrich patent mentions a large range of fat, it also gives a preferable range of two to five percent for increased antibiotic titer. Thus, if one wanted to draw any conclusions about the production of salinomycin from the Dietrich patent, the narrow preferred range of between 2-5% would indicate, contrary to the teachings of the '698 reissue patent, that the amount of oil between 5-16% achieves lower performance than the lesser amounts in the range of 2-5%. FF F 35.

• U.S. Patent 3,869,346 to Vezina et al. ("the Vezina patent" or "Vezina") teaches the fermentation of an antimycin-producing Streptomyces, with the use of oil. FF F 40.

The total amount of soybean oil used in the Examples of Vezina was 7.5%. FF F 48. Thus, the amount of oil used in the Vezina patent does not approach 12 percent, the lower end of the range specifically disclosed in the '698 reissue patent. FF F 41, 49. In fact, the Vezina patent states a preferred amount of oil which is substantially below the amount used in the '698 reissue patent, and thus indicates to one of ordinary skill in the art that larger amounts of oil would have a negative effect on fermentation.[49] FF F 41.

• U.S. Patent No. 3,892,850 to Struyk et al. ("the Struyk patent") concerns the fermentation of Streptopimaricin, a polyene, and not related to polyether antibiotics. The Struyk patent does not allow one to draw any conclusions about what to expect when fermenting a salinomycins-producing Streptomyces microorganism in 12-25% oil. FF F 50.

The Struyk patent teaches the possibility of using oils and fats in fermentation in that it refers to small amounts of oil to enhance fermentation run on other carbon sources. However, it does not teach that high levels of oils will be rewarded with high titers of antibiotic. FF F 51.

• U.S. Patent No. 3,989,820 to Florent ("the Florent patent") was not the subject of extensive testimony during the hearing, however Respondents' expert witness relied on it in part. He testified that it taught that one could replace the carbohydrate carbon source with oil as the main carbon source, as well as the use of ammonium salts. FF F 53.

Although the Florent patent concerns an anticoccidial substance, the structure of that substance is undertermined from the patent. FF F 53. The

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[49] Contrary to the position taken by Respondents' expert during the hearing, the Vezina patent does not teach a "linear relationship" between the amount of fatty acid precursor used and the amount of antibiotic obtained. See FF F 42.

Florent patent would therefore be of only very limited use to one of ordinary skill in the art. Furthermore, as discussed below, oil and carbohydrate are not simple substitutes for one another, at least not with respect to salinomycins-producing microorganisms.

• British Patent 1,083,546 ("the '546 patent") discloses the use of a moenomycin-producing Streptomyces. FF F 54. The British '546 patent teaches the doubling in the formation of moenomycin by the use of fats as the sole source of carbon in the range of 0.1 to 10%, preferably 0.5 to 5%. FF F 56. It also teaches the use of ammonia or an ammonium salt. FF F 55.

A person of ordinary skill in the art would know from the preferred low range that the production would be detrimentally affected as the amount of fat increased above 5%. FF F 56. As with the Dietrich patent, there is not an awareness in the British '546 patent of a linear relationship between the addition of oil and antibiotic titer. FF F 57. The British '546 patent does not add to the teaching of Dietrich with respect to the effect that an addition of oil in the 12-25% range might have on the fermentation of a salinomycins-producing microorganism. FF F 58.

• An article by Colin Ratledge, Fermentation Substrates, in 1 Annual Reports on Fermentation Processes, 49 (D. Perlman ed., 1977) ("the Ratledge article"), discusses, among other things, the addition of fats and oils to media containing carbohydrates. FF F 59. However, the Ratledge article does not indicate that an increase in antibiotic titer can be obtained by using 12 percent or more oils (fatty acid precursor) in fermentation. FF F 60.

• British Patent 1,500,965 ("the '965 patent") states on its face that the complete specification was published on February 15, 1978. Thus, it is not in and of itself prior art to the invention of the '698 reissue patent

based upon the patent's foreign priority filing date. FF F 61. Although foreign counterparts were allegedly published before 1977, there does not appear to be evidence of that in the record. Furthermore, the British '965 patent would be of only limited value if it were considered as a prior art reference.

The British '965 patent reports on polyether antibiotics, homologues of Lasalocid A, obtained through the use of a Streptomyces. FF F 62. It does not teach the use of ammonia or an ammonium salt. FF F 65. It teaches the use of carbohydrate such as sugar or molasses, with brown sugar being most preferred, and an addition of an oil such as soybean oil or lard oil as a carbon and surfactant (to control foam) and to improve yields. However, the British '965 patent does not disclose titers resulting from specific oil amounts. FF F 66.

• U.S. Patent No. 4,366,147 to Hamill et al. ("the Hamill patent") reports on a non-polyether, sulphur containing antibiotic, Antibiotic A-7413. The Hamill patent does not disclose the structure of the antibiotic. FF F 67.

The Hamill patent teaches the use of ammonia or an ammonium salt (ammonium sulfate), and that dextrose, glucose, fructose, maltose, sucrose, and the like can be used as carbon sources. It also teaches that, "[a]lthough not essential for growth, an oil such as corn oil improves antibiotic titer. Other useful sources of carbon include peanut oil, soybean oil, fish oil, and the like." FF F 71.

The teachings of the Hamill patent are general in nature, if not vague. Furthermore, without more information about the antibiotic involved, it is difficult to put the teachings of the Hamill patent into context. However, it

is clear that the Hamill patent does not involve the use of a Streptomyces microorganism. FF F 68.

• An article by Stark et al., Monensin, A New Biologically Active Compound, II. Fermentation Studies, in Antimicrobial Agent and Chemotherapy, 353-358 (1967) ("the 1967 Stark article")[50] states that the addition of oils to the fermentation medium "markedly increased" monensin production, with soybean oil being the best tested. Monensin is a polyether antibiotic produced by a Streptomyces microorganism. FF F 72.

The 1967 Stark article states that several factors influencing the biosynthesis of monensin were discovered in the study reported therein. The article listed several factors as "most important," including "strains of the culture," "concentration of selected minerals in the medium," and last on the list, "supplementation of the medium with oils." FF F 72.

The teachings of the 1967 Stark article concerning the use of oils do not include the use of oil in the range of the claimed invention. Furthermore, there was no testimony at the hearing concerning the 1967 Stark article. FF F 72-73.

• Canadian Patent 823,631 ("the '631 patent") concerns kasugamycin, which is an aminoglycoside. The structure of kasugamycin is extremely unlike that of salinomycin. FF F 77.

The Canadian '631 patent teaches the use of small amounts of oil of about 5%. It would not teach one of ordinary skill in the art the use of oil in the

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[50] A 1969 article by Stark, Monensin, A Biologically Active Compound Produced by a Fermentation Process, Fermentation Advances, pp. 517-40, was considered by the Patent Examiner during the reissue prosecution. The article describes a culture medium for monensin production which contains up to 4% of a fatty acid and a fatty acid precursor. FF F 74-75.

12-25% range, especially in connection with a Streptomyces microorganism such as that used in the '698 reissue patent.[51] FF F 78.

D. No Reasonable Expectation Of Success Prior To The Claimed Invention

The question presented is whether the prior art taken as a whole would permit one of ordinary skill in the art to have a reasonable expectation of success. See O'Farrell, 853 F.2d 894 at 903. In this case, success would not necessarily mean that one could obtain the dramatically high titers expressed in the specification of 60,000 μ/ml or 80,000 μ/ml which are cited in the '698 reissue patent specification, e.g., Patent Example 3. It has already been determined in this Initial Determination that those yields require vastly improved microorganism strains, or strains which have been obtained through mutation such as the SLS-K-7-68 strain. In other patent Examples, the yields reported are more modest, but represent genuine improvement. Notwithstanding the role played by improved microorganism strains, such as the withheld SLS-K-7-68 strain, the patent informs the public that high titers can be obtained using an oil medium. FF F 103. For example, while the 80614 strain of Streptomyces albus, as deposited, would not be expected to achieve a yield of 60,000 μ/ml, with present technology one could expect to achieve over 20,000 μ/ml, and higher using this strain, with the use of ammonia or ammonium salt. FF F 104-107.

The prior art would not lead one of ordinary skill in the art to a reasonable expectation that a salinomycins-producing Streptomyces, such as Streptomyces albus, could be successfully cultured with large amounts of oil in the range of 12-25%. In fact, the art directed to polyether antibiotics

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[51] It is not evident that the Canadian '631 patent teaches one of ordinary skill how to achieve high yields of kasugamycin. FF F 79-80.

available as of May 31, 1977, including Berg and Boeck, would lead one of ordinary skill in the art to predict that use of 12-25 percent oil would not be a good concentration to use for the production of salinomycin. FF F 82.

The levels of oil used throughout the prior art tend to be small and do not approach the 12-25% of the invention as claimed, or in the case of the Dietrich patent disclose the use of 16% oil while finding substantially smaller amounts to be preferable. FF F 81, 83. If one tried to make a determination of what would occur if a salinomycins-producing Streptomyces were cultured with the large amount of oil used in the claimed invention, one would learn that none of the prior art relied on in this investigation used high levels with their respective microorganisms, i.e, 12% and above, without showing that those high levels are less useful than lower levels. FF F 83.

For example, one might place special emphasis on the Berg patent because it teaches culturing a type of Streptomyces that produces 4-methyl salinomycin with oil and ammonia or ammonium salt. Certainly Respondents take the position that it makes out a prima facie case of obviousness. Berg caused Kaken to request a reissue patent. Yet even Berg fails to teach the use of a large amount of oil, or to indicate what would happen if a large amount of oil were used. FF F 84.

The lack of teachings about large amounts of oil in the prior art is crucial because of the fact it is not a general principle in the fermentation of antibiotics that if a little oil is good, a lot of oil is going to be better. See FF F 86. As seen in some of the prior art relied on by Respondents and discussed herein, sometimes a preferred range of oil is stated which is lower than the larger amounts of oil which had been tested and reported on in the patent or article. FF F 83, 86. Thus, one of ordinary

skill in the art would see that antibiotic yields do not necessarily increase with increases in the amounts of oil used.

Furthermore, none of the patents or articles uses a Streptomyces albus, i.e., a salinomycins-producing streptomyces of the type disclosed in the patent. This is significant in the relevant art because it is known that if the antibiotic one seeks to obtain differs from the antibiotic in the prior art, or if the microorganism species used to obtain the antibiotic differs from that in the prior art, the prior art may be of limited use. Additionally, various microorganisms react differently to oil as a carbon source with respect to their production of antibiotics. Even different species of Streptomyces react differently in this respect to oil as a carbon source. FF F 87, 90, 93.

Thus, for example, the Dietrich patent is relevant to the inquiry at hand, yet because it seeks to obtain an antibiotic which is quite dissimilar to salinomycin it would be of limited importance to one of ordinary skill in the art. FF F 36, 92. Similarly, the Vezina, Florent and Struyk patents, as well as the Canadian '823 patent are directed to the fermentation of antibiotics unrelated to salinomycin, and use microorganisms different from those that produce salinomycins. FF F 92.

The prior art to the '698 reissue patent also contain certain statements that may direct on of ordinary skill in the art away from using larger quantities of oil in the fermentation process. For example, the Vezina patent, the Florent patent, the Ratledge article, the Dietrich patent, and the Struyk patent indicated that carbohydrates could be substituted for oils, and at least in some cases the teaching was that carbohydrates would perform as a carbon source in a fashion parallel to that of fatty acids and fatty acid

precursors. FF F 94. However, oil and carbohydrate are not interchangeable in the production of salinomycin, at least with respect to the titer obtained. FF F 96.

That fact was also illustrated by tests performed by Respondents. Upon issuance of the '698 reissue patent, Hoechst AG began a series of tests designed to find a non-fatty acid precursor substrate for fermentation of salinomycin. FF F 97. However, Hoechst AG was unable to find any substrate other than a fatty acid or fatty acid precursors suitable for the production of salinomycin through fermentation. FF F 98-99.

In conclusion, the evidence does not show that one of ordinary skill in the art, based on the prior art as a whole, would have a reasonable expectation of successful fermentation of a salinomycins-producing Streptomyces with the use of fatty acid or fatty acid precursor in large amounts such as 12-25%, as claimed in the '698 reissue patent.

E. Objective Indicia Of Nonobviousness

As discussed above, secondary considerations such as commercial success, long felt but unsolved needs, failure of others, etc., may serve as indicia of obviousness or nonobviousness. See Graham, 383 U.S. at 17. Secondary considerations are also referred to as "objective evidence of nonobviousness," and may include other factors such as prior art teaching away. See Perkin-Elmer Corp. v. Computervision corp., 732 F.2d 888, 894 (Fed. Cir. 1984); In re Hedges, 783 F.2d 1038, 1041 (Fed. Cir. 1986). The Federal Circuit has observed that in some cases, objective indicia may constitute the most important evidence available when making the determination as to alleged obviousness. Simmons Fastener Corp v. Illinois Tool Works, Inc., 739 F.2d 1573, 1575 (Fed. Cir. 1984).

In this case, several objective indicia demonstrate the nonobviousness of the claimed invention of the '698 reissue patent.

The claimed invention has enjoyed substantial commercial success. Kaken continues to use the process recited in claim 2 of the '698 reissue patent to prepare salinomycin. FF F 108, H 1. Furthermore, the claimed invention has been the subject of extensive licensing by Kaken. Pfizer International is licensed under the '698 reissue patent from Kaken. FF F 110. Hoechst had a license under the original patent and its foreign counterparts from their issuance until 1992.[52] FF F 111. A.H. Robbins, and the successor-in-interest thereto, American Home Products, also had a license under the '698 reissue patent. FF F 112. Hoffmann-LaRoche took a license under the '698 patent, and continues to pay royalties under its license in addition to payments for product. FF F 113.

In addition, the invention of the '698 reissue patent as first disclosed in the '942 original patent, has had what may be described as a "revolutionary impact" on the field of polyether antibiotic fermentation. As discussed in detail above, the prior art suggested that the use of large amounts of oil in polyether antibiotic fermentations might be harmful to the growth of the microorganism or inhibit high antibiotic titers. However, the '698 reissue patent (or the '942 original patent) is truly a teaching patent for those in the fermentation industry. The disclosure of the invention directed the field to the extensive use of oils in polyether fermentations. FF F 114-115, 117.

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[52] Furthermore, it is found in this Initial Determination that Hoechst AG uses a process which is covered by claim 2 of the '698 patent, and the process would infringe the patent if the best mode requirement were satisfied and the patent were enforceable.

The importance of the invention disclosed in the '698 reissue patent is recognized in the fermentation industry. The teachings of the '698 reissue patent have been widely followed throughout the polyether antibiotics industry and changed the way people develop polyether antibiotic fermentations. FF F 116.

Salinomycin is the leading coccidiostat in the United States, and salinomycin sales account for about 30% to 35% of all domestic coccidiostat sales. FF F 109, G 1. Consequently, there were rewards to be had for an improved process. The objective fact, apart from an analysis of the prior art, is that before the disclosure of the claimed invention, an extensive use of oils had not been made to achieve industrial fermentation of salinomycin. Furthermore, the claimed invention has had a substantial impact on the industrial fermentation of microorganisms which produces salinomycin and other polyether antibiotics.

F. Conclusion On Nonobviousness

Based upon the evidence adduced in this investigation, including evidence concerning the prior art and objective indicia of nonobviousness, the Administrative Law Judge finds that it has not been demonstrated by clear and convincing evidence that the '698 reissue patent is invalid for obviousness.

VII. CLAIM 2 OF THE '698 REISSUE PATENT IS NOT INDEFINITE

Respondents take the position that claim 2 of the '698 reissue patent is invalid for indefiniteness under 35 U.S.C. § 112. Respondents' Post-Hearing Br. at 44-45. Complainant and OUII take the position that the claim is not invalid.

Respondents' position is based on their argument that there are three possible interpretations of the 12-25% oil limitation incorporated into

claim 2 from independent claim 1, and that there is disagreement as to how the oil percentages are to be calculated. In particular, respondents argue that Complainant's "passing through" or "window" theory of the claim would mean that there is no upper limit of the range.

In the sections of this Initial Determination on claim construction and domestic industry, including both the opinion and numbered findings of fact, the Administrative Law Judge has found that there is a clearly preferred reading of the claim to one of ordinary skill in the art with respect to the meaning of the 12-25% range of fatty acid or its precursor (oil), and how the amount of oil is to be calculated. Therefore, the claim is not invalid for indefiniteness. However, the proper construction of the claim is narrower than Complainant's proposed construction, and Complainant's "passing through" theory is rejected.

VIII. RESPONDENTS' MISUSE DEFENSE

Respondents take the position that Kaken used the leverage of its process patent to require licensee A.H. Robins ("Robins") to agree to buy unpatented bulk salinomycin from Kaken. Respondents rely on Zenith Radio Corp. v. Hazeltine Research, Inc., 395 U.S. 100, 136 (1969)(A patentee "may not condition the right to use his patent on the licensee's agreement to purchase. . . another article of commerce not within the scope of his patent monopoly."). Respondents argue that salinomycin is the subject of an expired Kaken patent and thus is not an article of commerce within the scope of Kaken's present patent rights.[53] Respondents' Post-Hearing Br. at 45-46.

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[53] Respondents agrue that to the extent Kaken's acts must be given a rule-of-reason analysis, Kaken unreasonably eliminated Hoechst as a salinomycin supplier to Robins and to Hoffmann-LaRoche ("HLR"), Robins' (continued...)

Complainant and OUII take the position that Kaken has not engaged in patent misuse.

The amendments to the Patent Act made by the Patent Misuse Reform Act of 1988 provide in pertinent part, as follows:

> No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent by reason of his having . . . (4) refused to license or use any rights to the patent; or (5) conditioned the license of any rights to the patent or the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

35 U.S.C. § 271(d) (emphasis added).

Respondents argue that the relevant market in this case is "coccidiostats containing salinomycin sold in the United States." Respondents' Post-Hearing Br. at 46. Their argument as to the relevant market is based on alleged admissions of Complainant. See Respondents' Post-Hearing Br. at 46. In particular, Respondents rely on the statement that "[t]he U.S. market for salinomycin-containing poultry feed premix has historically been met solely by the sale of BIO-COX®." Id. (citing Complainant's Revised Mem. in Support of Complainant's Mot. for Temporary Exclusion Order at 30).

Complainant argues that the statement relied on by Respondents is irrelevant to the misuse issue because in that statement Complainant was merely demonstrating that because Kaken possesses the manufacturing capacity

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[53](...continued)
assignee, and Kaken sought a monopoly position as the sole source of salinomycin because Robins was the only FDA-approved seller of salinomycin premix at the time of the alleged misuse. Respondents' Post-Hearing Br. at 46.

to satisfy existing demand for the foreseeable future, the public interest would not be harmed by entry of a temporary exclusion order. Complainant's Reply Br. at 23.

The Administrative Law Judge does not find that the statements relied on by Respondents can fairly be read as admissions as to the relevant market applicable to a patent misuse analysis. Nor do Complainant's statements provide probative evidence of the relevant market in which to assess alleged market power. Furthermore, there is insufficient evidence in the record to make a relevant market determination.[54]

Since such a finding is a predicate to the patent misuse offense, the Administrative Law Judge does not find that the '698 reissue patent is unenforceable due to patent misuse.

IX. DOMESTIC INDUSTRY

A. Background

Section 337(a)(1)(B), which is asserted against Respondents in this investigation, applies "only if an industry in the United States, relating to the articles protected by the patent. . . exists or is in the process of being established." 19 U.S.C. § 1337(a)(2).

The requisite domestic industry is defined in section 337 as follows:

> (3) For purposes of paragraph (2), an industry in the United States shall be considered to exist if there is in the United States, with respect to the articles protected by the patent . . . --

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[54] Complainant also argues that "the relevant market is the market for coccidiostats generally," in which salinomycin premixes have "only a 30-35% market share." Complainant's Reply Br. at 24. The record evidence is similarly insufficient to determine whether Complainant's asserted relevant market is correct. Furthermore, although it is found that sales of salinomycin account for about 30 to 35 percent of coccidiostat sales in the United States, FF G 1, there is insufficient record evidence to determine whether Kaken and its domestic licensee have the requisite market power.

(A) significant investment in plant and equipment;

(B) significant employment of labor or capital; or

(C) substantial investment in its exploitation, including engineering, research and development, or licensing.

19 U.S.C. § 1337(a)(3).

The domestic industry requirement is satisfied by meeting the criteria of any one of the three factors listed above. Certain Concealed Cabinet Hinges and Mounting Plates, Inv. No. 337-TA-289, Comm'n Op. at 19-20 (1990). Complainant bears the burden of establishing that the domestic industry requirement is satisfied. Id. at 22.

Respondents take the position that no domestic industry exists as required by section 337. Respondents argue that no one practices the claimed method in the United States, and that Complainant Kaken does not practice it in Japan. Respondents argue further that Complainant has not proved that the activities and investments of Complainant's domestic licensee, Hoffman-LaRoche ("HLR"), satisfy the statutory requirements. Respondents' Post-Hearing Br. at 46-47.

Complainant Kaken takes the position that it practices the method of the '698 reissue patent in Japan, and that the activities and investments of HLR in the United States satisfy the requirements of section 337. Complainant's Post-Hearing Br. at 8-9.

The Commission investigative staff also takes the position that there is a domestic industry as required by section 337. OUII Post-Hearing Br. at 45-49.

B. Kaken Practices Claim 2 Of The '698 Reissue Patent In Japan

The record evidence demonstrates that Kaken practices the process of claim 2 of the '698 reissue patent in Japan to obtain salinomycin.

There is no dispute that Kaken obtains its salinomycin through the fermentation of a salinomycins-producing microorganism. Kaken carries out the fermentation with soybean oil in the amount of approximately 24 to 27 percent, depending on the particular fermentation run.[55] Kaken also uses ammonium tartrate (which is an ammonium salt).[56] Kaken then recovers salinomycin from the mycelial mass. FF H 1-2.

The amount of oil used in Kaken's process is either literally within the claimed range of 12-25%, or within the range of equivalents which extends at least through [C] See Infringement Section, supra.

Therefore, Kaken practices claim 2 of the '698 reissue patent in its production of salinomycin.

C. The Activities And Investments Of Kaken's Licensee In The United States

There is no evidence that the method of the '698 reissue patent is practiced in the United States. Complainant Kaken obtains salinomycin through fermentation in Japan. FF H 1. However, Hoffman-LaRoche ("HLR"), a licensee of Kaken in the United States, purchases bulk salinomycin from Kaken, imports and warehouses the salinomycin, blends it, tests it for quality, bags it, ships it, and also invoices and services its customers. FF H 21.

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[55] The calculated percentage of oil based upon Kaken's DMF filed with the federal Food and Drug Administration is 24.8%. FF H 3.

[56] Kaken also uses urea. FF H 1. It is not disputed in this investigation that urea is an equal to ammonia or an ammonium salt.

The product that HLR blends with Kaken's salinomycin is Bio-Cox, an anticoccidial for veterinary use. Under current registrations of the Food and Drug Administration, bulk salinomycin biomass must be formulated into premix forms and the premix then mixed with animal feed before it can be administered, for example, to broiler chickens. FF H 11, 13, 18, 20. The only commercial use for Kaken's salinomycin is in the production of Bio-Cox premix as a veterinary pharmaceutical product. FF H 25.

As is evident from the plain language of the statute, quoted at length above, a domestic industry exists with respect to the "article protected by the patent." 19 U.S.C. § 1337(a)(2). In this case, the article protected by the patent is certainly not the Kaken process. Nor is it the salinomycin biomass obtained directly from the process, which without further processing cannot be sold to end-users or administered as a pharmaceutical product. Rather, the article protected by the patent is the premix, Bio-Cox, which puts Kaken's salinomycin to use as a veterinary pharmaceutical, and which results in sales to end-users. Such a definition of the article protected by the patent is consistent with, among other authorities, the most recent Commission precedent.

Earlier this year in Certain Diltiazem Hydrochloride and Diltiazem Preparations, Inv. No. 337-TA-349 (1995), the Administrative Law Judge ruled that the domestic industry requirement was satisfied in the case of a foreign manufacturer that practiced the claimed process to obtain a bulk product that was then imported into the United States for further processing and sale by a domestic company. The Commission determined not to review the domestic industry portion of the Initial Determination, 60 Fed. Reg. 17366 (1995),

which therefore became the determination of the Commission. See Diltiazem, Initial Determination (unreviewed portion) at 133-145.

In this case, as in Diltiazem, it is not necessary that the claimed process be carried out in the United States, nor is the article protected by the patent merely the immediate result of the claimed process -- i.e., the bulk compound, or in this case, bulk salinomycin. The article of commerce and the article protected by the patent by which the domestic industry is defined is the pharmaceutical product which is sold to end-users.

The determination in Diltiazem followed the plain language of the statute, as well as its legislative history and prior interpretation of the domestic industry requirement.

The 1988 amendments to the statute dealt in part with the definition of domestic industry. With respect to how one might satisfy the domestic industry requirement under the factors enumerated in section 337(a)(3), quoted above, the legislative history states in part, as follows:

> The first two factors in this definition have been relied on in some Commission decisions finding that an industry does exist in the United States. The third factor, however, goes beyond ITC's recent decisions in this area. This definition does not require actual production of the article in the United States if it can be demonstrated that significant investment and activities of the type enumerated are taking place in the United States.

H.R. Rep. 40, 100th Cong., 1st Sess. 157 (1987); S. Rep. No. 71, 100th Cong. 1st Sess. 129 (1987)(emphasis added). Therefore, Congress contemplated that the domestic industry requirement could be satisfied by foreign production under the patent at issue if coupled with activities and investments in the United States.[57]

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[57] Furthermore, it is noted that the statute makes no distinction between product and process patents with respect to the domestic industry requirement.

The application of the domestic industry requirement, both before and after the 1988 amendments, supports protection of industries in which the patent is practiced in a foreign country and is further exploited by activities and investments in the United States.

In Schaper Mfg. Co. v. United States Int'l Trade Comm'n, 717 F.2d 1368 (Fed. Cir. 1983), the Federal Circuit found against a domestic industry based on the production of accessories for the article protected by the patent, yet held that "in proper cases 'industry' may encompass more than the manufacturing of the patent item . . . ." 717 F.2d at 1373. The Federal Circuit cited other instances in which activities other than the manufacture of the patented item were sufficient to constitute a domestic industry, i.e.: Certain Cube Puzzles, USITC Pub. 1334 (Jan. 1983), in which a domestic industry was based on quality control, repair and packaging of imported cube puzzles which added half of the puzzles' value; and Certain Airtight Case Iron Stoves, USITC Pub. 1126 (Jan. 1981) and Airless Paint Spray Pumps and Components Thereof, USITC Pub. 1199 (Nov. 1981), "in which substantial domestic repair and installation activities necessarily associated with imported stoves (Stoves), and frequent domestic product servicing under warranties as well as some domestic production (in Spray Pumps), were found by the Commission sufficient to warrant determinations that the 'industry' requirement was met." Schaper, 717 F.2d at 1372-73.

The Commission has consistently held that relief in a patent-based investigation depends on whether a complainant "is exploiting or practicing the patent in controversy." Certain Plastic Encapsulated Circuits, Inv. No. 337-TA-315, Comm'n Op. at 16 (1992). The variety of circumstances in which a domestic industry has been found to exist reflects the fact that the domestic

industry determination is not made by the application of a rigid formula. The determination is made by an examination of the facts in each investigation, the article of commerce, and the realities of the marketplace. Certain Double-Sided Floppy Disk Drives and Components Thereof, Inv. No. 337-TA-214, 227 U.S.P.Q. 982, 989 (United States Int'l Trade Comm'n 1985)(Comm'n Op. on temporary relief).

For example, in Certain Personal Computers and Components Thereof, Inv. No. 337-TA-140, 224 U.S.P.Q. 270, 284 (United States Int'l Trade Comm'n 1984), the patented and copyrighted elements were manufactured overseas yet were essential components of the personal computers assembled in the United States. The Commission found that the article of commerce was the complete personal computer, and thus required the domestic industry to be defined in terms of such computers.[58]

In this case, HLR's processing of bulk salinomycin produced by Kaken under the claimed process makes an article of commerce which can be used as a pharmaceutical product. Therefore, a domestic industry should be defined in terms of HLR's Bio-Cox, which is the HLR product containing Kaken's salinomycin. Furthermore, the evidence shows that HLR's involvement with Kaken's salinomycin satisfies the domestic industry requirement because it constitutes significant investment in plant and equipment, as well as

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[58] In Cabinet Hinges, a Complainant's product was manufactured overseas, and a domestic industry was found to be lacking. It was determined that "[t]he only domestic addition to the completed product is the addition of imported dowels, which is optional and, because the patent covers the completed imported hinge, not the dowel feature, [the addition] does not bear directly on the 'exploitation' of any claim of the . . . patent." Comm'n Op. at 22-23. However, it is significant that in Cabinet Hinges, Complainant's investment in the United States was not totally discounted. Rather, the Commission held that "[b]ecause of its indirect bearing on the patented features . . . we reduce the weight we otherwise would accord complainant's investment in plant and equipment." Id. at 23.

significant employment of labor or capital. HLR also made a substantial investment in research and development aimed at exploiting Bio-Cox and the salinomycin contained in it which it purchases from Kaken.[59]

HLR became involved with Bio-Cox when it acquired AgriBio from American Home Products for approximately [C] in 1994. FF H 16, 26. The production and sale of Bio-Cox was AgriBio's only business prior to its acquisition by HLR. FF H 15. HLR acquired tangible and intangible assets. Tangible assets included plant and equipment and inventories. Intangible assets included trademarks, patents, and licenses. FF H 17.

HLR has facilities in VanBuren, Arkansas and Gainesville, Georgia. HLR assigned a value of [C] as of September 1994 to the equipment located at the VanBuren blending plant and testing equipment at the Gainesville facility. All of this value is attributed to salinomycin. FF H 34-35, 30. HLR assigned a value of [C] as of September 1994 to the intangible assets it had acquired. All of this value is attributed to salinomycin. FF H 28.

Over[C] HLR employees perform activities related to salinomycin. FF H 39. Approximately[C] of these employees are employed in performing production

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[59] Domestic value added denotes the proportion of the total value of a patented article attributable to domestic activities. Cabinet Hinges, Comm'n Op. at 22. A value added analysis is one factor that may establish the significance of investment and employment. Id.; Certain Dynamic Random Access Memories and Products Containing Same, Inv. No. 337-TA-242, Comm'n Op. at 67-68 (1987).

In this investigation, a conservative calculation of the domestic value added is C percent. Such a calculation does not include amortization of intangibles, which were presumably accounted for in the purchase of HLR in 1994, nor does it include profits and royalties. The Commission has in the past declined to include certain elements in considering the domestic industry issue, such as profits and royalties. The Commission may not include profits and royalties for the purposes of a value added analysis. See DRAMS, Comm'n Op. at 68.

and distribution activities. FF H 40. Approximately [C] of these employees are employed in performing quality control and quality assurance activities. FF H 41.

HLR has invested additional resources to assure the success of salinomycin sales in the United States. FF H 44. Numerous HLR employees spend at least part of their time on research and development, and regulatory activities. FF H 42. Furthermore, HLR has made a substantial investment in terms of time, resources and money to develop additional uses for salinomycin in swine and cattle. FF H 45-47, 43.

D. Conclusion On The Domestic Industry Issue

The evidence of record demonstrates that a domestic industry exists which satisfies the requirement of section 337.

FINDINGS OF FACT

I. BACKGROUND

A. The Parties

FF A 1. The Complainant in this investigation is Kaken Pharmaceutical Company, Ltd. ("Complainant" or "Kaken"), a Japanese corporation located in Japan at 2-28-8 Honkomagome, Bunkyo-ku, Tokyo 113, Japan. Rev. Complaint, ¶ 4 at 2.

FF A 2. Kaken makes salinomycin in Japan and sells it to be mixed with inert ingredients for use as a veterinary antibiotic. Hori, Tr. 853, 855-858.

FF A 3. Respondents are three companies from the Hoechst family of companies: Hoechst Aktiengesellschaft ("Hoechst AG"), is located at Bruningstrasse 50, 65929 Frankfurt am Main, Germany; Hoechst Veterinär GmbH, is located at Rheingaustrasse 190, D-65203, Wiesbaden, Germany; and Hoechst-Roussel Agri-Vet Co., is located at Route 202-206, Somerville, NJ 08876-1258, U.S.A. Hoechst AG is the ultimate parent of the other two related companies. Collectively, these three Respondents are referred to as "Respondents" or "Hoechst." Hoechst Resp. to Rev. Complaint, ¶ 10 at 5-6, ¶ 13 at 8 (2/23/95); Hoechst Supp. Response to Commission Investigative Staff's First Set of Interrogatories at 3; Respondents' Notice of Appearance.

FF A 4. Merck and Company, Inc. ("Merck") formerly was a respondent. It has an agricultural chemical blending facility, the Merck Agvet Division facilities, located in St. Louis, Missouri. Merck Resp. to Rev. Complaint, ¶ 15 at 5 (2/23/95); Tr. 7.

FF A 5. Hoechst AG makes salinomycin in Germany, which Hoechst Veterinär GmbH sells in bulk to Hoechst-Roussel Agri-Vet Co., which imports it into the United States. Hoechst Resp. to Rev. Complaint, ¶ 11 at 6 (2/23/95).

FF A 6. Hoechst-Roussel Agri-Vet Co. has entered into a manufacturing agreement with Merck to mix this bulk active ingredient with inert material. Hoechst-Roussel Agri-Vet Co. then sells the mixture to poultry producers under the trademark SACOX. Hoechst Resp. to Rev. Complaint, ¶¶ 10-11 at 6 (2/23/95).

FF A 7. Beginning in 1975, Kaken licensed its trade secrets and patents relating to salinomycin to several companies, giving each company rights to those trade secrets and patents for various regions of the world. RX 853C; RX 266C; RX 503C.

FF A 8. Hoechst AG was Kaken's [C] for many countries in [C] as well as certain other countries [C] RX 853C; Hoechst Resp. to Rev. Complaint, ¶ 11 at 6-7 (2/23/95); Hori, Tr. 868.

FF A 9. A.H. Robins Co., Inc. ("Robins") was Kaken's licensee for the United States as well as certain other countries from 1975 to May 1994. In May 1994, that license was assigned to Hoffmann-LaRoche, Inc. ("Roche"). RX 266C; CX 566C; Heinle, Tr. 1041; Hori, Tr. 858.

FF A 10. Pfizer, Inc. has been Kaken's licensee for certain countries since 1975. RX 503C.

FF A 11. Kaken retained rights under its patents to make, use, and sell salinomycin in Japan and certain other countries. RX 276C, ¶ II.1(b) and Ex. B at 5, 28-29; RX 257C, ¶ 2.2.

B. Technological Background

FF A 12. An antibiotic is a chemical produced by microorganisms for presumed defensive uses or needs by inhibiting growth of, or killing, other microorganisms. RX 468C at 2.

FF A 13. Antibiotic production is not necessary for growth of the microorganism. Hutchinson, Tr. 1444.

FF A 14. Antibiotics are made within a microorganism and normally are eventually secreted into the growth media. RX 468C at 3.

FF A 15. Nutrients provide the building blocks for the chemical structure of an antibiotic as well as a food source for growth of the microorganism. Necessary nutrients for antibiotic production include carbon sources and nitrogen sources. Examples of carbon sources include sugars (such as glucose), starch, fatty acids and fatty acid precursors (such as oils). Examples of nitrogen sources include ammonium salts, proteins, sodium nitrate, and urea. RX 468C at 3.

FF A 16. Salinomycin is a veterinary antibiotic used as a coccidiostat to prevent a poultry disease called coccidiosis. Hori, Tr. 855; Rev. Complaint ¶¶ 7-8 at 3-4, ¶ 13 at 6-7.

FF A 17. Salinomycin is a polyether antibiotic, which is an antibiotic whose chemical structure contains more than one cyclic ring containing at least one oxygen atom. Hutchinson, Tr. 1415-1416, 1567-1568; RX 468C at 3.

FF A 18. A species of bacterial microorganism known as *Streptomyces* produces salinomycin. RX 468C at 3.

FF A 19. Morphology refers to the physical appearance of a microorganism, typically on agar media. Hutchinson, Tr. 1438.

FF A 20. Different strains of *Streptomyces* species have distinguishable characteristics such as color, morphology, nutrient requirements, amount of antibiotic produced, growth characteristics, and stability of antibiotic production, caused by genetic differences between the strains. RX 468C at 3; Hutchinson, Tr. 1435-1437.

FF A 21. Genetic differences are more commonly referred to as mutations. RX 468C at 3.

FF A 22. A mutant is a microorganism strain that has at least one distinguishable, clearly recognizable, and repeatably observable genetic difference from its parent.[1] Hutchinson, Tr. 1414, 1434-1435, 1435, 1436-1437; Demain, Tr. 2096, 2155-2156.

FF A 23. "Repeatedly observable" means more than a single observation that disappears the second time it is examined. Hutchinson, Tr. 1435, 1437; Demain, Tr. 2156.

FF A 24. A mutant strain need not show genes entirely different from those of the parent strain. Hutchinson, Tr. 1437.

FF A 25. A single, distinguishable, repeatable characteristic is enough to conclude that a strain is a mutant of its parent strain. Hutchinson, Tr. 1435-1438; Demain, Tr. 2155-2156.

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[1] Complainant argues that differences in antibiotic production could be "due to differential incorporation of plasmid bodies within the microorganism" which would not cause the microorganism to be classified as a mutant. See, e.g., Complainant's Comments on Respondents' Proposed Findings of Fact at 1. This subject matter was raised by Complainant's expert witness on validity, Dr. Demain, in criticizing the hearing testimony of Respondents' witness, Dr. Hutchinson, because it did not address plasmids. The subject of plasmids was not developed by counsel with Dr. Demain. Dr. Demain did not testify that plasmid differences explain the differences among strains relevant to this investigation. Demain, Tr. 2100-2103. Furthermore, as reflected in the citations contained in this Finding, Dr. Demain agreed with Dr. Hutchinson as to the definition of a mutant.

FF A 26. A mutant can be distinguished on the basis of yield alone as long as it is significantly different and repeatable. Hutchinson, Tr. 1436-1438; Demain, Tr. 2157; Hara, Tr. 268.

FF A 27. A 10% to 15% difference from a preceding value is significant and, as long as it is reproducible, is enough to conclude that a microorganism is a mutant from its parent. Hutchinson, Tr. 1765-1766; Demain, Tr. 2157-2160.

FF A 28. Potency is a term that is used interchangeably with titer and yield. Demain, Tr. 2238.

FF A 29. Mutants can be distinguished on the basis of color alone when grown and evaluated in the same medium. Hutchinson, Tr. 1438; Hara, Tr. 268

FF A 30. Mutants can be distinguished on the basis of pH alone. Hutchinson, Tr. 1438, 1486-1487.

FF A 31. Mutants can be distinguished on the basis of visual appearance alone. Hutchinson, Tr. 1438.

FF A 32. Mutants can be distinguished on the basis of growth in different types of media alone. Hutchinson, Tr. 1438.

FF A 33. Mutants can be distinguished on the basis of growth characteristics alone. Hutchinson, Tr. 1438.

FF A 34. Mutants can be distinguished on the basis of stability alone. Hutchinson, Tr. 1438.

FF A 35. Mutants can be classified on the basis of differences in morphology alone. Hutchinson, Tr. 1438-1439.

FF A 36. A difference between a microorganism and its parent in the rate at which soybean oil is converted to salinomycin is indicative of a mutation. Hara, Tr. 277-278; Demain, Tr. 2157.

FF A 37. An auxotroph is a strain that requires a certain nutrient in order to grow. Hutchinson, Tr. 1443-1444.

FF A 38. A mutagen is a chemical or physical treatment that increases the frequency of mutation. Demain, Tr. 2097; Hutchinson, Tr. 1414-1415.

FF A 39. Mutagenesis is the process by which one applies a mutagen to a microorganism and isolates, as a consequence, mutants. Hutchinson, Tr. 1415.

FF A 40. Mutations can occur naturally in the absence of artificial mutagens. Hutchinson, Tr. 1442-1443.

FF A 41. A wild-type microorganism strain is the strain as originally isolated from nature. Hutchinson, Tr. 1439.

FF A 42. Mutants are obtained from wild-type strains by either natural processes of mutation or the application of an artificial mutagen to the wild-type strain. Hutchinson, Tr. 1439; RX 468C at 4.

FF A 43. Without the application of a mutagenic technique, a mutation spontaneously or naturally occurs at a very low frequency. Demain, Tr. 2175; Hara, Tr. 281.

FF A 44. Artificial mutagens increase the frequency of mutations as compared to natural mutations by 100 to 10,000 fold. Hutchinson, Tr. 1414-14155, 1443; Demain Tr. 2175.

FF A 45. With respect to microorganisms which produce antibiotics, artificial mutagens include ultraviolet (UV) or higher energy radiation such as gamma or "X" radiation and heavy particle radiation, and about 10-15 various chemical treatments such as N-methyl-N-nitrosoguanidine (NTG), nitrous acid, ethyl methane sulfonate (EMS), methyl methane sulfonate (MMS), hydroxylamine, ethidium bromide, ethylene oxide, mitomycin C, or acridine orange. Hutchinson, Tr. 1414-1415, 1443; RX 468C at 4.

FF A 46. The purpose of using ultraviolet radiation is to increase the probability of getting a mutation. Hara, Tr. 281-282.

FF A 47. The development of microorganism strains that produce higher yields of antibiotics involves the isolation of higher-producing mutants of the microorganism and the development of suitable media for growing the microorganism. Hutchinson, Tr. 1434.

FF A 48. The isolation of mutants and the development of suitable fermentation media are often done at the same time during strain improvement programs. Hutchinson, Tr. 1434.

FF A 49. Natural (or spontaneous) mutant strains are found by a method called monospore isolation which physically identifies and separates individual cells called spores. Hutchinson, Tr. 1439-1440, 1442.

FF A 50. One round of the monospore isolation process begins with the suspension of a sample of the microorganism in liquid, followed by dilution such that when the solution is applied to a solid agar media, each individual spore will be separated from the others so an individual colony of the resulting organism can grow. Individual colonies are then transferred to another stage of agar-based media followed by transfer to a liquid-based media. The colonies are allowed to grow for perhaps 7-10 days. Then, a culture broth or extract is assayed for the desired property, such as antibiotic production. Hutchinson, Tr. 1440; RX 806C; RX 12C; Hara, Tr. 392-397.

FF A 51. Typically in a strain improvement program, in each round of the monospore isolation process, one skilled in the art would evaluate 200 to 500 individual isolates for the desired property. Hutchinson, Tr. 1440-1442; Hara, Tr. 392-394; RX 806C; RX 12C.

FF A 52. Each round of a monospore isolation process is repeated many times during the course of a strain development program. Hutchinson, Tr. 1441; RX 806C.

FF A 53. If a mutant showing an improved desired characteristic is found after a round of monospore isolation, it then serves as a starting point for the next round of the monospore isolation process. Hutchinson, Tr. 1441; RX 806C; Hara, Tr. 395-396.

FF A 54. The monospore isolation technique and the successive generation technique are the same; they would have no different consequence in terms of whether a mutant is produced in a strain improvement program. Hutchinson, Tr. 1470-1472.

FF A 55. Monospore isolation does not guarantee isolation of a high producing strain. RX 806C; RX 32C at 15534; Hara, Tr. 406-409.

FF A 56. When artificial mutation techniques are used, the first step in the search for a higher antibiotic-producing strain is to select the mutagen to be used. Hutchinson, Tr. 1447.

FF A 57. After an artificial mutagen is selected, an optimum dosage for that mutagen and microorganism is determined. Hutchinson, Tr. 1447.

FF A 58. The choice of an appropriate artificial mutagen and dose is essential for successful strain improvement. Hutchinson, Tr. 1447-1449; RX 463 at 157.

FF A 59. Once a particular mutagen and dosage is determined, the bacteria to be tested are subjected to that level of mutagen, and a select number of isolates, usually between 200-500, are tested for yield. Those showing a reproducibly higher and stable yield represent a new strain and are chosen for further study. The process is then continually repeated with the

same culture medium using either natural selection or artificial mutation, constantly looking for strains with increased production. RX 468C at 6-7; RX 806C.

FF A 60. No known selectable or easily identifiable traits are associated with polyether antibiotic production. Hutchinson, Tr. 1445-1446.

FF A 61. It is not possible to direct a mutagen to affect specifically only one property, such as antibiotic production. Hutchinson, Tr. 1447.

FF A 62. The isolation of mutants containing only mutations affecting antibiotic yields in positive ways is problematic because multiple genes are involved in controlling antibiotic yield. Hutchinson, Tr. 1444-1445; RX 462 at 184.

FF A 63. Most mutations which affect antibiotic productivity do so in a negative way. Hutchinson, Tr. 1444-1445; RX 462 at 185.

FF A 64. Mutagens most commonly decrease the level of antibiotic production. Hutchinson, Tr. 1444, 1459.

FF A 65. When increases are seen in antibiotic production following treatment with a mutagen, they are typically small and occur infrequently. Hutchinson, Tr. 1444.

FF A 66. The ability of a microorganism to produce antibiotics is not a permanent property of the microorganism. Hutchinson, Tr. 1444.

FF A 67. The ability of a microorganism to produce secondary products, like antibiotics, is easily lost by mutation. Hutchinson, Tr. 1446; RX 445 at 125.

FF A 68. Both artificial and natural mutations involve purely random changes in the bacterial genome. Hutchinson, Tr. 1448; RX 468C at 4.

FF A 69. The outcome of strain improvement programs is random because the mutagen's effect cannot be guided. Hutchinson, Tr. 1451-1452.

FF A 70. In the mid 1970s, strain improvement programs were not a routine process. Hutchinson, Tr. 1449.

FF A 71. A considerable amount of judgment and skill is necessary in choosing paths to follow in a strain improvement program. Hutchinson, Tr. 1450-1451.

FF A 72. Different teams of investigators would use different combinations and techniques in an attempt to arrive at a desired goal in a strain improvement program. Hutchinson, Tr. 1451.

FF A 73. Strain improvement programs are time consuming, complex, circuitous, and labor-intensive, and the results are very unpredictable. Hutchinson, Tr. 1449-1450; RX 806C.

FF A 74. The amount of time taken for a strain improvement program to be successful is uncertain, and although progress is expected, the rate of progress is not predictable. Demain, Tr. 2183-2184.

FF A 75. Even after years of effort, there is no guarantee that a strain improvement program will result in the discovery of an improved microorganism strain capable of antibiotic production at a commercially acceptable level. Hutchinson, Tr. 1449-1450, 1454.

FF A 76. The ability to reproduce a mutation that results in a specific antibiotic yield is improbable and highly unpredictable. Hutchinson, Tr. 1452.

FF A 77. The process of strain improvement is analogous to the search for a needle in the haystack. Hutchinson, Tr. 1453; RX 464 at 252.

FF A 78. The search for high antibiotic-producing microorganism strains in a strain improvement program is even more difficult than the search for a needle in a haystack because, unlike the needle, the microorganism target continually changes throughout the search as a result of the mutations. Hutchinson, Tr. 1453-1454.

FF A 79. Examples exist of unsuccessful strain improvement programs where microorganism strains capable of producing high levels of antibiotics were never found. Hutchinson, Tr. 1454-1455.

FF A 80. In the 1970s, as well as now, strain improvement programs require an unavoidably long period of time (on the order of years or even decades) to obtain improvements in antibiotic yield to commercially feasible levels. Hutchinson, Tr. 1455-1458; RX 411 at 993; RX 460 at 95-96; RX 463 at 158; RX 466 at 320; Demain, Tr. 2183-2185.

FF A 81. As a strain improvement program progresses, the frequency at which increases in yield are observed markedly declines. Hutchinson, Tr. 1458-1459.

FF A 82. It took about 24 years of strain improvement programs to raise the yield from about 1,000 to about 10,000 μg/ml of penicillin using techniques such as monospore isolation and artificial mutagenesis. RX 410 at 179; Demain, Tr. 2186-2188.

FF A 83. Using monospore isolation and artificial mutagenesis and starting with something that was pretty close to a wild-type strain, it took about 17 or 18 years to raise the yield from about 1,000 to about 8,000 μg/ml of streptomycin, including work for 7-10 years to double the yield from 1,500 to 3,000 μg/ml. RX 410 at 180; Demain, Tr. 2188-2189.

FF A 84. With respect to streptomycin, the improvement from 1,000-1,500 μg/ml to about 2,000-2,300 μg/ml was pretty lucky and a major improvement that resulted from work with an auxotrophic mutant. RX 410 at 184; Demain, Tr. 2189-2190.

FF A 85. Quite a bit of luck is involved in successfully finding an improved microorganism capable of producing high levels of antibiotic. Hutchinson, Tr. 1460.

FF A 86. Blind alleys and dead ends of strain improvement programs can not be avoided by program design or the choice of a particularly unique mutagen. Hutchinson, Tr. 1476.

FF A 87. If a parent strain were subjected to ultraviolet radiation and an isolate resulted that had a repeatedly different yield characteristic, the probability is very high and Dr. Demain would use as a working hypothesis that the result was due to the mutagen rather than a spontaneous mutation. Demain, Tr. 2175-2177.

FF A 88. A strain that was generated from a parent strain using artificial mutation techniques, such as UV, that gave repeatedly higher improved yields is a mutant strain that is different from the parent strain, regardless of any comparison between the histogram of the parent and the histogram of the isolates, so long as the histograms are not identical. Demain, Tr. 2177-2178.

FF A 89. Individual strains derived from monospore isolation and artificial mutagenesis are commonly assigned identification numbers and deposited in public culture collections. RX 468C at 9.

FF A 90. Dr. Hutchinson first became familiar with public culture collections or depositories for microorganisms early in the 1970s. Hutchinson, Tr. 1428.

FF A 91. Culture collections have developed methods to preserve the deposited strain's characteristics over many years. RX 468C at 9.

FF A 92. Preservation typically involves storage of a lyophilized (freeze-dried) strain, or a frozen strain culture kept at low temperatures. RX 468C at 9.

FF A 93. Microorganism strains are stored in depositories to make them available to the public and to ensure preservation of the strains over a long period of time. Hutchinson, Tr. 1428.

FF A 94. The conditions at a microorganism depository are normally selected to maintain the viability of the deposit. Demain, Tr. 2113.

FF A 95. Depositories are necessary because it would be impossible to reisolate from nature a microorganism that someone else had discovered inasmuch as there are a quadrillion or more microorganisms in the natural environment. Hutchinson, Tr. 1428-1429.

FF A 96. Dr. Hutchinson agrees with Dr. Demain's deposition testimony that it is unexpected and not highly likely that one could obtain a high antibiotic-producing microorganism directly from nature. Hutchinson, Tr. 1429-1430; RX 416 at 57.

FF A 97. Dr. Hutchinson agrees with Dr. Demain's publication that the fermentation industry would be inconceivable without the ability to preserve industrial cultures and their mutants. Hutchinson, Tr. 1430-1431; RX 416 at 60.

FF A 98. If public depositories did not exist, the fermentation industry of today would not have been developed because of its heavy reliance on valuable microorganisms. Hutchinson, Tr. 1431-1432.

FF A 99. Without public depositories, it is likely that microorganisms would die. Hutchinson, Tr. 1432.

FF A 100. The American Type Culture Collection is considered to be the premier depository in the United States. Hutchinson, Tr. 1433.

FF A 101. In the 1970s, if Dr. Hutchinson had developed a microorganism strain and wanted the public to have access to it, he would have deposited it at the ATCC. Hutchinson, Tr. 1433.

FF A 102. In the 1970s, if owners wanted the public to have access to a microorganism strain, they would deposit the microorganism strain in a public depository. Hutchinson, Tr. 1433-1434.

FF A 103. Dr. Demain testified that owners of improved mutant strains do not like to deposit their improved strains because it gives them a competitive advantage not to do so. Demain, Tr. 2217-2219. According to Dr. Demain, most mutants are not patented and not deposited, but rather are kept as trade secrets. Demain, Tr. 2218.

FF A 104. Dr. Hutchinson, on more than one occasion, has written to industrial owners of high-producing microorganisms requesting a sample of such a strain, but was always politely refused. Hutchinson, Tr. 1432-1433.

II. CONSTRUCTION OF CLAIM 2 OF THE '698 REISSUE PATENT

A. The Level Of Ordinary Skill In The Art

FF B 1. A person of ordinary skill in the art as of 1977 would have had a Bachelor's Degree and at least two years of experience in antibiotic fermentation and biosynthesis. Hutchinson, Tr. 1552; Demain, Tr. 2115-2116.

A person would still have ordinary skill in the art if one had more experience, which could make up for a lack of formal education, or vice versa. Hutchinson, Tr. 1553.

FF B 2. Typically in the period around 1977, persons or ordinary skill in the art worked on teams and contributed their unique skills to the work of the whole team. Hutchinson, Tr. 1553.

B. "A Salinomycins-Producing Streptomyces Microorganism"

FF B 3. The specification of the '698 reissue patent states as follows:

> The foregoing and other objects of the present invention have been attained by culturing a polyether type antibiotic-producing microorganism in a medium containing a fatty acid or its precursor and ammonia or an ammonium salt and urea.

CX 1 (RX 5), '698 Reissue Patent, col. 1, lines 66 - col. 2, line 2.

FF B 4. The specification specifically refers to the microorganisms of the invention, as follows:

> The microorganism used in the present invention include [sic] generally polyether type antibiotics producing strains belonging to the genus of Streptomyces as well as the strains described in said literatures and their natural or artificial mutant.

CX (RX 5), '698 Reissue Patent, col. 2, lines 55 - 59 (emphasis added).

FF B 5. The specification states further, as follows:

> The strains used in this invention include Streptomyces albus No. 80614 and its mutants artificially or naturally produced, as well as the other Streptomyces strains capable of producing salinomycins. However, some of the salinomycins can occasionally not be detected in the culture, depending on the strain and fermentation conditions.

CX 1 (RX 5), '698 Reissue Patent, col. 3, lines 22-27, lines 52-53 (emphasis added).

FF B 6. The Patent Examiner rejected claims 1-4 of the reissue application under 35 U.S.C. § 112, first paragraph. The basis for the section 112 rejection was stated as follows:

> Since the microorganism is essential to the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, the requirements of 35 USC § 112, first paragraph may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public.

RX 901 (Prosecution History of the '698 Reissue Patent) at 144 (emphasis added). See Witherspoon, Tr. 1846-1847; Hutchinson, Tr. 1520-1521.

FF B 7. With respect to the Patent Examiner's specific rejection under 35 U.S.C. § 112, first paragraph, counsel for Kaken stated merely that the microorganism had in fact been deposited. Counsel responded to the Patent Examiner's rejection in part by stating that the claims are not limited to the specific strain reflected in the examples, yet did not take exception to the Examiner's view that the microorganism is an essential part of the claimed invention. RX 901 (Prosecution History of the '698 Reissue Patent) at 151-56; Witherspoon, Tr. 1847-1848.

FF B 8. High yields are an object of the invention:

> It is an object of the present invention to provide a method of producing polyether type antibiotics in remarkably high yields with industrial advantages.
>
> Another object of the present invention is to provide a method of producing Salinomycin type antibiotics such as salinomycin, 4-methysalinomycin, SY-1, SY-2, SY-3, SY-4, SY-5, SY-6, SY-7 and SY-8 substances in high yield.

CX 1 (RX 5), '698 Reissue Patent, at col. 1, lines 58-65 (emphasis added).

FF B 9. Assertions of high yields were made at various points during prosecution of the reissue patent, as recorded in the prosecution history. RX 901, Prosecution History of the '698 Reissue Patent.

FF B 10. Two of the named inventors, Mr. K. Hara and Ms. Nakamura worked primarily on improvement of the strain, another group worked primarily on improvement of the medium. The group members consulted each other as one team with regard to the tests using jar fermenters. Named inventor Mr. M. Hara testified that Mr. K. Hara and Ms. Nakamura were named as inventors because the yield increase resulted from improvements in the strain as well as the culture medium. Hara, Tr. 243.

FF B 11. Mr. M. Hara admitted that the process described in the '698 reissue patent resulted from efforts to improve the strain, as well as to improve the media and culturing conditions. Hara, Tr. 138-141.

FF B 12. Not only M. Hara, but also two other named inventors, Dr. Miyazaki and Mr. Yoneda, as well as Dr. Demain, admitted that the yield improvement Kaken achieved was dependent upon both the strain and the media. RX 56C at 11; Hara, Tr. 296, 419; RPX 109C, Hara, Dep. Tr. 603-604; Yoneda, Tr. 617; RX 55C, Fig. 6, p. 14; Demain, Tr. 2170-2170; RX 793C; Inaba, Dep. Tr. 409.

FF B 13. M. Hara's 1983 Okochi Memorial Foundation article, he recognized that the microorganism plays a main role in the fermentation process. CX 1048, at 58; Hara, Tr. 273-274.

FF B 14. Mr. M. Hara wrote that the number one factor in order to produce as much salinomycin as possible is to select a strain having high productivity. He recognized that the amount of production of an antibiotic is

"largely increasable by varying the nature of the producing organisms." Hara, Tr. 273-274; CX 1048, at 58.

C. The Requirement Of 12-25% Fatty Acid Or Its Precursor

FF B 15. Claims 1 and 2 of the '698 reissue patent are as follows:

> 1. A method of producing salinomycins, which comprises culturing a salinomycins-producing Streptomyces microorganism in a medium containing *12-25%* fatty acid or its precursor and ammonia or an ammonium salt and recovering the salinomycins from the culture.
>
> 2. The method of claim 1 wherein salinomycin is recovered together with the mycelial mass from the culture.

CX 1 (RX 5) '698 Reissue Patent at col. 8, lines 53-61.

FF B 16. One of ordinary skill in the art as of May 1977, would understand the 12-25% limitation contained in claims 1 and 2 of the '698 reissue patent to refer to the total cumulative amount of fatty acid or its precursor put into the fermentation medium; i.e., the person of ordinary skill in the art would calculate the percentage by taking into account all the oil used in the medium from the beginning of the fermentation process through the end of the process. Hutchinson, Tr. 1634-1636, 1643-1644. See Sybert, Tr. 794; 813-814.

FF B 17. [C] is used in the process as a fatty acid precursor. CX 1 (RX 5), col. 2, lines 18- 26; Hutchinson, Tr. 1622; Joint Stipulation of June 9, 1995 (RX 919C) ¶ 3.

FF B 18. Alternative measurements of oil content may be expressed in terms of percentage similar to the range of percentages expressed in claim 1 of the '698 reissue patent. One could measure the amount of oil present at the beginning or end of the process, or at any time in the process. However, one of ordinary skill in the art would not understand the language in claims 1

and 2 of the '698 reissue patent to refer to such other measurements. Hutchinson, Tr. 1636-1637.

FF B 19. The 12-25% range was added to independent claim 1 during the reissue proceeding. The rest of the specification is identical to that of original U.S. Patent No. 4,212,942. CX 1 (RX 5); Witherspoon, Tr. 1827.

FF B 20. Respondents' technical expert witness, Mr. Sybert, viewed claim 1 of the '698 reissue patent as covering a "window" of 12-25% fatty acid or its precursor. Sybert, Tr. 785, 824.

FF B 21. The words "pass through" do not appear in the claims or elsewhere in the '698 reissue patent. CX 1 (RX 1); Sybert, Tr. 824.

FF B 22. The specification states that "[t]he addition amount [of fatty acid] is generally about 1-25%, particularly about 12-20% based on the medium." CX 1 (RX 5), col. 2, lines 32-33.

FF B 23. In Example 3 of the '698 reissue patent, where a total of 16% soybean oil is used, the specification teaches that "[i]n this case, the similar production amount is attained even when soybean oil is added in a small amount at the beginning and then the addition amount is increased [to 16%]." CX 1 (RX 5), col. 7, lines 32-44.

FF B 24. Mr. M. Hara and Mr. Yoneda, who are two of the Kaken inventors of the '698 reissue patent, agree that the correct interpretation of the claimed 12-25% fatty acid or fatty acid precursor range in claims 1 and 2 should be the total amount of oil added together through the end of the process, i.e., the total amount of oil which was placed in the medium initially plus the amount of oil which was added along the way. Hara, Tr. 431-432; Yoneda, Tr. 555-556. See Hutchinson, Tr. 1637.

FF B 25. In the Inaba Declaration submitted during the prosecution of the '698 reissue patent, the calculation of the percentage of fatty acid or fatty acid precursor in the fermentation medium was based on the total cumulative amount of oil added to the medium throughout the entire process. Hutchinson, Tr. 1635-1636; RX 901, Inaba Declaration, Report 1 at 33, Report 2 at 40, Report 3 at 46-49, Report 4 at 52; Inaba, Tr. 1272-1275.

FF B 26. With respect to its current commercial process for manufacturing salinomycin, Kaken calculated the oil content by summing the total amount of oil added to the fermentation tank, including the initial charge and all subsequent additions during the process. Nakamura, Tr. 968.

FF B 27. Dr. Hutchinson did not support the theory advanced by Mr. Sybert, i.e., that the claim covers a process passing through the 12-25% range for a substantial period of time between the beginning and end of the process. In fact, Dr. Hutchinson believed that the "sliding scale" interpretation advanced by Mr. Sybert does not relate to the claims which specify a clear upper limit of 25 percent for the process. Dr. Hutchinson testified that the interpretation advanced by Mr. Sybert is unconventional, and not reasonable to him or to one of ordinary skill in the art. Hutchinson, Tr. 1640-1644.

FF B 28. For each of the tests in the Inaba Declaration, Mr. Inaba determined the oil content of the medium by summing up each amount of oil added to the medium during that test (numerator) and dividing the total oil figure by the initial volume of the culture solution (denominator), rather than by a subsequent volume. That method of determining the percentage of a specific component, such as oil, is not the conventional method used with respect to commercial fermentation in which, for example, the total oil (numerator) is divided by the total culture solution (denominator), rather

than only the initial volume of the culture solution. RX 901, Inaba Declaration, Report 1 at 33, Report 2 at 40, Report 3 at 46-49, Report 4 at 52; Inaba, Tr. 1272-1275; Nakamura, Tr. 964, 968, 991-993; Hori, Tr. 880-881. However, the method used by Mr. Inaba in his testing is the basis for the information submitted to the PTO, and is part of the file history of the '698 reissue patent. RX 901; Inaba, Tr. 1272-1275.

FF B 29. Respondents' technical expert witness, Dr. Hutchinson, testified that when computing the percentage of a particular component, the starting volume is used as the basis for the percentage rather than taking into account additions to the volume of the media during the process. Hutchinson, Tr. 1674-1675.

FF B 30. Dr. Hutchinson, received a Ph.D in organic chemistry in 1970. Thereafter, he spent a year at Cambridge as a research doctoral student in the biosynthesis of natural products. Hutchinson, Tr. 1410.

FF B 31. As a university professor, Dr. Hutchinson has lectured many times on fermentation methods, strain improvement and other aspects of antibiotics production. He has occasionally taught a course entitled Industrial Microbiology. Hutchinson, Tr. 1411-1412.

FF B 32. Since 1975, Dr. Hutchinson has been involved in research projects involving microorganisms and the antibiotics they produce, including polyether antibiotics. Hutchinson, Tr. 1413, 1415-1416.

FF B 33. Dr. Hutchinson has been an active consultant for more than 20 years for various pharmaceutical companies with respect to antibiotic yield improvement, including strain improvement and fermentation media improvement. Hutchinson, Tr. 1413-1414.

FF B 34. Dr. Hutchinson has been elected to the editorial boards of journals in his field, and currently serves on the board of four journals which deal with topics such as antibiotic fermentation and industrial processes. Hutchinson, Tr. 1416-1417.

III. CLAIM 2 OF THE '698 PATENT WOULD BE INFRINGED

A. The Current Hoechst AG Process For The Fermentation Of Salinomycin

FF C 1. The [C] Hoechst AG commercial fermentation process for salinomycin was put into [C] CX 873C, Koenig, Dep. Tr. 76, 330-331, 343-346.

FF C 2. [C]

[C]

[C]

[C]

FF C 3. [C]

[C]

[C]

[C]

[C]

FF C 4. [C]

[C]

FF C 5. [C]

[C]

FF C 6. [C]

[C]

[C]

[C]

FF C 7. In the current Hoechst AG process for the fermentation of salinomycin, Hoechst AG cultures a salinomycin-producing Streptomyces microorganism for the production of salinomycin. Joint Stipulation of June 9, 1995 (RX 919C) ¶ 1.

FF C 8. In the current Hoechst AG process for fermentation of salinomycin, Hoechst AG recovers the salinomycin together with the mycelial mass from the culture. Joint Stipulation of June 9, 1995 (RX 919C) ¶ 2.

FF C 9. For purposes of the current investigation, respondents have withdrawn their arguments that the current Hoechst AG process does not use ammonia or an ammonium salt. Joint Stipulation of June 9, 1995 (RX 919C) ¶ 6; Respondents' Comments on OUII's Proposed Findings of Fact at Part IV, at 2.

FF C 10. The [C] Hoechst AG process for the fermentation of salinomycin uses [C] as the fatty acid precursor in its fermentation medium. Joint Stipulation of June 9, 1995 (RX 919C) ¶ 3.

FF C 11. [C]

[C]

[C]

FF C 12. The amount of [C] used in the fermentation medium at the [C] of fermentation for the current Hoechst AG process depicted in CPX 12C as [C] and extending through the [C] is [C] but is always [C] Joint Stipulation of June 9, 1995 (RX 919C) ¶ 5(A).

FF C 13. [C]

[C]

[C]

[C]

[C]

FF C 14. [C]

[C]

[C]

[C]

FF C 15. In the [C] Hoechst AG commercial fermentation process for salinomycin, the total cumulative amount of [C] used [C] of fermentation [C] CPX 9C; CPX 12C; Joint Stipulation of June 9, 1995 (RX 919C) ¶ 5(B).

FF C 16. The [C] process that Hoechst AG used [C] [C] is [C] [C] depicted in CPX 12C, [C]

[C]

[C]

[C]

[C]

FF C 17. [C]

[C]

[C]

[C]

[C]

FF C 18. There is no stipulation with respect to the Hoechst AG commercial process for the period after April 1995 because no discovery has been had. Joint Stipulation of June 9, 1995 (RX 919C) ¶ 4(D).

FF C 19. [C]

[C]

FF C 20. [C]

[C]

FF C 21. [C]

[C]

[C]

[C]

[C]

[C]

[C]

[C]

[C]

[C]

[C]

FF C 22. [C]

[C]

[C]

[C]

[C]

FF C 23. [C]

[C]

[C]

[C]

[C]

FF C 24. The amount of fatty acid precursor in Hoechst AG's [C] process for the production of salinomycin measured at the beginning of the fermentation process [C] the cumulative amount of fatty acid precursor measured at the end of the process is always greater than 25%, and the amount of fatty acid precursor measured [C] during the process is [C] CPX 9C; CPX 12C; Hutchinson, Tr. 1638-1640.

B. The Range Of 12 To 25% Fatty Acid Or Its Precursor In The Prosecution History

FF C 25. Claim 1 of original U.S. Letters Patent 4,212,942, is as follows:

> 1. A method of producing salinomycins, which comprises culturing a salinomycins-producing Streptomyces microorganism is a medium containing fatty acid or its precursor and ammonia or an ammonium salt and recovering the salinomycins from the culture.

RX 4 ('942 Patent), col. 8, lines 54-58.

FF C 26. Kaken's claims in its original '942 patent specified a fatty acid or fatty acid precursor in the fermentation medium, but did not specify any particular amount of fatty acid or fatty acid precursor. RX 4, ('942 patent), col. 8, lines 53-67.

FF C 27. Kaken filed an application for reissue of the '942 patent on January 29, 1993. RX 901 (Reissue File History) at 3.

FF C 28. Kaken sought to reissue its original patent to distinguish its claims from the prior art Berg et al. U.S. Letters Patent 4,035,481 patent, which describes culturing a Streptomyces in a medium that includes 0.46% soybean oil. RX 901 (Reissue File History), Reissue Declaration ¶ 3, at 16.

FF C 29. In a preliminary amendment to the claims of original '942 patent at the beginning of the reissue proceedings, Kaken requested that

independent claim 1 be amended to add the limitation that the medium contain "at least 12%" fatty acid or its precursor. RX 901 (Reissue File History), Preliminary Amendment (Jan. 29, 1993), at 60; Kelber, Tr. 1994.

FF C 30. Kaken, thorough its counsel, stated that the preliminary amendment adding the "at least 12%" limitation to the language of claim 1 was for the purpose of distinguishing its patent over the Berg '481 patent. Kaken stated that in contrast to the amount of oil added in Berg, "more substantial amounts, including the 12% by weight herein, confers on the process a dramatic increase in yield, that could not be predicted by those of skill in the art." RX 901 (Reissue File History), Preliminary Amendment (Jan. 29, 1993) at 61-62.

FF C 31. When Kaken filed its reissue application, the claims as presented in the reissue application did not have a 25% upper limit on the percentage of fatty acid or fatty acid precursor. RX 901 (Reissue File History) at 60; Kelber, Tr. 1993-1994.

FF C 32. In a June 30, 1993 Office Action in the '698 reissue proceedings, the Patent Examiner rejected the claims under § 112 (second paragraph) for indefiniteness because they did not have an upper limit on the percentage of fatty acid or fatty acid precursor. RX 901 (Reissue File History) at 147, See Kelber, Tr. 1994; Witherspoon, Tr. 1851-1852.

FF C 33. On June 30, 1993, the Patent Examiner issued an Office Action rejecting the claims of the reissue application, including the preliminary amendment of "at least 12%." RX 901 (Reissue File History) at 143-149.

FF C 34. In the June 30, 1993 Office Action, the Patent Examiner rejected all claims under 35 U.S.C. § 112, first paragraph, stating there was inadequate information that the microorganism essential to the claimed

invention was deposited and readily available to the public. RX 901 (Reissue File History) at 144-146.

FF C 35. In the June 30, 1993 Office Action, the Patent Examiner stated as follow:

> The reissue application filed January 29, 1993 is objected to under 35 U.S.C. § 132 because it introduces new matter in to the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the addition of fatty acid at a percentage of above 20%.

RX 901 (Reissue File History) at 146 (emphasis added).

FF C 36. In the June 30, 1993 Office Action, the Patent Examiner rejected all claims 35 U.S.C. § 112, first paragraph, stating that the disclosure of the patent was enabling only for claims limited to the specific strain exemplified within the specification and a fatty acid content of 12-20%. RX 901 (Reissue File History) at 146. The Examiner stated further that "[a]n amount above that percentage has not been shown [to] induce the production of salinomycins and it would be expected that percentage[s] above that range may actually be toxic to the microorganisms." Id. at 147.

FF C 37. In the June 30, 1993 Office Action, the Patent Examiner stated that all claims were rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner further stated that "[t]he specific percent of fatty acid to be added can not be determined since there is no upper limit stated within the claim." RX 901 (Reissue File History) at 147. See Witherspoon, Tr. 1851-1852.

FF C 38. In the June 30, 1993 Office Action, the Patent Examiner rejected all claims "under 35 U.S.C. § 103 as being unpatentable over Berg et al." RX 901 (Reissue File History) at 5-7.

FF C 39. On November 1, 1993, in response to the outstanding rejections, and as a result of discussions with the Patent Examiner and correspondence with Kaken's Japanese patent counsel, Mr. Kelber, Kaken's patent attorney in the United States, amended the claims to add the upper limit to the range of fatty acid or its precursor of 25%. RX 901 (Reissue File History), Amendment (Nov. 1, 1993), at 151-152; RX 828C; RX 829C; RX 830C; RX 875C; Kelber, Dep. Tr. 126-127.

FF C 40. In its Remarks submitted with the amendment of November 1, 1993, which added the "12-25%" range to claim 1, applicants noted that "[t]his upper limit of 25% is disclosed at column 2, line 30, the lower limit of 12% is disclosed at column 2, line 31." RX 901 (Reissue File History), Amendment (Nov. 1, 1993), at 152.

FF C 41. In its Remarks submitted with the amendment of November 1, 1993, applicants, through counsel, noted that the claims had been rejected on the ground that they introduced subject matter, and that the Examiner said the specification is limited to a fatty acid content of no greater than 20%. Applicants stated that "[t]his rejection has been met by insertion of a maximum amount of 25% (not 20%) as set forth in the specification, column 2, line 30. This amendment was discussed with Examiner Robinson and appears adequate to meet the rejection, without more." RX 901 (Reissue File History), Amendment (Nov. 1, 1993), at 153.

FF C 42. In its Remarks submitted with the Amendment (Nov. 1, 1993), adding the 25% upper limit, Kaken, through its counsel, took the position that

the Examiner's rejection under 35 U.S.C. § 112, second paragraph, was "mooted by the amendment setting a limit on the amount of fatty acid content." However, the applicants commented that: (1) the invention resides in the identification of a minimum limit, not the maximum limit; (2) the applicant has demonstrated that amounts in excess of 25% fatty acid are not toxic; (3) culturing at concentrations of 32% and 39% are also demonstrated (presumably in the Inaba Declaration); and (4) the upper limit is only of practical importance but not critical to patentability. RX 901 (Reissue File History), Amendment (Nov. 1, 1993), at 154-155.

FF C 43. Subsequent to the amendment inserting an upper limit of 25% for fatty acid or its precursor, the arguments presented by Kaken's attorney, and the formal surrender of the original U.S. Patent No. 4,212,942, the Patent Examiner issued a Notice of Allowability for the '698 reissue patent. RX 901 (Reissue File History) at 160; Witherspoon, Tr. 1855.

FF C 44. Mr. Sybert saw work reported in the file history of the '698 reissue patent which indicates to him that there were only small or insignificant differences between 25 and 32%. Sybert, Tr. 755-756, 804.

FF C 45. Mr. Sybert saw work reported in the file history of the '698 reissue patent which indicates that there were "very good yields and very high yields, at least up to 32 percent and perhaps somewhat beyond. Tests were shown up to 39 percent at which there was some tailing off but not a sharp increase that would be indicative of toxicity." Sybert, Tr. 795-796.

FF C 46. However, with respect to the 25% figure for, Mr. Sybert also testified as follows:

> In reviewing the file history, it appeared to me that there was a reasonable peak in the activity level without any sharp drop-off on [e]ither side. That plateau in activity level <u>centered around the 25 percent range</u> and, therefore, it would be one reason

> for selecting that number as part of the range. There possibly are other reasons relating to, as I saw in some of the documents, not wishing to adversely affect or dilute out the other nutrients.

Sybert, Tr. 755 (emphasis added). See RX 901, Prosecution History of the '698 reissue Patent, at 42-43.

FF C 47. While Kaken told the Patent Examiner that upper limit of 25% is one of "practical importance" and not meant critically to characterize the invention, Kaken stated that "an excess of fatty acid complicates retrieval, without securing any benefit. Note, for example, that maximum production obtained at 32% treatment is higher than the maximum production obtained at 39% and that further, maximum production as 25% may in fact be greater than the maximum production at 32%." RX 901 (Reissue File History), Amendment (Nov. 1, 1993), at 154.

C. The Contributions Of The Invention Of The '698 Patent

FF C 48. The '698 patent has contributed a substantial teaching to the industry of polyether antibiotics. It directed the field to the extensive use of oil in polyether fermentations. The '698 patent is "a real teaching patent in which the field has been generally impressed by this patent." Demain, Tr. 2145-2147.

FF C 49. The '698 reissue patent was a standard-setting innovation for those in the polyether antibiotic industry. Demain, Tr. 2147.

D. The Accused Hoechst AG Process Would Infringe Claim 2 Of The '698 Patent Under The Doctrine Of Equivalents

FF C 50. Complainant's expert testified that the difference between using a total of 25% oil vs. 32% oil in the fermentation to produce salinomycin is insignificant. The test data contained in the prosecution history of the '698 reissue shows that the differences between 25 and 32

percent soybean oil concentration mattered little in the final yield of the product. Sybert, Tr. 755-757.

FF C 51. The file history of the '698 patent states that there is no toxicity associated with using amounts of oil greater than 25% and at least up to 39% for the fermentative production of salinomycin. Sybert, Tr. 757-758.

FF C 52. The testing submitted with the Inaba declaration to the PTO during the reexamination does not contain evidence of any toxic effect of oil on the salinomycin-producing microorganism at least in the range of 25%-32%. Sybert, Tr. 757.

FF C 53. The prosecution history of the '698 reissue patent shows high yields of salinomycin with amounts of oil above 25%. Complainant's expert testified in part, as follows:

> Q. As to the result of a fatty acid range of 12 to 25 percent, does the same result occur with the range of 12 to 25 percent as a result would occur from the range of 25 to 39 percent?
>
> * * *
>
> THE WITNESS: Yes. As I understood the results of the previous studies that were done and reported in the file history, there is a gradation of effect within that range and I believe I saw that between 12 and something around 32 or something more percent that there is an increasing effect and then tailing off above 32 percent, somewhere up around the 39 percent range. So the function I believe to be a building block. The result I believe to be an increase in the amount of salinomycins produced.

Sybert, Tr. 799-800.

FF C 54. The '698 reissue patent directed the field to the extensive use of oil in polyether fermentations. Demain, Tr. 2145-2147.

FF C 55. Mr. Sybert testified for Kaken that, with respect to the [C] Hoechst AG process for the fermentation of salinomycin as stipulated by the parties in CPX 9C, Claim 2 of the '698 reissue patent was infringed because in reaching [C] cumulative amount of oil used by

Hoechst AG, the process had to pass through the claimed range of 12-25 percent. CPX 9C; Sybert, Tr. 814-815.

FF C 56. Mr. Sybert testified that the Hoechst AG process as depicted in CPX 9C falls within the scope of Claim 2 [C]

[C]

[C]

FF C 57. A production run at Hoechst AG can [C] CX 873C, Koenig, Dep. Tr. 346.

FF C 58. With respect to his understanding of the 12-15% range for fatty acid or its precursor, Complainant's technical expert witness on the infringement issue, Mr. Sybert, testified as follows:

> Q. Now, Mr. Sybert, let's look at chart CPX-9C. Do you see that the total cumulative amount of soybean oil that's represented on this chart as being added in the fermentation process is 30 percent?
>
> A. Yes, sir, I do.
>
> Q. And, in your view, the process represented by chart CPX-9C would infringe Claim 2 of the '968 patent, correct?
>
> A. My position as stated earlier is that a significant portion of that fermentation process encompasses the range of 12 to 25 percent, that during that portion of the fermentation process, a cumulative amount of 12 to 25 percent was added to the medium.
>
> Q. But just let me make sure that I understand what you're saying. The total cumulative amount of soybean oil added is [C] and it's your contention and your view that the Claim 2 of the '698 patent is still infringed, correct?
>
> A. I believe it was infringed because in order necessarily to get [C] by the method that Hoechst practices in my understanding, the process had to have passed through the range of 12 to 25 percent.
>
> Q. Now, Mr. Sybert, if the final total cumulative amount of [C] were [C] would that infringe Claim 2 of the '698 patent in your view?

A. If the process were practiced as I understand it in which the [C] were added incrementally and it passed through the range of 12 to 25 percent, then I believe that the claim was infringed by that passage through the range of 12 to 25 percent.

Q. So even if the final total cumulative amount of oil were 40 percent at the end of the process, it's your view that the claim limitation 12 to 25 percent is met, correct?

A. I believe that by passing through that range, that was what was intended, in my opinion, by the statement was that the additive amount of 12 to 25 percent was what was shown in the analytical -- in the research studies to produce the high [C] [C]

Q. So, in other words, sir, if the final cumulative amount were 50 percent, in your view, Claim 2 was infringed, is that what you're saying?

A. Yes, sir.

Q. And if the total cumulative amount were 60, 70, 80, 90 or 100 percent total at the end of the process, it's your view that this claim would be infringed, is that right?

A. Given that it passed through the range of 12 to 25 percent in getting there, it's my opinion that it contained 12 to 25 percent during the growth phase of the culture during the productivity phase for the salinomycin.

Q. So in your view it's irrelevant, the final total cumulative amount of oil that's added?

A. My understanding is, as I would read this, that the medium contained 12 to 25 percent of fatty acid or its precursor during that block of time that's shown there on the chart.

Q. So, then, in your view there is no upper limit to the amount of cumulative oil added to the fermentation process that would escape the reach of Claim 2 in your view, correct?

A. That's correct, as long as it passed through the range of 12 to 25 percent, it would be covered by that claim in my opinion.

Q. And there is no upper limit, correct?

A. I don't see an upper limit, no.

Sybert, Tr. 814-817.

FF C 59. Mr. Sybert testified that if the fermentation process were begun at 26 percent, that this would not literally infringe the claims having the 12-25 percent limitation because although it would 12-25 percent oil as part of the larger percentage, it would not "pass through window" of 12-15% which he perceived to be claimed by the reissue patent. Sybert, Tr. 785, 822-824.

FF C 60. With respect to a process that began at 26% oil, Mr. Sybert testified in part, as follows:

> JUDGE HARRIS: I think you should answer from the perspective of your experience in the field, what it means to you as a person with your training and your experience in the field of fermentation. What does it mean if you start with 26 percent and go on from there.
>
> THE WITNESS: To someone like myself who has practiced fermentation for many years, there is a difference in meaning between starting at that time 26 percent and going up and starting at some number like we have here, 12 percent to 25 percent. They are different ranges, the results could very well be different. I don't know that they are, I do not know that they're not.
>
> But I do know that as a practitioner of fermentation, if I read a separate paper that said a medium containing 26 to whatever percent, I would practice that in a different way than I would practice the 12 to 25 percent.

Sybert, Tr. 830-831.

FF C 61. Mr. Sybert stated that in his experience there is a difference in meaning between starting with 26 percent and going up as opposed to starting at some number within a 12-25 percent range, because they are different ranges and the results could very well be different. Mr. Sybert did not know whether the results would be different or whether they would not. Sybert, Tr. 830.

FF C 62. The words "pass through" are not in the '698 reissue patent. CX 1 (RX 5).

FF C 63. The words "pass through" are not in Claims 1 or 2 of the '698 reissue patent. They derive from Mr. Sybert's interpretation. CX 1 (RX 5); Sybert, Tr. 824.

FF C 64. Respondents' technical expert, Mr. Sybert, testified the "increasing effect" of oil on salinomycin production is not capped at 25% oil but continues up to about 32% oil. Mr. Sybert's testified that his conclusion to this effect was upon his reading of the prosecution history. Sybert, Tr. 795.

FF C 65. The Hoechst AG fermentation records [C]

[C] were the fermentation records that Mr. Sybert testified about as characterizing the Hoechst AG process for production of salinomycin. [C]

[C]

FF C 66. [C]

[C]

[C]

[C]

[C]

FF C 67. With the exception of run [C]

[C]

[C] which were merely those runs in [C]

[C] excepted by the Joint Stipulation, only one run, [C]

[C] of the cited fermentation records that Mr. Sybert testified about as characterizing the Hoechst AG process was a run shown in [C] as being from the first quarter of 1995. Joint Stipulation of June 9, 1995 [C]

[C]

FF C 68. Mr. Sybert is not a patent lawyer. He had only a layman's understanding of what the term "claim construction" means. He as not familiar with the legal rules regarding claim construction. Sybert, Tr. 802.

FF C 69. Mr. Sybert had reviewed only one file history--the one here at issue--in any detail. Sybert, Tr. 802-803.

FF C 70. Mr. Sybert had never heard the term prosecution file history estoppel before he testified at the trial. Sybert, Tr. 803.

FF C 71. Mr. Sybert did not know what a Section 112 rejection was. Sybert, Tr. 803.

FF C 72. Mr. Sybert had only a layman's understanding of the significance of amending claims in response to Patent Office rejections. Sybert, Tr. 803-804.

FF C 73. Mr. Sybert had no understanding of the legal effect of inserting a 25 percent upper claim range limit as was done in the file history of the '698 reissue patent. Sybert, Tr. 805.

FF C 74. Kaken's only expert witness on infringement, Mr. Sybert, admitted he had no specific expertise as a microbial nutritionist, whose area of study is the cause-and-effect relationship of individual nutrients in the fermentation mixture. He testified that although he understood that the fatty acids provide a needed metabolic building block that the microorganism uses for the production of salinomycins during its growth and production phase, he further testified that he did not know the specific pathway followed: "within the many pathways that one can plot out, I don't know." Sybert, Tr. 797-798,

801. Kaken's only other technical expert witness, Dr. Demain, did not testify on the infringement issues.

FF C 75. Other than to say generally that the fatty acids are metabolic building blocks, Mr. Sybert did not know what specific pathways were followed within the many pathways that could be plotted. Sybert, Tr. 797-800.

FF C 76. It is not the case in fermentation technology that if a little bit of oil is good, a lot of oil is better. Demain, Tr. 2138-2139.

FF C 77. Patents showing how to obtain antibiotics through fermentation usually show a range which is understood to be the preferable range of oil to be used to obtain the highest titers of antibiotics. In fact, it is understood that using more than the amount of oil in the preferable range will decrease the amount of antibiotics recovered and will be detrimental to the microorganism. Demain, Tr. 2123-2125, 2138, 2223-2228.

FF C 78. When people write a patent application it is common for them to extend their claimed range of oil in both directions, higher and lower, usually to expand the use of their invention. However, it is the preferable range that is important because if one states a preferable range in a patent the reader has a higher number for the limit. One of ordinary skill in the art would conclude that the use of oil higher than that level is detrimental as compared with the use of the preferred level. Demain, Tr. 2223-2224.

FF C 79. The optimal amount of oil for the invention disclosed in the '698 patent is 16%. Hara, Tr. 164.

IV. THE '698 REISSUE PATENT IS INVALID FOR FAILURE TO DISCLOSE THE BEST MODE

A. The Patent Specification And The Emphasis On Commercially High Yields

FF D 1. Hoechst AG's Dr. Rathscheck testified that in 1982 Hoechst did not attach importance to the question of whether it was accurate to state that its production strain was stored as ATCC 21838. Rathscheck Dep. (CX 874C) Tr. 344-349.

FF D 2. In 1995, during the pendency of this investigation, Hoechst corrected its FDA submission with regard to the microorganism stain used to produce salinomycin. Hoechst stated that the strain is a mutant, and not the ATCC 21838 strain as deposited. RX 882C.

FF D 3. The '698 reissue patent concerns a method of producing "salinomycins." RX 5, col. 1, lines 11-13, 33-36 and col. 2, lines 6-12.

FF D 4. The term "salinomycins" is defined in the patent as including salinomycin, 4-methylsalinomycin (narasin), SY-1, SY-2, SY-3, SY-4, SY-5, SY-6, SY-7, and SY-8. RX 5, col. 1, lines 33-36, and col. 2, lines 6-12; Hutchinson, Tr. 1625-1626.

FF D 5. The stated objectives of the '698 patent are to provide a method of producing polyether-type antibiotics in remarkably high yields with industrial advantages and a method of producing salinomycin-type antibiotics in high yield. Hutchinson, Tr. 1521; RX 5, col. 1, lines 11-13, 58-65.

FF D 6. The specification of the '698 reissue patent states as follows:

> It is an object of the present invention to provide a method of producing polyether type antibiotics <u>in remarkably high yields with industrial advantages</u>.
>
> Another object of the present invention is to provide a method of producing Salinomycin type antibiotics such as salinomycin, 4-methysalinomycin, SY-1, SY-2, SY-3, SY-4, SY-5, SY-6, SY-7 and SY-8 substances <u>in high yield</u>.

RX 5 at col. 1, lines 58-65 (emphasis added).

FF D 7. Kaken asserted such high yields during the prosecution of the reissue application. Hutchinson, Tr. 1594-1598; RX 901C at 17, 26, 61-62, 155-56.

FF D 8. The '698 reissue patent states that yields are increased to the range of about 50,000 to 80,000 μg/ml when the fermentation medium contains soybean oil in the stated range along with an ammonium salt. Hutchinson, Tr. 1522.

FF D 9. The '698 reissue patent indicated that the invention disclosed therein results in "remarkably increased" yields of salinomycin over the prior art. Hutchinson, Tr. 1522. The '698 reissue patent states, as follows:

> According to the present invention the production amount of polyether type antibiotics, particularly Salinomycin type antibiotics can be remarkably increased. For example, the yield of Salinomycin is generally 100-300 μ/ml in known method, whereas the yield is about 10,000-20,000 μ/ml in the medium containing fatty acid or its precursor, and the yield is further increased to about 50,000-80,000 μ/ml when said medium is further aided by ammonia or ammonium salt.

CX 1, '698 Reissue Patent, col. 3, lines 7-12.

FF D 10. Reference Example 1 reciting a yield of 100-300 μg/ml does not represent the conditions set forth in the claims of the '698 reissue patent because the culture medium did not contain a fatty acid or its precursor, or ammonia or an ammonium salt. Hutchinson, Tr. 1514-1515.

FF D 11. Reference Example 2 reciting a yield of 20,000 μg/ml does not represent the conditions of the claims of the '698 reissue patent because only 10% soybean oil and no ammonia or ammonium salt were used in the culture medium. Hutchinson, Tr. 1515.

FF D 12. Example 1 reporting a yield of 20,000 μg/ml does not represent the conditions of the claims of the '698 reissue patent since 10% soybean oil

and no ammonia or ammonium salt were used in the culture medium. Hutchinson, Tr. 1515-1516.

FF D 13. Example 2 of the '698 reissue patent does not recite a yield as it merely illustrates recovery, not production, of the antibiotic. Hutchinson, Tr. 1516.

FF D 14. Example 3 of the '698 reissue patent reciting a yield of 60,000 μg/ml represents the culturing conditions of the claims because 16% soybean oil and ammonium sulfate were used in the fermentation medium. The culturing reported in Example 3 was carried out in a fermenter. Hutchinson, Tr. 1516-1517; RPX 109C, Hara, Depo. Tr. 423.

FF D 15. Example 4 of the '698 reissue patent reporting yields ranging from 34,000 to 39,000 μg/ml represents the culturing conditions of the claims of the '698 reissue patent because 12% soybean oil and an ammonium salt were used in the fermentation medium. The culturing reported in Example 4 was carried out in a flask. Hutchinson, Tr. 1516-1517; Hara, Tr. 161.

B. The Only Microorganism Deposited And Disclosed Is The Wild-Type Strain

FF D 16. Kaken's '698 reissue patent identifies only one deposited microorganism, the *Streptomyces albus* waxman and henrich No. 80614 strain (the "80614 strain"). RX 5, col. 1, lines 39-40; col. 4, lines 63-65; col. 5, lines 11, 32; RX 901C at 58-59 and 152-53.

FF D 17. Kaken previously disclosed the 80614 strain in its '948 salinomycin product patent, which issued in 1974 based on a 1972 application. That patent explains that salinomycin may be prepared by "culturing *Streptomyces albus* 80614 to form Salinomycin in a medium." RX 3, col. 1, lines 28-30.

FF D 18. Kaken deposited the 80614 strain at a Japanese culture depository under the identification number FERM-P. No. 419 and at a U.S. depository (American Type Culture Collection ("ATCC")) under the identification number ATCC 21838. RX 11C at 06557; RX 85C at Kaken 05202; RX 901C at 58-59.

FF D 19. Kaken deposited the 80614 strain at the Japanese depository in 1969. The 80614 strain was originally isolated by Kaken in 1968. RX 11 at Kaken 06557; RX 96 at Kaken 21782.

FF D 20. The 80614 strain became publicly available at least as early as December 31, 1974, when Kaken's '948 product patent issued. RX 3; RX 901C at 58-59, 153.

FF D 21. The '698 reissue patent tells the reader that the deposited 80614 strain was the only strain used in the Examples of the patent. RX 5 at col. 4, lines 63-64, col. 5, lines 11-12, 32-33; Hutchinson, Tr. 1507, lines 7-14; Inaba [30(b)(6)] Depo. Tr. 11.

FF D 22. Reference Example 1 of the '698 reissue patent states that the "Streptomyces albus waxman and henrich No. 80614 strain (FERM-P. No. 419)" was used to carry out the work reported in that reference Example. RX 5, col. 4, lines 63-65; Hutchinson, Tr. 1507.

FF D 23. Reference Example 2 states that "[t]he 80614 strain which is the same strain as described in [Reference] Example 1" was used to carry out the work reported in that reference Example. RX 5, col. 5, lines 11-12; Hutchinson, Tr. 1508.

FF D 24. Example 1 states that the inventors used "[t]he 80614 strain which is the same strain as described in [Reference] Example 1" to carry out

the work reported in that Example. RX 5, col. 5, lines 32-33; Hutchinson, Tr. 1508.

FF D 25. Example 2 states that the inventors used the 80614 strain for that Example because salinomycin was "cultured in the same manner as described in Example 1." RX 5, col. 6, lines 19-20; Hutchinson, Tr. 1508.

FF D 26. Example 3 refers one to the 80614 strain for use in that Example because it refers to "[t]he second-stage pre-culture liquid of Example 1," which contained the 80614 strain. RX 5, col. 7, lines 26-28; Hutchinson, Tr. 1508.

FF D 27. Example 4 refers one to the 80614 strain for use in that Example because it refers to "[t]he third-stage pre-culture liquid in Example 3," which contained the 80614 strain. RX 5, col. 8, lines 26-28; Hutchinson, Tr. 1508.

FF D 28. Although the '698 reissue patent mentions that artificially or naturally-produced mutants of the 80614 strain can be used, the reference to mutants does not indicate to one of ordinary skill in the art that anything other than the 80614 strain was used in the Examples and does not allow one of ordinary skill in the art to obtain a mutant capable of achieving the yields reported in Examples 3 and 4. Hutchinson, Tr. 1511-1512; RX 5, col. 2, lines 55-59 and col. 3, lines 22-25.

FF D 29. The '698 reissue patent's recitation of mutants artificially or naturally produced does not disclose how to obtain the desired mutants. It does not eliminate the necessity for one skilled in the art to go through a strain improvement program to find a strain which achieves the yields reported in the '698 reissue patent. Hutchinson, Tr. 1513.

FF D 30. Conducting a strain improvement program does not guarantee success in finding a strain capable of the antibiotic yields described in Examples 3 or 4 of the '698 reissue patent. Hutchinson, Tr. 1513.

FF D 31. In fact, the strain used by the inventors in the Patent Examples was not the 80614 strain. See Subsections E and F, infra; RX 673, Kaken Req. Adm. 6-9.

C. The SLS-K-7-68 Strain Was Developed After At Least Four Years Of An Extensive Strain Improvement Program

FF D 32. Kaken dug up and isolated a salinomycins-producing *Streptomyces* microorganism from a soil sample in Japan in 1968, designating it *Streptomyces albus* waxman and nenrich No. 80614 ("the 80614 strain"). Hara, Tr. 280, 381; RX 11C at 06557; RX 85C at 05202; RX 806C.

FF D 33. Kaken isolated salinomycin from that wild-type strain by at least 1971. Hara, Tr. 381.

FF D 34. In tests of the 80614 strain, Kaken found that it produced low yields of salinomycin. Hutchinson, Tr. 1495-1496; Hara, Tr. 209; RX 793C, Inaba, Depo. Tr. 110-111.

FF D 35. For testing purposes, Kaken reproduced from the 80614 strain several identical samples. Kaken called the samples "original strain" numbers 1 through 6, each of which was the same as the 80614 strain. Hara, Tr. 372, 415; Hutchinson, Tr. 1463; RX 806C.

FF D 36. While results before 1974 are not known because Kaken claimed that those records could not be found, some of the earliest examples of the low yields Kaken found from the 80614 strain are jar fermentation experiments Kaken rar between April and July of 1974 using original strain 6 in media including approximately 10 to 12% oil and approximately 0.3 to 0.5% ammonium salt. The yields from those experiments with original strain 6 were 13,000

μg/ml (RX 188C), 12,500 μg/ml (RX 186C), 8,000 μg/ml (RX 189C), 12,500 μg/ml (RX 190C), and 14,000 μg/ml (RX 191C), resulting in an average yield of about 12,000 μg/ml. Yoneda, Tr. 618-619; RX 791C, Yoneda, Depo. Tr. 181-194; RX 788C, Hara, Depo. Tr. 119, 141, 144-145; RX 807C.

FF D 37. By at least as early as 1972, Kaken directed significant efforts toward developing an improved microorganism strain. RX 806C; Hara, Tr. 381-382; Hutchinson, Tr. 1462; Hara, Tr. 145-146, 289-294; RX 336C, Kaken Resp. Interrog. 7; RX 788C, Hara, Depo. Tr. 55-56.

FF D 38. Kaken's scientists concluded that both an improved microorganism strain, and not just an improved culture medium, were required to obtain acceptable yields. RPX 788C, Hara, Depo. Tr. 604.

FF D 39. Kaken continued its search for the best producing salinomycin-producing strain through at least 1977. Yoneda, Tr. 613-614; RX 792C, Miyazaki, Depo. Tr. 184-185.

FF D 40. Respondents' Strain Tree Chart exhibit illustrates a portion of Kaken's efforts to develop an improved microorganism strain; the efforts from 1974 through 1977. RX 806C; Hara, Tr. 416.

FF D 41. Respondents' Strain Tree Chart exhibit does not include Kaken's work prior to 1974 because documents from that period were not available for discovery. RX 806C.

FF D 42. Kaken does not dispute any of the facts on the Strain Tree Chart, nor does it dispute that it conducted the strain improvement experiments represented on that chart. RX 806C; RPX 6; Hara, Tr. 389-391.

FF D 43. Kaken began its strain improvement program using the wild-type 80614 strain. RX 806C; Hara, Tr. 382-383; Hutchinson, Tr. 1462-1463.

FF D 44. Kaken first tried monospore isolation techniques to improve the 80614 strain. RX 806C; Hara, Tr. 383-384.

FF D 45. Kaken then also tried artificial mutation techniques to obtain microorganisms yielding higher production of salinomycin. RX 806C; Hara, Tr. 141, 150, 159.

FF D 46. Kaken's typical procedure in selecting and testing small samples of microorganisms, referred to as "isolates," after use of monospore isolation or an artificial mutation technique involved the following: (1) a number of isolates (e.g., 400) were selected randomly from the larger sample that had been subjected to the technique; (2) each individual isolate was inoculated into a liquid culture medium; (3) salinomycin productivity was examined for each of the isolates; and (4) individual isolates having better activity were selected for further testing. RX 806C; RX 12; Hara, Tr. 392-397.

FF D 47. Mr. M. Hara was the person who headed the researchers working on Kaken's strain improvement program based on the 80614 strain. By 1973, he was in the group Kaken called its Second Research Lab. Hara, Tr. 137-138, 140-141; RX 788C, Hara, Depo. Tr. 51.

FF D 48. Focusing on strain improvement and maintenance in Kaken's Second Research Lab as part of Kaken's program were Mr. Kaoru Hara and Ms. Y. Nakamura, as well as four or five equipment operators. Yoneda, Tr. 500; Hara, Tr. 146, 159.

FF D 49. Many of the strains M. K. Hara and Ms. Nakamura developed were tested in fermentation jar tests, the results of which are shown on the Yield Chart exhibit. RX 807C; RX 902C; Yoneda, Tr. 610-611.

FF D 50. Between 1973 and the middle of 1977, Kaken ran at least 118 jar tests on isolates as part of its strain improvement efforts. The results of those tests were reported to Mr. M. Hara. Yoneda, Tr. 612.

FF D 51. Mr. Yoneda also worked in the Second Research Lab. His responsibilities included assisting Mr. M. Hara in identifying the best salinomycin producing strain. During the period of 1973 through 1977, Mr. Yoneda spent most of his time working on jar tests on microorganism strains that were being conducted under his supervision. He also supervised five or six people who ran fermentation apparatus 24 hours a day to perform those salinomycin jar tests. Yoneda, Tr. 610-611, 614-616.

FF D 52. One branch of Kaken's strain improvement program began with original strain 1, exposing it to the artificial mutagen NTG, leading to 384 isolates. Choosing one of those isolates, Kaken treated it with ultraviolet irradiation, resulting in 735 isolates. Choosing one of those isolates again led to another series of isolates. However, Kaken did not further study that line of strains. Hutchinson, Tr. 1463-1464.

FF D 53. In another branch of Kaken's strain improvement program, Kaken performed monospore isolation on original strain 2, and made a series of successive isolates from those results. Eventually, Kaken wound up with a series of isolates that it did not investigate further. Hutchinson, Tr. 1465.

FF D 54. Inasmuch as the original strain numbers 1-6 do not reflect the order in which experiments were conducted and Kaken has not produced documents from the period before 1974, presumably original strains 3-5 were used prior to 1974. See Hutchinson, Tr. 1465.

FF D 55. Using original strain 6, Kaken's strain improvement program followed several paths, including monospore isolation, ultraviolet

irradiation, and heavy particle irradiation, as well as the creation of auxotrophic mutants. Hutchinson, Tr. 1465-1467.

FF D 56. In the course of this work, in 1974 Kaken developed at least eight new strains (strains 13 to 18 and 20 to 22) by subjecting samples of the 80614 strain to monospore isolation or successive generation culturing. Kaken obtained over 2,600 isolates of these strains. RPX 6; RX 806C; Hara, Tr. 383-384, 387-388, 392-402, 405-406.

FF D 57. In jar tests using ammonium salt and at least 10% oil, the tested isolates from these new strains generated in 1974 achieved an average yield of about 16,900 μg/ml, with the highest yield being 26,500 μg/ml. RX 807C; RX 745C.

FF D 58. In 1975, Kaken developed at least seven more strains (strains 23 to 29) from strains previously developed from the 80614 strain by using various techniques, including artificial mutation by ultraviolet irradiation and heavy particle irradiation, as well as monospore isolation. It created over 2,500 isolates of these strains. RX 806C; Hara, Tr. 410-415.

FF D 59. In jar tests using ammonium salt and at least 10% oil (some using at least 12% oil), the tested isolates from 1975 achieved an average yield of about 16,800 μg/ml, with the highest yield being 28,500 μg/ml. RX 807C; RX 745C.

FF D 60. In 1976, Kaken continued its strain improvement program using various techniques, such as artificial mutation, resulting in Kaken's development of at least nine more new strains (strains 30 to 35, A-1, A-2, 7, and 9), from which it produced over 2,500 isolates. RX 806C; Hara, Tr. 415-416.

FF D 61. With the exception of isolate number 68 of the strain designated number 7 -- i.e., the "SLS-K-7-68" strain, and its descendants -- in jar tests using ammonium salt and at least 10% oil (most using at least 12% oil), the tested isolates achieved an average yield of about 20,500 μg/ml, and the highest yield achieved was 31,000 μg/ml. RX 807C; RX 745C.

FF D 62. The immediate parent of the SLS-K-7-68 strain is the A2-54 strain. Kaken developed the A2-54 strain by performing monospore isolation on original strain 6. RX 42C; RX 806C; Hara, Tr. 313-316; Hutchinson, Tr. 1467.

FF D 63. In April or May 1976, named inventor K. Hara developed the SLS-K-7-68 strain by subjecting the A2-54 strain to ultraviolet irradiation. Hutchinson, Tr. 1467; Hara, Tr. 187-188, 211, 231, 330; RX 41C at 18456, 18458; RX 42C at 18117, 18120; RX 43C at 18324; RX 44C at 18112; RX 788C, Hara, Depo. Tr. 346-348, 350-351, 388-389.

FF D 64. The SLS-K-7-68 strain showed very significant yield improvement over the other strains that Kaken's program had developed. RX 807C.

FF D 65. The SLS-K-7-68 strain was the first strain tested by Kaken to achieve a salinomycin yield that exceeded 30,000 μg/ml. RX 902C; Yoneda, Tr. 617.

FF D 66. Through August 1976, only one other strain (30-379) achieved a yield of over 30,000 μg/ml, and the average yield with that strain was only 28,500 μg/ml. RX 807C.

FF D 67. A Kaken monthly report appears to indicate that one isolate of strain 36, out of the 735 isolates tested, achieved a yield of 35,000 μg/ml. When it was tested again but with more care, however, it obtained a significantly lower yield of 19,000. RX 76C at 15413, 15415; RPX 788C, Hara, Depo. Tr. 541-543.

FF D 68. As illustrated on the Strain Tree Chart compiled by Respondents, Kaken's strain improvement program involved many different parallel lines of investigation, most of which led to dead-ends. Hutchinson, Tr. 1449-1450, 1472-1473; RX 806C; see also Tr. 1712.

FF D 69. To say that it took only one to four months to develop the SLS-K-7-68 strain is analogous to laboriously working one's way through a maze to reach the end, and then arguing that completion of the maze took only the time required to open the door that successfully let one out at the end. Hutchinson, Tr. 1473.

FF D 70. Dr. Demain's article demonstrates that strain improvement programs are measured from the beginning, not the end. Demain, Tr. 2186-2188.

FF D 71. Kaken's strain improvement program for salinomycins-producing Streptomyces strains was extensive and took over four years from 1972 to 1976 to arrive at the SLS-K-7-68 strain. Hutchinson, Tr. 1472; RX 806C; RX 807C.

FF D 72. A pictorial presentation of Kaken's strain improvement program appears in a 1980 article of M. Hara and Miyazaki. An annotated presentation appears as Figure 6. RX 55C at H200 00062.

D. The Named Inventors And Kaken Recognized The SLS-K-7-68 Strain As A Superior Mutant Strain

FF D 73. The SLS-K-7-68 strain was characterized as a superior mutant in an October 15, 1976 technical know-how report that Kaken sent to Hoechst under a license agreement: "[t]he superior mutant, SLS-K7-68 [sic] was obtained by UV irradiation." RX 48C at H031 00552; Demain, Tr. 2165-2166.

FF D 74. The information in the October 15, 1976 technical know-how report was based on reports and other information provided by Kaken's Second Research Lab, headed by named inventor M. Hara. RX 48C; Hara, Tr. 335-337; RX 788C, Hara, Depo. Tr. 398, 400.

FF D 75. Mr. M. Hara received a copy of the October 15, 1976 technical know-how report, and does not recall criticizing the information disclosed in that report. RX 48C; Hara, Tr. 338.

FF D 76. Kaken admits that the information contained in the October 15, 1976 technical know-how report was known to at least one of the named inventors before June 1, 1977. RX 673C, Kaken Resp. Req. Adm. 51.

FF D 77. Similarly, the SLS-K-7-68 strain was characterized as a superior mutant in a June 1, 1977 Kaken technical know-how report that Kaken provided to its licensees. That report reveals some of the mutation techniques used by Kaken in its strain development program which resulted in the SLS-K-7-68 strain. In a section entitled "The isolation of mutants," Kaken's report explains:

> The isolation of mutants for salinomycin production were continued to obtain "Improved" strains. Ultraviolet-ray, X-ray, [gamma]-ray radiations and N.T.G., $NaNO_2$ treatments were used for the mutagenic techniques. The selection of mutants among the survivors were made by the morphological [sic, morphological] changes, methionine auxotrophs, speed of comsumption [sic, consumption] of oil and salinomycin producing ability, but the mutants superior to SLS-K-7-68 have not been obtained as yet.

RX 50C at Kaken 04249 (emphasis added); Hara, Tr. 300, 302, 417-418; Yoneda, Tr. 562-563, 578.

FF D 78. The information in the June 1, 1977 technical know-how report came from Kaken's Second Research Lab, headed by Mr. M. Hara. It is based on data from jar reports by named inventor Yoneda. RX 50C; Hara, Tr. 298-299; Yoneda, Tr. 562-563, 568-572; RX 788C, Hara, Depo. Tr. 402-404, 405-406.

FF D 79. Mr. M. Hara's group provided the figures and test data for the June 1, 1977 know-how report. Mr. M. Hara approved all the information his group contributed to the know-how report. Mr. M. Hara received a copy of the report around the time it was written. Hara, Tr. 297-303.

FF D 80. Mr. Yoneda did not tell anyone, nor did anyone tell him, that the statement in the June 1, 1977 technical know-how report that "mutants superior to strain SLS-K-7-68 had not been obtained as yet" was incorrect or wrong in any way. RX 50C; Yoneda, Tr. 567.

FF D 81. The June 1, 1977 technical know-how report shows the views of the named inventors at the time of filing for patents on the method claimed in the '698 reissue patent and '942 parent patent. It is dated the same day as the second Japanese priority application, and the day after the filing of the first priority application, which formed the basis for those patents. RX 50C; RX 5; Hara, Tr. 297-304.

FF D 82. Kaken admits that the information in the June 1, 1977 technical know-how report was known to at least one of the named inventors before June 1, 1977. RX 673C, Kaken Resp. Req. Adm. 52; see also Hara, Tr. 303.

FF D 83. Another contemporaneous example of how the named inventors viewed the SLS-K-7-68 strain is an article published in 1982 by named inventors Mr. M. Hara and Dr. Miyazaki. It, too, referred to a "superior mutant strain," and specifically identified only one strain, the SLS-K strain. RX 56 at 12; Hara, Tr. 296-297.

FF D 84. In accordance with these views, named inventors Mr. Hara and Dr. Miyazaki referred to an "improved mutant strain" in draft Examples for the 1977 Japanese patent applications upon which the '698 patent is based. They provided the draft Examples to Mr. Shibuya, who drafted the background portion of Japanese Patent Applications 52-62802 and 52-63215. RX 277; RX 796C, Shibuya, Depo. Tr. 30-32, 32, 37-38, 97-98, 165-166.

FF D 85. Given Kaken's admission that the SLS-K-7-68 strain was actually used to carry out Patent Example 3, it is clear that the SLS-K-7-68 strain was

the "improved mutant strain" referred to in the draft patent Examples that the named inventors provided to Mr. Shibuya. RX 673C, Kaken Resp. Req. Adm. 6-9; Order No. 16 (6/2/95), Undisputed Fact No. 4, at 12; Hara, Tr. 304, 310; Yoneda, Tr. 584; RX 875C, Kelber, Depo. Tr. 123.

E. The SLS-K-7-68 Strain Was Recognized By Kaken And The Named Inventors As Being Significantly Different From, And Superior To, Prior Strains, Including The Parent Strain, In Carrying Out The Claimed Invention

FF D 86. Two of the named inventors, Dr. Miyazaki and Mr. M. Hara, wrote an article published in 1980. That article, reflecting information the inventors knew before filing for a patent in 1977, graphically demonstrates the dramatic increase resulting from the use of the SLS-K-7-68 strain. Mr. M. Hara prepared Figure 6 in that article. The improvement in yield achieved through use of the SLS-K strain (Point D) exceeded the combined improvement of adding both oil (i.e., fatty acid precursor) and an ammonium salt (Points A and B).[2] RX 53C at 08836; RX 55C at H200 00062; CX 75C at 13; Hara, Tr. 239; RX 788C, Hara, Depo. Tr. 434-435, 437-440, 614-615; RX 792C, Miyazaki, Depo. Tr. 115; RX 53C at 08835.

FF D 87. A similar chart appears in a 1982 article by the same two named inventors, Dr. Miyazaki and Mr. M. Hara, which also describes work done in the 1970s. In that article, Point D of Fig. 4 refers to the SLS-K-7-68 strain, and point C refers to new strains which are improved strains. CX 75C (RX 56C); Hara, Tr. 238-239; RX 788C, Hara, Depo. Tr. 426-427.

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[2] Kaken offered as a proposed exhibit a modified version of the graph from the 1980 article by named inventors, Dr. Miyazaki and Mr. M. Hara, Figure 6. That proposed exhibit was excluded from evidence because, the Administrative Law Judge found, it did not accurately represent the article and contained "features which are at least misleading if viewed apart from all portions of the transcript related to it. . . ." Order No. 18 at 4.

FF D 88. Pointing out the yield improvement due to the SLS-K strain, Dr. Miyazaki's and Mr. M. Hara's 1980 and 1982 articles state that the "improved SLS-K strain" produced a 1.5 fold conversion efficiency increase and notes that the SLS-K strain produced a "dramatic" increase in production. Indeed, Kaken's trial translator translated the "dramatic" increase as "leaps and bounds." RX 55C at H200 00062; RX 53C, (original Japanese language version); Hara, Tr. 296, 342, 347; RX 788C, Hara, Depo. Tr. 423, 426-434, 450; RX 792C, Miyazaki, Depo. Tr. 110-111, 114-115; RX 56C at H200 00035; RX 54C; Hutchinson, Tr. 1527.

FF D 89. Dr. Miyazaki, in an article published in 1984, also stated that the SLS-K strain "is far more efficient than other strains at converting soybean oil in to [sic] salinomycin, and resulted in a dramatic increase in production." RX 86C; RX 87C at H200 00091; RX 792C, Miyazaki, Depo. Tr. 124-128.

FF D 90. Dr. Miyazaki testified that the "dramatic increase" pointed out in his article was based upon a comparison with the 80614 strain, and that he "saw a clear difference between the SLS-K strains and the parent strains," including the 80614 strain. RX 792C, Miyazaki, Depo. Tr. 126-128.

FF D 91. These 1980, 1982, and 1984 articles written by named inventors after the filing date of the patent application reflect results achieved, and known by the inventors, prior to the filing date. RX 788C, Hara, Depo. Tr. 426-427, 437-438.

FF D 92. At trial, Mr. M. Hara tried to dismiss the significant difference between the SLS-K-7-68 strain and the parent 80614 strain described in his 1980 and 1982 articles, as "some exaggeration." RX 56; Hara, Tr. 311-312. Mr. Hara's 1995 testimony on this point at the hearing is not

credible, given that he authored the several articles in the 1980s extolling the virtues of the SLS-K strain, and given that other contemporaneous documentation is consistent with the description of the SLS-K strain that appears in these articles.

FF D 93. Other contemporaneous writings by named inventors express similar views as to the superiority of the SLS-K-7-68 strain. For example, named inventor K. Hara in a July 1976 report demonstrates that the SLS-K-7-68 strain achieved yields 1.68 times greater than the average of the other strains, and achieved significantly higher yields than its parent, the A2-54 strain (in at least one instance, almost twice the yield of its parent). RX 42C at 18117; Hara, Tr. 321-322; RX 788C, Hara, Depo. Tr. 348, 351, 355, 384-386.

FF D 94. Several contemporaneous documents by the named inventors note differences between the SLS-K-7-68 strain and other strains in terms of oil conversion. The more efficient the microorganism is at converting the oil to salinomycin, the higher the salinomycin yield. The SLS-K strains, which include the SLS-K-7-68 strain, were singled out by the inventors as being the most efficient in this regard. Hara, Tr. 279; CX 1048[3]; RX 43C; RX 45C.

FF D 95. Mr. K. Hara in his September 1976 research report, describes beneficial differences between the SLS-K-7-68 strain and its parent strain, including oil consumption:

1. Difference in bacterial strain

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[3] During the hearing, Respondents examined witnesses on various exhibits which were originally offered by Complainant. See Order No. 3, Ground Rule 6(b) (requesting the parties to avoid unnecessary duplication in their hearing exhibits). Complainant subsequently withdrew CX 1048. Complainant's Comments on Respondents' Proposed findings of Fact at C5. However, after the hearing Respondents provided for the record copies of CX 1048 and certain other exhibits originally offered by Complainant.

> In regard to the differences between the mutant strain 7-68 which was obtained by UV irradiation and its parent strain, the differences as shown in Table 1 are the following three points: In the mutant strain; 1. pH is higher, 2. Average value in SL is higher, 3. Variation coefficient is lower. The reason for higher pH is that the consumption of oil is quicker (this will be explained later). It is thought that the reason for the higher SL value is the mutation caused by UV irradiation, or that the wild type characteristic has been lost. For that reason, the variation coefficient is also lower.

RX 43C at 18324; Hara, Tr. 257-261; RX 788C, Hara, Depo. Tr. 360-363, 379-383.

FF D 96. Similarly, contemporaneous documents from named inventor M. Hara also recognize the superiority of the SLS-K-7-68 strain. His October 1976 report noted that the SLS-K-7-68 strain had rapid oil consumption, a high pH, a low variation coefficient, and high potential, based on a report by K. Hara. RX 45C at 18320; Hara, Tr. 330-332.

FF D 97. Mr. M. Hara also prepared a 1983 article in which the SLS-K strains are discussed, which includes the SLS-K-7-68 strain:

> As a result, on several occasions, we obtained new strains, in which positive differences against the parent strain were recognized. Particularly, one strain, which we named SLS-K, displays a better utilizability of an oil in a medium. The conversion rate of soybean oil to salinomycin increased widely as much as 1.5 times compared with conventional strains, thus contributing much to the improvement of productivity.

CX 1048C at 58 (emphasis added). Mr. Hara testified that 1.5 times difference was a "wide difference," and represents a dramatic increase in production of salinomycin. CX 1048; Hara, Tr. 272-273, 276-277, 280-281.

FF D 98. Earlier in that article, Mr. M. Hara noted that salinomycin was isolated in 1971 from Streptomyces albus. CX 1048C at 56. However, when referring to the most efficient organism for converting oil into salinomycin, Mr. Hara did not discuss the 80614 strain. Rather, he concluded that the most

efficient organisms for converting oil to salinomycin were the SLS-K strains, which included the SLS-K-7-68 strain. Hara, Tr. 280; CX 1048 at 58.

FF D 99. Similarly, Mr. M. Hara admitted at trial that the SLS-K strains, including the SLS-K-7-68 strain, were far more efficient in converting oil into salinomycin than the 80614 strain. Hara, Tr. 287-288.

FF D 100. Mr. M. Hara also testified that, as shown in his contemporaneous documents, did not remember a strain that produced a higher yield than SLS-K-7-68. Hara, Tr. 445.

FF D 101. Kaken admitted based on information supplied by the inventors that as of the effective filing date of the '698 reissue patent at least one of the named inventors considered at least one of the SLS-K strains to be the best microorganism to carry out the claimed method. RX 5; RX 673C, Kaken Resp. to Req. for Adm. Nos. 28 and 29.

FF D 102. In accordance with the contemporaneous views by the named inventors, Kaken chose the SLS-K-7-68 strain as the parent strain from which it developed all its production strains. RX 74C; RX 812C; RX 788C, Hara, Depo. Tr. 505-508; Hutchinson, Tr. 1475; RX 793C, Inaba, Depo. Tr. 47-48.

FF D 103. The named inventors, as well as Kaken, recognized that the SLS-K-7-68 strain achieved yields far superior to prior strains. RX 44C at 18112; RX 788C, Hara, Depo. Tr. 389-390.

FF D 104. Consistent with contemporaneous evidence, Kaken admits that, by May 31, 1977, it had not developed a microorganism strain superior to the SLS-K-7-68 strain. RX 673C, Kaken Resp. to Req. for Adm. 47, 48.

FF D 105. In all experiments conducted prior to the May 31, 1977 and June 1, 1977 filing dates of the relevant Kaken applications, the original 80614 strain produced significantly lower yields than had been obtained with

SLS-K-7-68. RX 186C; RX 187C; RX 188C; RX 189C; RX 190C; RX 191C; RX 791C, Yoneda, Depo. Tr. 181-194; RX 788C, Hara, Depo. Tr. 119, 141, 144-145; RX 807C; RX 902C; RX 754C; RX 716C.

FF D 106. As shown in the Yield Chart compiled by Respondents, the SLS-K-7-68 strain achieved significantly higher yields than the other strains resulting from Kaken's strain development efforts, averaging a yield of about 44,160 μg/ml with a high of 80,000 μg/ml. RX 807C; RX 745C; RX 902C; RX 716C.

FF D 107. The yields of salinomycin for the SLS-K-7-68 strain ranged from 40,000 μg/ml to 80,000 μg/ml. Hutchinson, Tr. 1473-1474; RX 745C; RX 716C; RX 902C.

FF D 108. The fermentation media used to achieve yields in the range of 40,000 μg/ml to 80,000 μg/ml with the SLS-K-7-68 strain contained at least 12% oil and an ammonium salt. Hutchinson, Tr. 1474; RX 902C; RX 745C; RX 716C.

FF D 109. The fermentation medium used to achieve an 80,000 μg/ml yield with the SLS-K-7-68 strain contained 16% oil and .3 to .5% ammonium salt. Hutchinson, Tr. 1474; RX 902C; RX 238C.

FF D 110. In June or July 1976, Mr. K. Hara performed tests comparing the yield of the SLS-K-7-68 strain to that of its immediate parent, strain A2-54, in three different media, referred to as SLM-9, 11 and 12. He found the SLS-K-7-68 strain provided significantly improved yields. RX 42C.

FF D 111. In medium SLM-9, the A2-54 strain gave a yield of 18,800 units, while the lowest yield of the SLS-K-7-68 strain was 22,500 units, about a 19% difference; the highest yield for the SLS-K-7-68 strain was 26,800 units, about a 42% difference. In medium SLM-11, the A2-54 strain gave a yield of 20,200 units, while the lowest yield of the SLS-K-7-68 strain was 23,800, about an 18% difference; the highest yield for the SLS-K-7-68 strain

was 27,300, about a 35% difference. In the SLM-12 medium, the A2-54 strain yielded 14,800 units, while the lowest yield of the SLS-K-7-68 strain was 19,300, about a 30% difference; the highest yield for the SLS-K-7-68 strain was 27,800, about an 88% difference. RX 42C; Hara, Tr. 316-317; Demain, Tr. 216C.

FF D 112. Kaken's expert, Dr. Demain, tried to dismiss the test in the SLM-12 medium because the report indicated that there was abnormal growth, and that there were differences in the volume of the inocula. However, substantial evidence exists to support the accuracy and reliability of the results of these tests. RX 42C at Kaken 18117; Demain, Tr. 2160-2161.

FF D 113. In contrast to Dr. Demain, named inventor M. Hara admitted that nothing was wrong with the data reported in M. K. Hara's June or July 1976 report comparing the A2-54 strain and the SLS-K-7-68 strain. RX 42C; Hara, Tr. 362-363. Mr. M. Hara was M. K. Hara's supervisor, and the report was written to M. Hara. Hara, Tr. 144-145, 312.

FF D 114. Contradicting himself at the hearing, Mr. M. Hara also tried to dismiss Mr. K. Hara's results from 1976, testifying that he felt the comparison between the A2-54 parent strain and the SLS-K-7-68 strain was inappropriate. However, that testimony is not credible. Mr. M. Hara relied on these results at least in part to report large scale increases in salinomycin in his subsequent articles in the 1980s. Moreover, he also relied on M. K. Hara's comparison data during presentations within Kaken discussing work on salinomycin in the 1970s. RX 55; RX 56; Hara, Tr. 361-362; RX 14 at 15484; Hara, Tr. 362-365.

FF D 115. Mr. M. Hara also tried to dismiss those results by testifying that the side-by-side comparison between the A2-54 and SLS-K-7-68 strains was

not proper because, according to Mr. M. Hara, Mr. K. Hara had used a 1 year old sample of strain A2-54 but a new sample of the SLS-K-7-68 strain. This testimony also is not credible, given Mr. M. Hara's reliance on Mr. K. Hara's data. Moreover, the contemporaneous documents contradict this testimony. According to those documents, the A2-54 strain had only been isolated a few months prior to the side-by-side comparison between A2-54 and SLS-K-7-68. RX 33; RX 42C; RX 39; Hara, Tr. 320-321, 356, 357-36. In addition, Mr. M. Hara testified that he did not recall ever asking Mr. K. Hara to repeat the comparison between A2-54 and SLS-K-7-68 reported in the June or July 1976 experiments. Hara, Tr. 365.

FF D 116. In about October 1976, soon after Mr. K. Hara's June or July 1976 comparison between the SLS-K-7-68 and its immediate parent, named inventor Yoneda compared the SLS-K-7-68 strain to another strain that Kaken's strain improvement program had developed, called strain 30-248. Under the same fermentation conditions, in a medium containing 12% soybean oil, the SLS-K-7-68 strain produced a yield of 33,000 μg/ml, while strain 30-248 produced a yield of only 19,500 μg/ml. RX 48C at H031 00559; Hara, Tr. 338-339; Yoneda, Tr. 593; Hara, Tr. 464-465; RX 225C.

FF D 117. Mr. Yoneda admitted that for the comparison in his experiment between strains SLS-K-7-68 and 30-248, the strains were run under the same conditions with respect to the percent of inoculum, the percent of soybean oil, and the composition of the preculture medium prior to the main fermentation step. RX 48C; RX 225C; Yoneda, Tr. 594, 596.

FF D 118. Mr. Yoneda suggested his 1976 comparison may have been inappropriate because of a difference in the seed culture media. However, Mr. Yoneda testified that he never told anyone that a difference between the

seed culture media used in his comparison prevented a valid comparison between the two strains. Yoneda, Tr. 596-597.

FF D 119. Corroborating the validity of Mr. Yoneda's comparison, his results were included in an October 15, 1976 know-how report from Kaken to its licensees. RX 48C. There is no indication in that report that the differences in seed culture between the runs of the SLS-K-7-68 strain and strain 30-248 would prevent a valid comparison from being made. Mr. Yoneda testified that he did not recall telling anybody or anybody telling him that the comparison between strains SLS-K-7-68 and 30-248 in the October 15, 1976 Kaken report to licensees was incorrect or inappropriate in any way. Yoneda, Tr. 593, 597, 600; RX 225C.

FF D 120. At trial, Kaken witness Mr. Yoneda and its expert witness, Dr. Demain, suggested that the SLS-K-7-68 strain was unstable. Yoneda, 539-545; Demain, Tr. 2099-2100, 2168, 2234-2236. However, contrary to that suggestion, contemporaneous and other evidence shows that Kaken and the named inventors considered the SLS-K-7-68 strain to be stable.

FF D 121. Kaken chose the SLS-K-7-68 strain as the parent strain later to develop Kaken's commercial production strains. RX 74C; RX 812 C; RX 788C; Hara, Depo. Tr. 508; Hutchinson, Tr. 1475; Yoneda, Tr. 539-544; RX 793C, Inaba, Depo. Tr. 47-48.

FF D 122. Mr. Yoneda testified that Kaken chose the SLS-K-7-68 strain to use in its efforts to optimize the fermentation media conditions. It was the one standard strain to be used when testing characteristics of different media by varying the media but not the strain. He testified that unless Kaken used one strain, it would have been impossible to compare the effect on yields by changing the media characteristics. Mr. Yoneda also testified that he never

said or wrote to anyone that he disagreed with the selection of the SLS-K-7-68 strain for use in those tests to optimize the fermentation media conditions. Yoneda, Tr. 550, 582-583.

FF D 123. The SLS-K-7-68 strain provided consistently high yields in virtually every test Kaken ran. RX 902C; RX 716C; RX 745C.

FF D 124. The named inventors, which included Mr. Yoneda, used the SLS-K-7-68 strain to carry out Example 3 in their '698 reissue patent. Mr. Yoneda and Mr. Hara testified at trial that Example 3 was the best way they knew to practice the claimed invention. RX 673C, Kaken Resp. Req. Adm. 6-9; Hara, Tr. 310; Yoneda, Tr. 584; Order No. 16 (6/2/95), Undisputed Fact No. 4, at 12; RX 875C, Kelber, Depo. Tr. 123. Mr. Yoneda, Mr. Hara and Dr. Miyazaki submitted affidavits in opposition to Hoechst Respondents' Motion for Summary Determination stating that Example 3 was the best way of practicing their invention.

FF D 125. Kaken's June 1, 1977 know-how report to its licensees, almost a year after Mr. K. Hara isolated the SLS-K-7-68 strain, told the licensees that "mutants superior to SLS-K-7-68 have not been obtained as yet," and that "[i]n many tests of various conditions of cultivation in 30 l. jar fermentor, excellent experimental data above ca. 60,000 units were obtained frequently." Mr. Yoneda provided all the jar test data for the SLS-K-7-68 strain that appear in the June 1, 1977 report. Moreover, all the data (15 examples) provided in the report were generated with the SLS-K-7-68 strain. Hara, Tr. 303, 417-418; Yoneda, Tr. 568-572; RX 50C at Kaken 04249, 04251, 04254-04268.

FF D 126. Kaken's June 1, 1977 technical know-how report does not indicate that the 7-68 strain was considered to be an unstable strain, and

Mr. Yoneda did not recall anyone saying at the time the work reported upon was done that the SLS-K-7-68 strain was an unstable strain. RX 50C at Kaken 04249; Demain, Tr. 2166-2167; Yoneda, Tr. 566-567.

FF D 127. Mr. Yoneda's and Dr. Demain's testimony as to instability was premised on five fermentation runs with the SLS-K-7-68 strain that achieved lower yields. Yoneda, Tr. 539-545; Demain, Tr. 2099-2100. However, more than sixty runs with SLS-K-7-68 achieved higher yields, and Mr. Yoneda testified that the five low runs were not important enough to include in Kaken's June 1, 1977 know-how report to its licensees. Yoneda, Tr. 573-574; RX 902C.

FF D 128. Further contrary to Kaken placing any significance on five low yielding runs as indicating instability, Mr. Yoneda admitted that two of those runs using the SLS-K-7-68 strain that produced 11,500 and 9,100 μg/ml were unusually low yielding because of a stoppage of the air passage in the fermentation vessels, and that such a comparison between these runs and other successful runs was unfair. Yoneda, Tr. 608-610; Hutchinson, Tr. 1491-1494.

FF D 129. Dr. Hutchinson testified that the SLS-K-7-68 strain is more stable than the 80614 strain. RX 43C; Hutchinson, Tr. 1485.

FF D 130. The SLS-K-7-68 strain, under various fermentation conditions, produced significantly greater yields of salinomycin than the 80614 strain, the A2-54 (its parent strain), and other strains resulting from Kaken's strain improvement efforts. RX 902C; RX 50C at Kaken 04251.

FF D 131. Respondents' Exhibits RX 807C and RX 902C graphically set forth the yields Kaken researchers obtained in jar tests using strains developed in its strain improvement program from 1974 through 1976. RX 807C; RX 902C; RX 745C; RX 716C. Exhibit RX 807C lists only the highest yield achieved by each strain tested in a jar. These jar tests typically provide a

higher yield than flask tests. RX 788C, Hara Depo. Tr. 354; RX 793C, Inaba, Depo. Tr. 280, 604-605.

FF D 132. Kaken contended that the yields shown for various runs of strains could not validly be compared because the volume of inoculant used in the runs varied. However, substantial evidence showed that the volume of inoculant used did not always lead to a higher salinomycin yield. Exhibit RX 807C lists only the highest yield achieved by each strain tested in a jar. These jar tests typically provide a higher yield than flask tests. RX 788C, Hara, Depo. Tr. 354; RX 793C; Depo. Tr. 280, 604-605.

FF D 133. The amount of inoculum is the amount of seed culture placed in a fermentation stage, expressed as a percentage of the total volume of the fermentation stage. Yoneda, Tr. 527-528.

FF D 134. Mr. Yoneda testified that raising the amount of inoculum reduces the time it takes for culturing. Yoneda, Tr. 528.

FF D 135. According to Mr. Yoneda, by changing the inoculum quantity, Kaken was trying to determine the optimum inoculum quantity. Yoneda, Tr. 529.

FF D 136. Mr. Yoneda testified that use of an increased amount of inoculum raises the maximum possible productivity of a particular strain. That testimony is contradicted by his own admission and by evidence from Kaken jar test reports, which show that increased inoculum does not necessarily lead to increased salinomycin productivity. Yoneda, Tr. 513-514, 524, 527-529, 601-603, 606-608; RX 224C; RX 191C.

FF D 137. Mr. Yoneda also testified that Kaken began using large amounts of inoculum in experiments after August 1976 because it realized that larger amounts of inoculum gave larger yields. That testimony is contradicted by evidence that the amount of inoculum Kaken used both before and even after

August 1976 varied from 1 to 10%. Yoneda, Tr. 534; RX 224C (CX 198) (strain 30-379 used 10% and 1% inoculum in July 1976 jar tests); RX 234C (jar test SL-108, strains 9-6, 9-39, 7-68 used 1% and 10% in November 1976 testing); RX 191 (July, 1974 jar tests on original strain 6 using both 1% and 10% inoculum).

FF D 138. Kaken has admitted that as of May 31, 1977 and June 1, 1977, at least one of the inventors considered at least one of the SLS-K strains to be the best for practicing the claimed method. RX 673, Kaken Resp. Req. Adm. Nos. 28-29.

F. The SLS-K-7-68 Strain Is A Mutant Strain Generated By Ultraviolet Irradiation

FF D 139. Mr. K. Hara's June 1976 report includes a paragraph titled "Mutation induced by UV irradiation" that describes an irradiation procedure used to generate SLS-K-7-68. It includes a table titled "Mutation induced by UV irradiation" that lists a number of strains and their corresponding yields, including the SLS-K-7-68 strain, which gave a yield of 29,000. RX 41C at 18456, 18458; RX 788C, Hara Depo. Tr. 346, 350, 355.

FF D 140. Similarly, Mr. K. Hara's July 1976 report, in a section titled "Mutation induced by UV irradiation," compares the yield of the SLS-K-7-68 strain with that of its immediate parent, the A2-54 strain. That report states that the SLS-K-7-68 strain achieved yields 1.68 times greater than the average of the other strains, and achieved significantly higher yields than its parent, the A2-54 strain (in at least one instance, almost twice the yield of its parent). It concludes from those experiments that, "[i]n view of the above results, it is considered that the [SLS-K-]7-68 strains are mutant." RX 42C at 18117; Hara, Tr. 321-322; RX 788C, Hara, Depo. Tr. 348, 351, 355, 377, 384-386.

FF D 141. Mr. M. Hara testified that he may have verbally criticized Mr. K. Hara for referring to the SLS-K-7-68 strain as a mutant after receiving K. Hara's July 1976 monthly report. RX 788C, Hara Depo. Tr. 361-362, 618-619. However, substantial evidence establishes that this testimony is not credible. For example, an August 1976 M. Hara report described results from K. Hara's July 1976 report stating that "Among 200 pieces treated with UV irradiation, 29 pieces are sent for the second test. Among the above, (7-68) showed high potency (it is 1.7 times of the average value)." Mr. M. Hara did not recall questioning or doubting any of the conclusions that Mr. K. Hara reached concerning the SLS-K-7-68 strain. Mr. M. Hara's report did not criticize Mr. K. Hara's conclusion that the SLS-K-7-68 strain was a mutant and did not criticize K. Hara's work. RX 43; RX 44C at Kaken 18112; Hara, Tr. 261, 321-322.

FF D 142. A September 1976 research report by Mr. K. Hara describes differences between the SLS-K-7-68 strain and its parent strain, and refers to the SLS-K-7-68 strain as a mutant with mutation caused by ultraviolet irradiation:

> 1. Difference in bacterial strain
>
> In regard to the differences between the mutant strain 7-68 which was obtained by UV irradiation and its parent strain, the differences as shown in Table 1 are the following three points: In the mutant strain; 1. pH is higher, 2. Average value in SL is higher, 3. Variation coefficient is lower. The reason for higher pH is that the consumption of oil is quicker (this will be explained later). It is thought that the reason for the higher SL value is the mutation caused by UV irradiation, or that the wild type characteristic has been lost. For that reason, the variation coefficient is also lower.

RX 43C at 18324 (emphasis added); Hara, Tr. 257-261; RX 788C, Hara, Depo. Tr. 360-361, 379-383.

FF D 143. Describing results from Mr. K. Hara's September 1976 report, as earlier noted, Mr. M. Hara's October 1976 report stated that the SLS-K-7-68 strain had rapid oil consumption, a high pH, a low variation coefficient, and high potential. This report, which M. Hara provided to his supervisor, however, does not criticize K. Hara's description of the SLS-K-7-68 strain as a mutant. RX 45C; Hara, Tr. 330-332.

FF D 144. Although Mr. M. Hara testified that he may have verbally criticized Mr. K. Hara's use of the term mutant for the SLS-K-7-68 strain, he testified that he never objected in writing to reports he received from Mr. K. Hara that characterized the SLS-K-7-68 strain as different from other strains and described it as a "mutant." Hara, Tr. 255; RX 788C, Hara, Depo. Tr. 360-363, 379-383, 618-619; see, e.g., RX 43C.

FF D 145. According to Mr. M. Hara, he did not correct Mr. K. Hara in writing because he wished to avoid an unpleasant atmosphere. However, he testified that he would verbally criticize monthly reports to his superior. Nevertheless, Mr. M. Hara received a copy of Mr. K. Hara's report stating that the SLS-K-7-68 strain is a mutant around the time it was written; and Mr. M. Hara approved it. Hara, Tr. 213, 297-303 322-324.

FF D 146. There is no genuine factual dispute that Mr. K. Hara was knowledgeable in his field. Complainant's Comments on Respondents' Proposed Findings of Fact at C1. Mr. M. Hara believed that, as of 1974, M. K. Hara had significant experience in strain improvement work. M. K. Hara also had at least the equivalent of several years of college. Hara, Tr. 254-255, 424-425. Dr. Demain stated that the people in the Japanese pharmaceutical companies back in the 1970s were excellent technologists, and that included Kaken. Demain, Tr. 2195.

FF D 147. In an October 15, 1976 technical know-how report that Kaken sent to Hoechst under a license agreement, Kaken characterized the SLS-K-7-68 strain as a superior mutant strain: "[t]he superior mutant, SLS-K7-68 [sic] was obtained by UV irradiation." RX 48C at 552. The report includes a genealogy chart that shows that the SLS-K-7-68 strain was obtained by subjecting its parent strain to UV irradiation. The information provided in the report was based on a report by K. Hara. Mr. M. Hara testified that he himself had provided information disclosed in the technical know-how report. RX 48C; Hara, Tr. 335-338; see, Demain, Tr. 2165-2166.

FF D 148. The 1980 article published by two of the named inventors, Dr. Miyazaki and Mr. M. Hara, states that "Monospore isolation and artificial mutation technology was then used to produce a strain called SLS-K...." RX 55C at 61-62.

FF D 149. In a 1982 article by the named inventors, Dr. Miyazaki and Mr. M. Hara, the SLS-K strains were similarly described as being obtained by using artificial mutation techniques:

> 1) Identification of productive strains
>
> One of the great dreams of industrial fermentation is the promise of productivity gains by the use of improved strains. Once a strain with even slightly elevated salinomycin productivity is isolated, monospore isolation can be used to select individual spores (equivalent to the seeds of a plant) of the microbe (in this case, a member of the Actinomycetes), culture the spores, and check their productivity. This technique is often combined with artificial mutation, in which mutations are induced artificially for a deliberate purpose. In our case, we used ultraviolet, gamma-ray, and alpha-ray radiation, as well as mutagens such as N-methyl-N'-nitro-N-nitrosoguanidine. In addition to checking for daughter strains which produced more target substance than their parents, we also made selections based on our knowledge of the biosynthetic pathway and resistance or sensitivity to various drugs. As a result, we obtained daughter strains that were significantly different from the parent. We thereby developed a strain called SLS-K which, when cultured in the oil medium to be described below, is 1.5 times more efficient at converting soybean

oil into salinomycin. This resulted in a dramatic increase in production.

The article also referred to a "superior mutant strain," and the only strain specifically identified in the article is the SLS-K strain. RX 56C at 34-35 (emphasis added) and 37; RX 54C (original Japanese language version); Hara, Tr. 294-297; RX 788C, Hara, Depo. Tr. 426,-427, 432-434, 450; RX 792C, Miyazaki, Depo. Tr. 110-115.

FF D 150. Draft patent examples by the named inventors for the Japanese patent applications on which the '698 reissue patent is based similarly refer to a mutant, as noted above. Mr. Shibuya, from Kaken's patent group, drafted the background portion of Japanese Patent Applications 52-62802 and 52-63215. Named inventors Dr. Miyazaki and Mr. M. Hara provided him with draft examples and a draft example written by M. Hara included a description of an "improved mutant strain." RX 796C, Shibuya Depo. Tr. 30-32, 37-38, 97-98, 165-166, 273; RX 277.

FF D 151. Although Mr. M. Hara testified at the hearing that he included strains in addition to the 80614 in his draft patent application "thinking that it may be better to make a slightly broader range," it is also true that the SLS-K-7-68 strain was used in the experimentation that in fact led to the Patent Examples. Hara, Tr. 245-246, 310; RX 673C, Kaken Resp. Req. Adm. 6-9; Yoneda, Tr. 584.

FF D 152. A 1983 Okochi Memorial Foundation article, which Mr. M. Hara wrote in part, states that by employing "the following conventional or new selection procedures: monospore culture, artificial mutation," Kaken obtained "new strains," and states SLS-K was one of those new strains. CX 1048C at 58; Hara, Tr. 272-273.

FF D 153. A 1984 article published by named inventor Dr. Miyazaki states that "monospore isolation and artificial mutation technology can be used to produce a daughter strain that is significantly different from the parent. By this means we developed a strain called SLS-K . . . ." RX 87C at 91; RX 792C, Miyazaki, Depo. Tr. 124-128.

FF D 154. The SLS-K-7-68 strain was obtained by subjecting the A2-54 strain to UV radiation. RX 42C; Hara, Tr. 211, 317; see also Hara, Tr. 187-188.

FF D 155. Mr. M. Hara admitted that ultraviolet irradiation is a technique designed to increase the probability of a mutation occurring. Hara, Tr. 281-282; RX 788C, Hara, Depo. Tr. 301.

FF D 156. Without a mutagenic technique, spontaneous or natural mutation occurs infrequently, and mutagenic techniques increase this frequency by 100 to 10,000 fold. Hutchinson, Tr. 1414-1415; 1443; Demain, Tr. 2175.

FF D 157. With ultraviolet irradiation, if it works in a particular situation with the right dose and the right amount of time, mutation rates could be increased by a thousand fold. Demain, Tr. 2175.

FF D 158. A mutant is genetically different from its parent. Demain, Tr. 2156.

FF D 159. A mutant is a strain that differs from its parent strain in at least one characteristic that can be repeatedly observed. Repeatedly observed means more than a single observation that disappears the second time it is examined. Hutchinson, Tr. 1435-1437; Demain, Tr. 2096, 2155-2157.

FF D 160. Any one different characteristic is sufficient to indicate whether there is a genetic difference from the parent and whether the microorganism is a mutant. That conclusion is reinforced if there is more

than one observable difference. Hutchinson, Tr. 1435-1438, 1487; Demain, Tr. 2155-2156.

FF D 161. For example, a significant and repeatable difference in yield between a microorganism and its parent indicates a mutation. Hutchinson, Tr. 1436-1438; Hara, Tr. 268; Demain, Tr. 2157.

FF D 162. Dr. Demain testified that if a strain generated from a parent strain by artificial mutation techniques such as UV irradiation gave repeatedly higher yields, then he would consider it to be a mutant strain that was different from the parent strain. Dr. Demain would consider the probability to be very high, and take it as a working hypothesis, that the result was due to the mutagen rather than a spontaneous mutation. Demain, Tr. 2178, 2175-2177.

FF D 163. Because of the higher salinomycin yield produced by the SLS-K-7-68 strain, M. K. Hara concluded that strain was a mutant. Hara, Tr. 191-192; CX 61C; RX 43C.

FF D 164. The SLS-K-7-68 strain repeatedly produced significantly higher yields of salinomycin than its parent or prior strains, as discussed above. See, e.g., Order 16 (6/2/95), Undisputed Fact No. 1, at 12.

FF D 165. A 10% to 15% difference from a preceding value is significant and, as long as it is reproducible, is enough to conclude that a microorganism is a mutant from its parent. Hutchinson, Tr. 1765-1766; Demain, Tr. 2157-2160.

FF D 166. Showing a difference exceeding that range, Mr. K. Hara's September 1976 research report shows a yield of 20,500 for strain A2, which is the parent of SLS-K-7-68, whereas the SLS-K-7-68 strain achieved a yield of

28,350, which is a difference of about 39 percent. RX 43C at 18325; Demain, Tr. 2164.

FF D 167. Also showing a difference exceeding that range, an August 1976 M. Hara report states that "Among 200 pieces treated with UV irradiation, 29 pieces are sent for the second test. Among the above, (7-68) showed high potency (it is 1.7 times of the average value)." RX 44C; Hara, Tr. 321-322.

FF D 168. A significant difference between a microorganism and its parent in the rate at which soybean oil is converted into salinomycin is indicative of a mutation. Dr. Demain testified that if it can be determined that one organism is one and a half times more efficient in converting oil into salinomycin, that is sufficient information to conclude that the organism is a mutant if repeatedly observed. Demain, Tr. 2157; Hara, Tr. 271-272, 277-278.

FF D 169. In the Miyazaki and Hara 1980 article it is stated that the improved SLS-K strain improved by 1.5 times the ratio for converting oil into salinomycin resulting in a dramatic increase of production. RX 55C at 62; Demain, Tr. 2169-2170.

FF D 170. Such a difference is also shown in the 1983 Okochi Memorial Foundation article, which states that the SLS-K strain was 1.5 times more efficient at converting oil into salinomycin. CX 1048 at 58.

FF D 171. Another feature of microorganisms is the variation coefficient, which is a measure of the stability or reproducibility in terms of a specific characteristic. Hutchinson, Tr. 1483-1485.

FF D 172. M. K. Hara considered the variation coefficient to be lower for the SLS-K-7-68 strain than for its parent. CX 61C; RX 43C; Hara, Tr. 201.

FF D 173. The pH is a characteristic that, if different from that of another strain, can be used to conclude that a strain is a mutant. Hutchinson, Tr. 1438, 1486-1487; Hara, Tr. 268-269.

FF D 174. Because the SLS-K-7-68 strain had a higher pH than its parent, M. K. Hara concluded that the SLS-K-7-68 strain was a mutant. CX 61C; RX 43C; Hara, Tr. 191.

FF D 175. A difference in color, when the medium is the same, is indicative of a mutation. Hutchinson, Tr. 1438; Hara, Tr. 268; RX 410, 180; Demain, Tr. 2237-2238.

FF D 176. The SLS-K-7-68 strain had a difference in physical appearance, compared to other isolates of its parent strain observed at the same time. Hutchinson, Tr. 1488-1491; RX 41C.

FF D 177. According to Dr. Hutchinson, the SLS-K-7-68 strain is very clearly different from the 80614 strain. Hutchinson, Tr. 1480. Indeed, inventor Dr. Miyazaki admitted as much when he testified in his deposition that he saw a clear difference between the SLS-K strains and the parent 80614 strain. RX 792C, Miyazaki, Depo. Tr. 127-128.

FF D 178. Dr. Hutchinson testified that the SLS-K-7-68 strain differs from the 80614 strain in the following characteristics: reproducibly higher yield, pH, stability, color, and morphology. Hutchinson, Tr. 1480-1481, 1789.

FF D 179. The notation in one of Mr. K. Hara's reports concerning the SLS-K-7-68 strain mentions the color orange in a chart. There is not a written explanation in the report of what the notation means, and one must rely on the testimony of others to interpret the late Mr. K. Hara's report. There is testimony to indicate that the SLS-K-7-68 strain was orange. See Hara, Tr. 264. However, the notation may indicate that the microorganism was

orange, or it may indicate that the microorganism did not obscure an orange background provided by the medium. See Nakamura, Tr. 2029-2030, 2047-2048; Inaba, Tr. 2051-2055.

FF D 180. Dr. Hutchinson testified that the SLS-K-7-68 strain is a mutant of the 80614 strain. Hutchinson, Tr. 1480.

FF D 181. Dr. Demain testified that significant reproducible differences in characteristics indicate a mutant. Demain, Tr. 2155-2157.

FF D 182. Dr. Demain admitted that strain improvement resulting in the SLS-K-7-68 strain, along with media improvements, permitted significantly higher yields to be achieved by the SLS-K-7-68 strain than those for the 80614 strain, as reported in Figure 6 of Miyazaki et al. (1980). Dr. Demain admitted that the new strains indicated on Figure 6 of Miyazaki et al. (1980) were different strains from the 80614 wild-type strain, and that the SLS-K-7-68 strain was the result of the strain improvement indicated in Figure 6. RX 55C, Fig. 6, 14; Demain, Tr. 2170-2171.

FF D 183. Dr. Demain also admitted that, in connection with his testimony, he had not taken into account the 1984 article by Dr. Miyazaki stating that there were SLS-K daughter strains that were significantly different from the 80614 parent strains in efficiency of converting oil into salinomycin. RX 87C, 16; Demain, Tr. 2171-2173.

FF D 184. Dr. Demain admitted that he had not seen the article published by Kaken stating that "[p]articularly, one strain, which we named SLS-K, diaplays [sic] a better utilizability of an oil in a medium. The conversion rate of soybean oil to salinomycin increased widely as much as 1.5 times compared with conventional strains, thus contributing much to the improvement of productivity," and that such statement would be indicative of SLS-K strain

being a mutant if it were repeatedly observed. CX 1048C, 58; Demain, Tr. 2173-2174.

FF D 185. As a basis for asserting that the SLS-K-7-68 strain was not a mutant of the 80614 strain, Dr. Demain referred to histograms comparing two microorganisms, appearing in Exhibit CX 33C. Unknown to Dr. Demain, however, the histograms which appear in CX 33C do not represent histograms for the parent of SLS-K-7-68 strain or the isolates that were generated as a result of the ultraviolet radiation procedure that was used to produce SLS-K-7-68. Thus, those histograms do not support Dr. Demain's conclusion. CX 33C; RX 25C; Demain, Tr. 2179-2180.

FF D 186. Dr. Demain also admitted that if one used an artificial mutation technique, such as UV irradiation on a parent strain, obtained a higher producer, and determined that the higher producer could reproduce the higher yield, the probability is that the higher producer was obtained because of the mutagen, regardless of any comparison between the histogram of the parent and the histogram of the isolates, so long as the histograms are not identical. Demain, Tr. 2177-2178.

G. The Yields Asserted In The Examples Of The Kaken Reissue Patent Were Generated By Use Of The SLS-K-7-68 Strain

FF D 187. The '698 reissue patent specification contains Reference Examples 1 and 2, and Examples 1 through 4. RX 5, col. 4, l. 62 to col. 8, l. 52.

FF D 188. The Reference Examples and Examples state that the deposited 80614 strain was used in those Examples. RX 5;RX 877C, Miyazaki, Depo. Tr. (5/15/95) 53-54; Hutchinson, Tr. 1517; Kelber, Tr. 1951-1952; Demain, Tr. 2204-2209, 2199-2202.

FF D 189. Kaken admits that the only microorganism strain actually used in patent Examples 1-4 was the SLS-K-7-68 strain. RX 336 C, Kaken Resp. Int. 4; see also RX 673C, Kaken Resp. Req. Adm. 6-9; Order No. 16.

FF D 190. Examples 3 and 4 of the patent describe processes producing yields of 34,000 to 60,000 μg/ml, allegedly using the claimed invention. RX 5, col. 7, lines 39-41, col. 8, lines 40-48.

FF D 191. Not only Mr. M. Hara, but also two other named inventors, Dr. Miyazaki and Mr. Yoneda, as well as Dr. Demain, admitted that the yield improvement Kaken achieved was dependent upon both the strain and the media. RX 56C at 11; Hara, Tr. 296, 419; RPX 109C, Hara, Depo. Tr. 603-604; Yoneda, Tr. 617; RX 55C, Fig. 6, 14; Demain, Tr. 2170; RX 793C; Inaba, Depo. Tr. 409.

FF D 192. In Mr. M. Hara's 1983 Okochi Memorial Foundation article, he recognized that the microorganism plays a main role in the fermentation process. He recognized that the amount of production of an antibiotic is "largely increasable by varying the nature of the producing organisms." CX 1048 at 58; Hara, Tr. 273-274.

FF D 193. Mr. M. Hara testified that the number one factor in order to produce as much salinomycin as possible is to select a strain having high productivity. Hara, Tr. 273-274.

FF D 194. In 1974, Kaken found that the 80614 strain yielded only 9,000 to 14,500 μg/ml. Hutchinson, Tr. 1495-1496; RX 807C.

FF D 195. The wild-type strain is not capable of the yields recited in Examples 3 and 4 when fermented under the culturing conditions described in those Examples. Hutchinson, Tr. 1517-1518.

FF D 196. Dr. Demain testified that "the development of the oil medium allowed a much easier exploitation of strains so that they could demonstrate

their potential to a greater extent." However, Dr. Demain admitted that even with today's technology the deposited 80614 strain cannot achieve yields of 60,000 μg/ml. Demain, Tr. 2216.

FF D 197. In the time period before filing for patents on May 31, 1977 and June 1, 1977, Kaken's scientists, including the named inventors, chose to work exclusively with the SLS-K-7-68 strain in their yield improvement experiments because it showed better productivity compared to other strains. RX 807C; Hara, Tr. 180, 182-183; Yoneda, Tr. 579-581, 617.

FF D 198. The inventors used the SLS-K-7-68 strain to carry out the patent Examples. Order No. 16 (6/2/95), Undisputed Fact No. 4, at 12; RX 673C, Kaken Resp. Req. Adm. 6-9.

FF D 199. Mr. M. Hara and Mr. Yoneda testified that Example 3 of the reissue patent describes the best way they knew to practice the claimed invention. They and Dr. Miyazaki, stated this in affidavits submitted in opposition to the Hoechst Respondents' Motion for Summary Determination. RX 5; Hara, Tr. 161, 163, 169-170, 310, 443; Yoneda, Tr. 549, 586.

FF D 200. The SLS-K-7-68 strain was the strain used to carry out Example 3 of Kaken's patents. Order No. 16 (6/2/95), Undisputed Fact No. 4, at 12; RX 336C, Kaken Resp. Int. 4; RX 673C, Kaken Resp. Req. Adm. 6-9.

FF D 201. Mr. M. Hara and S. Yoneda were involved in generating the June 1, 1977 know-how report (RX 50C), which states that "mutants superior to SLS-K-7-68 have not been obtained as yet." They also were involved in generating the October 1976 know-how report (RX 48C) which refers to "[t]he superior mutant, SLS-K7-68 [sic]." Those writings, contemporaneous with the patent filing in 1977, further demonstrate that they considered the SLS-K-7-68

strain to be part of the best way they knew to carry out their invention. RX 48C at 2; RX 50C at 1; Hara, Tr. 298-299, 335-337; Yoneda, Tr. 563, 585.

FF D 202. The praise for the SLS-K strain that named inventors M. Hara and Y. Miyazaki gave in their 1980, 1982, 1983 and 1984 articles, which describe their earlier work, shows that they considered the SLS-K-7-68 strain to be part of the best way they knew to carry out their invention. RX 53C/RX 55C; RX 54C/RX 56C; RX 86C/RX 87C; CX 1048.

H. There Is Not Adequate Disclosure Of The SLS-K-7-68 Strain In The Kaken Patents, And The Patents Misleads Those Skilled In The Art Concerning The Best Microorganism Strain Used In The Invention

FF D 203. The '698 reissue patent and '942 parent patent disclose only one strain, the 80614 strain. RX 5.

FF D 204. The patents do not even mention the SLS-K-7-68 strain. RX 5.

FF D 205. Dr. Demain testified that in his patents, if he uses a mutant, he makes a public deposit of the microorganism or at least gives detailed information on how one could obtain the microorganism. Demain, Tr. 2196-2199. He also testified that if he says in a patent that he used a particular microorganism, then that is the microorganism he used. For example, if he says that a deposited microorganism was used, then he used that microorganism as deposited. Demain, Tr. 2198.

FF D 206. Example 3 of the patents discloses the use of the claimed method to obtain a yield of 60,000 μg/ml, the highest yield of any patent example. RX 5.

FF D 207. Example 4 of the patents discloses the use of the claimed method to obtain a yield of up to 39,000 μg/ml. RX 5.

FF D 208. The Examples of the '698 reissue patent state and disclose to one skilled in the art that the 80614 strain was used to carry out the process

reported in those Examples. RX 5; Demain, Tr. 2204-2205; Hara, Tr. 442-443; RPX 144C, Inaba, Depo. Tr. (6/2/95) 11; Hutchinson, Tr. 1517.

FF D 209. Kaken admits that each of Examples 1 through 4 was carried out with the SLS-K-7-68 strain. RX 673, Kaken Req. Adm. 6-9; see Order No. 16 at 12.

FF D 210. There is no indication in the Examples or the patents that any strain other than the deposited 80614 strain was used in carrying out the Examples. RX 5; Demain, Tr. 2199-2202, 2205-2209; Hara, Tr. 440-443; RX 877C, Miyazaki, Depo. Tr. (5/15/95) 53-54.

FF D 211. Kaken's May 1994 testing using 18% soybean oil showed an average yield of 9700 μg/ml for the 80614 strain. RX 98C; RPX-11C; Hutchinson, Tr. 1496-1498, 1523-1524; Inaba, Tr. 1238-1239. Kaken's December 1994 testing using 12% soybean oil showed a yield of 12,600 μg/ml for the 80614 strain, and its December 1994 testing using 18% soybean oil showed a yield of 16,700 μg/ml. Hutchinson, Tr. 1499-1500; RX 101C at 20648. The yields reported for the 80614 strain in the May 1994 and December 1994 testing are low yields as were the yields reported for original strain 6 as tested in 1974.

FF D 212. In another set of tests run in December 1994, Kaken reported salinomycin yields for the 80614 strain of 33,100 μg/ml in a jar test using a fermentation medium containing 35% oil and an ammonium salt. (35% oil is well outside of the range of the claims of the '698 reissue patent.) In the same report, in a side-by-side test, the production strain 2-57 gave a yield of 99,500 μg/ml in the fermentation medium containing 35% oil. Hutchinson, Tr. 1501-1507; RX 101 at 20658.

FF D 213. Kaken's 1995 testing reported in CX 1160, CX 1161 and CX 1169 has been excluded from evidence because late production of the tests denied Hoechst adequate discovery. Tr. 1705, 1714, 1794-1804. Kaken obtained a sample of strain FERM P-419 from the depository approximately one year before it conducted the 1995 testing. It is not clear whether the sample was subjected to monospore isolation before the testing. The testing is unreliable. Inaba, Tr. 2068-20074. Furthermore, regardless of what Kaken did to the strain obtained in April 1994 from the FERM depository, it was not able to reproduce the yields reported in Example 3 of the reissue patent using the deposited strain. Inaba, Tr. 2085.

FF D 214. As Mr. Inaba admitted, Kaken has never been able to repeat Example 3 of the patent with the deposited 80614 strain, which produces low yields. RPX 144C, 6/2/95, Inaba, Depo. Tr. 25, 110-111; Inaba, Tr. 1187, 2076-2077.

FF D 215. The specification of the patents reports that the claimed process obtained yields of 50,000 to 80,000 μg/ml. RX 5, col. 3, lines 4-12; RX 4, col. 3, 11. 3-11.

FF D 216. The 80614 strain has not and could not produce yields of 50,000 to 80,000 μg/ml. Inaba Tr. 1187, 2076-2077, 2085; RX 793C, Inaba Depo. Tr. 110-111; RPX 144C, Inaba, 6/2/95 Depo. Tr. 25.

FF D 217. Dr. Demain testified that with the 80614 strain, one could achieve higher yields using the medium taught in the patent than with media taught in the prior art. Demain, Tr. 2203.

FF D 218. As with the Examples, Kaken's patents do not disclose that any strain other than the 80614 strain was used to obtain yields of 50,000 to 80,000 μg/ml. RX 5.

FF D 219. The failure to indicate that a strain other than the disclosed 80614 strain, i.e., the undisclosed SLS-K-7-68 strain, was needed to obtain the yields of 50,000-80,000 μg/ml misleads one skilled in the art to believe the 80614 strain could obtain those yields. Hutchinson, Tr. 1785-1786.

FF D 220. The SLS-K-7-68 strain, a mutant of the 80614 strain, was not disclosed by implication. The specification of the patent does not describe any mutants. While the specification includes a general statement that strains used in the claimed invention include the 80614 strain, "its mutants artificially or naturally produced," and other Streptomyces strains, the specification does not describe any mutation techniques Kaken used to obtain its improved SLS-K strains, or identify any specific mutants (or even any other Streptomyces strains). RX 5, col. 3, lines 22-25; RX 4, col. 3, lines 21-24; Hutchinson, Tr. 1519; Hara, Tr. 181.

FF D 221. The reference to "mutants artificially or naturally produced" in the specification of the '698 reissue patent does not inform one skilled in the art that any strain other than the deposited 80614 strain was used in the Examples. RX 5, col. 3; Demain, Tr. 2208-2209.

I. Even With The Kaken Patents, Not Only Would It Take Those Skilled In The Art At Least As Long As It Took Kaken To Develop A Strain Comparable To The SLS-K-7-68 Strain In 1977 Or Today, They Might Never Obtain Such A Strain

FF D 222. Though Kaken's patents mention "mutants," they do not describe any details or procedure, or even any mutagenic technique, for obtaining any mutants from the 80614 strain. RX 5; RX 4; Demain, Tr. 2190-2191.

FF D 223. Drs. Hutchinson and Demain agreed that a research team in 1977-78 starting with the teachings of Kaken's patents (RX 5; RX 4) in front of them would have taken about the same amount of time that it took Kaken, and possibly even longer, to go from the wild-type strain to a strain capable of

commercial levels of antibiotic production. RX 5; RX 4; Hutchinson, Tr. 1476-1479; Demain, Tr. 2192-2195.

FF D 224. A mutant producing yields comparable to that of the SLS-K-7-68 strain could not readily be obtained by monospore isolation. Monospore isolation allows selection of strains naturally mutated. However, natural mutations occur rarely. Hara, Tr. 281.

FF D 225. In addition, monospore isolation does not guarantee isolation of a high-producing strain. RX 806C; RX 32 at 15534; Hara, Tr. 226, 406-409.

FF D 226. Ms. Nakamura used monospore isolation on the 80614 strain but was unable to develop a strain with high productivity. Hara, Tr. 209-211, 227.

FF D 227. In 1974-1975, Ms. Nakamura performed three sequential monospore isolations starting with original strain 6, isolating and testing a total of almost 900 isolates. The best strain she isolated after the final monospore isolation yielded only approximately 19,000 μg/ml. RX 806C; RX 25; Hara, Tr. 400-402.

FF D 228. Again in 1974-1975, Ms. Nakamura attempted to improve yield by performing monospore isolation. She performed four sequential monospore isolations starting with original strain 6, isolating and testing a total of over 1,000 isolates. After the final monospore isolation, Ms. Nakamura concluded that the final isolates were not good in terms of yield and therefore did not retain them. RX 806C; RX 32 at 15534; Hara, Tr. 405-408.

FF D 229. Similarly, artificial mutation techniques known in 1977 and even now do not guarantee isolation of a high-producing strain. In 1977, and currently, there is no guarantee of ever isolating a strain with the 50,000 to

80,000 μg/ml salinomycin yields that the SLS-K-7-68 strain exhibits because of the unpredictability of mutagenic techniques. Hutchinson, Tr. 1476.

FF D 230. When increases are seen in antibiotic production following treatment with a mutagen, they are typically small and occur infrequently. Hutchinson, Tr. 1444; RX 463 at 156.

FF D 231. Mutagens most commonly decrease the level of antibiotic production. Hutchinson, Tr. 1444, 1459.

FF D 232. Ms. Nakamura's efforts with mutation techniques demonstrate the unpredictability of those techniques. Starting with original strain 6, from 1974 to 1975, Ms. Nakamura used monospore isolation followed by ultraviolet irradiation to induce mutations for strain improvement. Well over 500 individual isolates were tested. The highest yielding isolates yielded only from 14,000 units to approximately 15,500 units. RX 806C; RX 25; Hara, Tr. 410-411.

FF D 233. In the mid-1970s, strain improvement programs were not a routine process. Hutchinson, Tr. 1449.

FF D 234. Strain improvement programs are time consuming, complex, circuitous, and labor-intensive, and the results are unpredictable. Moreover, different teams of investigators would use different combinations and techniques in an attempt to arrive at a desired goal in a strain improvement program. A considerable amount of judgment and skill is necessary in choosing paths to follow in a strain improvement program. Blind alleys and dead ends cannot be avoided by program design or the choice of a particularly unique mutagen. Hutchinson, Tr. 1449-1451, 1476; RX 806C.

FF D 235. As a strain improvement program progresses, the frequency at which increases in yield are observed usually markedly declines. Hutchinson, Tr. 1458-1459.

FF D 236. In the 1970s, as well as now, strain improvement programs require an unavoidably long period of time (on the order of years or even decades) to obtain improvements in antibiotic yield to commercially feasible levels. Hutchinson, Tr. 1455-1458; RX 411 at 993; RX 460 at 95-96; RX 463 at 158; RX 466 at 320; Demain, Tr. 2183-2185.

FF D 237. Mr. M. Hara testified that it would be very difficult to find a mutant strain that would significantly increase the productivity of salinomycin, comparing it to the similar difficulty in finding a new antibiotic. Hara, Tr. 185-186, 188; see also RPX 144C; Inaba, 6/2/95 Depo. Tr. 39-40.

FF D 238. Illustrating the difficulty in increasing yields of microorganisms through a strain improvement program, Dr. Demain stated in one of his articles that "a newly discovered aminoglycoside may be produced at very low levels, such as 10 micrograms per milliliter, and a traditional strain improvement program might take years to raise the titer to an economically feasible one, such as 10 milligrams per milliliter." RX 411, 993; Demain, Tr. 2184-2185.

FF D 239. As another example, with respect to improving the antibiotic penicillin yields from microorganisms, an article by Dr. Demain stated that it took about 24 years of strain improvement programs to go from about 1,000 to about 10,000 μg/ml using techniques such as monospore isolation and mutagenic techniques. Dr. Demain measured the length of time from the beginning of the program in 1946. RX 410, 179; Demain, Tr. 2186-2188.

FF D 240. The same article by Dr. Demain states that using monospore isolation and other mutagenic techniques for microorganisms to produce the antibiotic streptomycin, it took about 17 or 18 years to raise the yield from about 1,000 to about 8,000. That program started with a microorganism that was close to a wild-type strain, and included work for 7-10 years to double the yield from 1,500 to 3,000. RX 410, 180; Demain, Tr. 2188-2189.

FF D 241. Not only is success of a strain improvement program to develop a strain capable of producing commercial-level yields uncertain, but even if success ultimately is achieved, the amount of time the program takes to result in success is uncertain. Moreover, although progress usually is expected, the rate of progress is not predictable. Demain, Tr. 2183-2184. Hutchinson, Tr. 1449-1453.

FF D 242. Confirming the unpredictability of such programs, even Mr. M. Hara referred to M. K. Hara's ability to obtain a high-producing strain, in what Mr. Hara said he viewed as a onetime trial, as a "world record." Hara, Tr. 227-228.

FF D 243. Part of the unpredictability results from the nature of mutations. The outcome is random because a mutagen's effect cannot be guided, and both artificial and natural mutations involve purely random changes in the bacterial genome. Hutchinson, Tr. 1448, 1451-1452.

FF D 244. Kaken's own search for an improved salinomycin-producing Streptomyces microorganism evidences the unpredictability of strain improvement programs. Specifically, the identical procedures which resulted in the discovery of the SLS-K-7-68 strain were used a year earlier to try to progress from original strain 6 to the 17 series and then to try to progress to the 23 series. The result: a strain having an antibiotic yield lower than

original strain 6. Although identical methods were used for developing the SLS-K-7-68 strain, markedly different results were obtained, demonstrating the randomness of the process. Hutchinson, Tr. 1467-1470; RX 806C; RX 807C.

FF D 245. Dr. Demain concluded that it would be very hard to predict how long it would take another research team, starting with the teachings of the '698 reissue patent and the wild-type deposited strain, to develop the SLS-K-7-68 strain. RX 5; Demain, Tr. 2191. At trial, Dr. Demain called Mr. K. Hara's finding of the SLS-K-7-68 strain "lucky." Demain, Tr. 2189-2190.

FF D 246. Quite a bit of luck is involved in successfully finding an improved microorganism capable of producing high levels of antibiotic. Hutchinson, Tr. 1460.

FF D 247. Further evidencing the unpredictability of artificial mutation techniques, Mr. M. Hara felt that "luck was on" Kaken's scientists when Mr. K. Hara developed the high-producing SLS-K-7-68 strain by ultraviolet irradiation. Hara, Tr. 211. Like Dr. Demain, Mr. Hara later unconvincingly attempted to retract his testimony. Hara, Tr. 225-228.

FF D 248. Even after years of effort, there is no guarantee that a strain improvement program will result in the discovery of an improved microorganism strain capable of antibiotic production at a commercially acceptable level. Hutchinson, Tr. 1449-1450, 1454.

FF D 249. The process of strain improvement is analogous to the search for a needle in the haystack, except it is even more difficult than the search for a needle in a haystack because, unlike the needle, the microorganism target continually changes throughout the search as a result of the mutations. Hutchinson, Tr. 1453-1454; RX 464 at 252.

FF D 250. Some unsuccessful strain improvement programs never found microorganism strains capable of producing high levels of antibiotics. Hutchinson, Tr. 1454-1455.

FF D 251. It is entirely possible that in the mid to late 1970s, a person of ordinary skill in the art, starting with the wild-type strain, would have been unsuccessful in developing an improved strain capable of a commercial level of antibiotic production. Hutchinson, Tr. 1452-1453.

FF D 252. There is no guarantee or predictability that those of skill in the art, even with the '698 reissue patent (RX 5) in front of them, would have been as successful as Kaken in going from the wild-type strain to a strain capable of commercial levels of antibiotic production in the 1977-1978 time period. Hutchinson, Tr. 1479.

V. THE '698 REISSUE PATENT IS UNENFORCEABLE DUE TO INEQUITABLE CONDUCT

A. The SLS-K-7-68 Strain Was Not Deposited Because Kaken Viewed It To Be Of Significant Commercial Value And Wanted To Retain It As A Trade Secret

FF E 1. Most mutants are not patented and not deposited, but rather are kept as trade secrets. Demain, Tr. 2218.

FF E 2. Owners do not like to deposit their improved mutant strains, because it gives them to other people in a competitive business, and the owners obtain significant competitive advantages if they do not deposit the strains but keep them as trade secrets. Demain, Tr. 2217-2219.

FF E 3. Those skilled in the art must bear the onerous burden and expense of engaging in a strain improvement program to develop high-producing microorganism strains themselves if the owner of such a strain does not make it publicly available. Hutchinson, Tr. 1433; Demain, Tr. 2217-2219.

FF E 4. On more than one occasion, industrial owners of high-producing microorganism strains have refused to provide Dr. Hutchinson with samples of their strains. Hutchinson, Tr. 1432-1433.

FF E 5. Kaken did not in the 1970's, and does not today, make its production strains available to the public. RX 792C, Miyazaki Dep. Tr. 146-147.

FF E 6. Kaken considers production strains to be a very important asset. Hori, Tr. 895; RX 796C, Shibuya Dep. Tr. 57-60.

FF E 7. Kaken treats production strains as trade secrets because they are considered to be such an important asset. Inaba, Tr. 1290. Dr. Miyazaki stated that Kaken did not reveal high yielding production strains to the public. RX 792C, Miyazaki Dep. Tr. 146-147. Mr. Inaba, a Kaken scientist, testified that Kaken considered these production strains to be trade secrets and that they were not made publicly available. RX 793C, Inaba Dep. Tr. 6, 464. Mr. Kobayashi, Kaken's Director of New Product Development in the mid-1970s, also testified that Kaken considered its production strains to be a trade secret. RX 797C, Kobayashi Dep. Tr. at 33-34, 156-157, 201-202, 232-234. Kaken's President, Mr. Wakiyama, testified that it was Kaken's policy to maintain as a secret the production strains it uses to make antibiotics. RX 895C, Wakiyama Dep. Tr. at 121.

FF E 8. Kaken's production strains require "the highest level of secrecy and the highest level of stringent control." RX 797C, Kobayashi Dep. Tr. 232-233.

FF E 9. When Kaken provided production strains to its licensees, Kaken's basic policy was to try to maintain proprietary ownership rights in those production strains. RX 796C, Shibuya Dep. Tr. 57-60.

FF E 10. Mr. Kobayashi, the former head of Kaken's licensing department, was in charge of negotiating Kaken's salinomycin licenses with Hoechst, A. H. Robins Company ("Robins"), and Pfizer Corporation ("Pfizer"). RX 797C, Kobayashi Dep. Tr. 66-67.

FF E 11. Mr. Kobayashi testified that Kaken routinely included secrecy clauses in its contracts with licensees. RX 797C, Kobayashi Dep. Tr. 232-234.

FF E 12. Mr. Kobayashi testified that if he had forgotten to include a strict secrecy clause in a license agreement, he would be "disqualified as the head of the licensing department, [he] would be probably fired. And, furthermore, the president of [Kaken] would never give approval on such a request." RX 797C, Kobayashi Dep. Tr. 233-234.

FF E 13. Kaken's salinomycin licenses with Hoechst, [C] all state that the production strain "shall remain the property" of Kaken, require strict secrecy in connection with the strain, and place substantial restrictions on the licensee's use of the strain. [C]

[C]

[C]

[C]

[C]

[C]

FF E 14. Kaken's licenses contain these restrictions, although the agreements were entered into after the 80614 strain became publicly available. RX 257C; RX 385C; RX 275C; RX 276C; RX 901 at 58-59; RX 3.

FF E 15. The 80614 strain was not a production strain. The first production strain used at Kaken was the SLS-K-7-68 strain or a strain derived from SLS-K-7-68, and the production strains Kaken used through 1994 were all

descendants of SLS-K-7-68. RX 74C; RX 793C, Inaba Dep. Tr. 44-48; RX 788C, Hara Dep. Tr. 507-508.

FF E 16. Kaken has never publicly deposited an SLS-K strain. Kelber, Tr. 1931.

FF E 17. Kaken continued its efforts to maintain the secrecy of its production strain in 1990 when it sent a draft license agreement to Hoechst that asserted proprietary rights for Kaken in the production strain and contained restrictions on Hoechst's use and disclosure of the production strain. RX 474 at Articles 10 and 12; Hori, Tr. 905-906.

FF E 18. At least as late as December 19, 1991, Kaken asserted trade-secret rights in its production strain when it warned Hoechst that its agreement with Kaken prohibited Hoechst from providing the salinomycin production strain to any third party without prior written consent of Kaken. RX 476C at 2.

B. The Kaken Reissue Patent Examples Were Intentionally Falsified

FF E 19. The SLS-K-7-68 strain was the strain actually used to carry out the work reported in all the Patent Examples showing Kaken's claimed process. RX 675C, Kaken's Resp. to Respondents' Interog. No. 4. See Order No. 16, Established Fact No. 4; RX 673C, Kaken's Resp. to Respondents' Req. for Admis. Nos. 6, 7, 8, 9.

FF E 20. The Hoechst Respondents' Request for Admission No. 6, and Kaken's response thereto is, as follows:

> 6. An SLS-K strain was the strain actually used by Kaken when it carried out the work reported in Example 1 of the '698 reissue patent and the '942 patent.
>
> RESPONSE
> Admitted

RX 673 at 3.

FF E 21. The Hoechst Respondents' Request for Admission No. 7, and Kaken's response thereto is, as follows:

> 7. An SLS-K strain was the strain actually used by Kaken when it carried out the work reported in Example 2 of the '698 reissue patent and the '942 patent.
>
> RESPONSE
> Admitted

RX 673 at 3.

FF E 22. The Hoechst Respondents' Request for Admission No. 8, and Kaken's response thereto is, as follows:

> 8. An SLS-K strain was the strain actually used by Kaken when it carried out the work reported in Example 3 of the '698 reissue patent and the '942 patent.
>
> RESPONSE
> Admitted

RX 673 at 3.

FF E 23. The Hoechst Respondents' Request for Admission No. 9, and Kaken's response thereto is, as follows:

> 9. An SLS-K strain was the strain actually used by Kaken when it carried out the work reported in Example 4 of the '698 reissue patent and the '942 patent.
>
> RESPONSE
> Admitted

RX 673 at 4.

FF E 24. Kaken's process is described in the specifications of Japanese Patent Application Nos. 52-62802 and 52-63215, on which the '698 reissue patent in part relies for priority. The Japanese applications were drafted by Mr. Shibuya, a Kaken employee. RX 5; RX 277C; RX 796C, Shibuya Dep. Tr. 30-32, 37-38, 97-98, 165-166.

FF E 25. Two of the named inventors, Mr. M. Hara and Dr. Miyazaki, participated in the preparation of the Japanese patent applications by writing

draft examples for Mr. Shibuya that describe embodiments of Kaken's process. Embodiment 2 of the draft examples substantially tracks Example 1 of the '698 reissue patent, Embodiment 3 substantially tracks Example 3 of the patent, and Embodiment 4 substantially tracks Example 4 of the patent. RX 5, col. 5, line 30 to col. 6, line 16, col. 7, line 25 to col. 8, line 52; RX 277C; Hara, Tr. 243-245; RX 796C, Shibuya Dep. Tr. 30-32, 37-38, 97-98, 165-166, 273.

FF E 26. The draft examples prepared by M. Hara, list three strains: (1) the "80614 strain;" (2) the strain "divided" from the 80614 strain; or (3) the "improved mutant strain." RX 277C at 17762; RPX 97C at 17762; Hara, Tr. 245, 304; RPX 117C, Shibuya Dep. Tr. 276-277.

FF E 27. While preparing that draft example, M. Hara was aware of the information provided by his research group that formed the basis for Kaken's statement in the June 1, 1977 technical know-how report that it had not obtained mutants superior to the SLS-K-7-68 strain. RX 50C; Hara, Tr. 307, 309-310.

FF E 28. As established by the specification of the '698 reissue patent and the testimony of Drs. Miyazaki, Hutchinson, and Demain and Mr. Kelber, the '698 reissue patent discloses to one skilled in the art that the 80614 strain was used in the patent Examples and does not disclose the "improved mutant strain," SLS-K-7-68. RX 5, col. 5, 32, col. 6, lines 20-21, col. 7, line 25, col. 8, line 25; RX 877C, Miyazaki Dep. Tr. (5/15/95) 53-54; Hutchinson, Tr. 1517; Demain, Tr. 2204-2209, 2199-2202; Kelber, Tr. 1973. See RPX 144C, Inaba Dep. Tr. 11.

FF E 29. Mr. Shibuya was aware of the best mode requirement of U.S. patent law before filing the Japanese patent applications. RX 796C, Shibuya Dep. Tr. 82-83.

FF E 30. Mr. Shibuya testified that Mr. Kobayashi, a Kaken employee but not one of the named inventors, deleted the reference to the "improved mutants" from the patent application. RX 796C, Shibuya Dep. Tr. 181-183.

FF E 31. Mr. Shibuya's testimony does not provide any evidence of good faith since Mr. Shibuya did not know why the key words were deleted. RPX 117C, Shibuya Dep. Tr. 183-185.

FF E 32. Dr. Demain admitted that even with today's technology, the 80614 strain could not achieve the yield of 60,000 μg/ml reported in Example 3 of the '698 reissue patent. RX 5; Demain, Tr. 2216.

FF E 33. Dr. Demain's opinion is confirmed by testing Kaken conducted with the 80614 strain in April 1994 and December 1994 that produced an average yield of 9,700 μg/ml and a yield of 12,600 μg/ml, respectively. RX 96C at 21817; RX 793C, Inaba Dep. Tr. 351-352; RX 101C at 20648, 20656; RX 793C, Inaba Dep. Tr. 349-353, 367-369, 374.

C. Kaken's Attorney Misrepresented To The PTO Office That The Deposited Strain Was Used In The Patent Examples

FF E 34. Kaken filed its reissue application with claims 1-4 on January 29, 1993, containing Examples from the original '942 patent purporting to report work done with the 80614 deposited strain, along with the Inaba Declaration reporting tests with Kaken production strains 91-2-57 and 26-71. RX 793C, Inaba Dep. Tr. 108-110.

FF E 35. The United States Patent and Trademark Office ("PTO") issued an Office Action in the reissue prosecution on June 30, 1993, which rejected claims 1-4 under 35 U.S.C. § 112, first paragraph, because, among other things, "the microorganism is essential to the claimed invention" and "[t]he strains of Streptomyces albus used within the Examples of the specification have not been properly deposited." RX 901 at 144, 146.

FF E 36. In September 1993, Mr. Kelber wrote to his counterpart in Japan, Mr. Shimada, and asked if the 80614 strain had been deposited "or is otherwise available to those of skill in the art," and inquired if the two strains used in the Inaba Declaration examples "are publicly available in some fashion." RX 138C; Shimada, Tr. 670-671.

FF E 37. The September 1993 response to Mr. Kelber's letter from Mr. Shimada stated that the 80614 strain was deposited as ATCC 21,838, and that the US-91-2-57 and US-26-71 Inaba "strains are mutants of Streptomyces albus 80,614, and they are not deposited and thus not publicly available." RX 139C; Shimada, Tr. 677-678; Kudo, Tr. 1372-1373.

FF E 38. Mr. Kelber did not disclose the above information concerning the mutant strains to the Patent Examiner in the reissue prosecution. RX 875, Kelber Dep. Tr. 123-125.

FF E 39. Mr. Kelber's November 1, 1993 response to the June 30, 1993 Office Action stated that the 80614 strain was widely available, contained no disclosure that the SLS-K-7-68 strain was used in any Example, and did not disclose how the SLS-K-7-68 strain could be obtained or provide any disclosure that would enable one skilled in the art to use it. RX 901 at 151-156. See Witherspoon, Tr. 1849.

FF E 40. Kelber's November 1, 1993 Amendment responsive to the June 30, 1993 Office Action stated in pertinent part:

> The claims stand rejected under 35 USC § 112, first paragraph, on the grounds that the referenced microorganism, *Streptomyces albus* 80,614 has not been guaranteed as available. It should be noted that this microorganism has been deposited, with all restrictions or conditions on access thereto long irrevocably waived under ATCC Deposit 21,838. This deposit is referenced in U.S. Patent 3,857,948, and the deposit continues to be available to members of the public without restriction, which access will continue upon issuance

> of this patent. Enclosed herewith is the Promise of Unrestricted Distribution filed in connection with prosecution of the '948 Patent. It should be noted that this strain is widely available.

PX 901 at 152-53.

FF E 41. At his deposition, Kaken's attorney, Mr. Kelber admitted that as of the November 1, 1993 response to the June 30, 1993 Office Action, he knew that the deposited 80614 strain was not used in Example 3:

> Q. As of November 1, 1993, your response to the office action as of that date you had known or you knew that the strain used in example 3 of the patent was not the 80614 strain as deposited, correct?
>
> A. That's correct.

RX 875C, Kelber Dep. Tr. 123. See RX 875C, Kelber Dep. Tr. 22, 28.

FF E 42. Mr. Kelber knew in 1993 that Example 3 was performed using the concealed SLS-K-7-68 strain:

> Q. And you knew that the SLS-K-7-68 strain had been used in reality to generate the data in example 3, is that correct?
>
> A. I believe that's correct.

RX 875C, Kelber Dep. Tr. 123. See RX 875C, Kelber Dep. Tr. 15-18; Kelber, Tr. 1925; Kelber, Tr. 1950.

FF E 43. In the November 1, 1993 response to the June 30, 1993 Office Action, Mr. Kelber failed to tell the Patent Examiner that the deposited 80614 strain was not used in the Example. Instead, he expressly misrepresented that it was used, as reflected in his deposition testimony, as follow:

> Q. Now, the examiner was telling you that the strains used in the examples have not been properly deposited, and you wrote back to him indicating that 80614 was properly deposited, is that correct?
>
> A. That's correct.

RX 875C, Kelber Dep. Tr. 117.

FF E 44. Mr. Kelber knew during the reissue prosecution that the SLS-K-7-68 strain was "not identical" to the deposited 80614 strain. RX 875C, Kelber Dep. Tr. 21.

FF E 45. Mr. Kelber knew during the reissue prosecution that ultraviolet irradiation was used in the process of obtaining the SLS-K-7-68 strain. Kelber, Tr. 1919. See Kelber, Tr. 1916-1917; RX 48C.

FF E 46. Mr. Kelber knew during the reissue prosecution that ultraviolet irradiation was used in connection with microorganisms to induce mutation. Kelber, Tr. 1949-1950.

FF E 47. Mr. Kelber knew during the reissue prosecution that the use of ultraviolet irradiation increased the probability of mutation occurring. Kelber, Tr. 1950.

FF E 48. Mr. Kelber knew during the reissue prosecution that at least one of the inventors considered the SLS-K-7-68 strain to be a mutant. RX 875C, Kelber Dep. Tr. 123; Order No. 16, Established Fact No. 6.

FF E 49. Mr. Kelber knew during the reissue prosecution that the use of the term mutant in connection with the SLS-K-7-68 strain had originally been arrived at by one of the inventors of the '698 reissue patent. RX 50C; Kelber, Tr. 1922.

FF E 50. Mr. Kelber was never told before the issuance of the '698 reissue patent that the deposited strain could achieve the yields reported in Example 3. Kelber, Tr. 1930. See Kelber, Tr. 1973, 1975.

FF E 51. Mr. Kelber received a 1976 Kaken technical report (RX 48C) during the reissue prosecution which indicates that "[t]he superior mutant, SLS-K7-68 [sic], was obtained by UV irradiation." RX 48C; RX 875C, Kelber Dep. Tr. 36-38.

FF E 52. Mr. Kelber was provided with a June 1, 1977 Kaken technical report before the conclusion of the reissue prosecution which indicates that "mutants superior to SLS-K-7-68 have not been obtained as yet." RX 50C; RX 875C, Kelber Dep. Tr. 38-39.

FF E 53. Mr. Kelber knew during the reissue prosecution of the reference in the 1982 Miyazaki et al. article (RX 56) that the authors believed that the SLS-K-7-68 strain was significantly different from the parent strain. Kelber, Tr. 1920-1922; RX 56C; RX 57C.

FF E 54. Mr. Kelber knew during the reissue prosecution of publications by inventors dated after 1977 where at least two of the inventors had characterized the SLS-K strain as an improved strain that resulted in a dramatic increase in yield. RX 55, RX 56C, RX 57C; RX 875C, Kelber Dep. Tr. 14-15. Kelber, Tr. 1919-1920; Kelber, Tr. 1922.

FF E 55. Kaken never told Mr. Kelber that the statements by the inventors that the SLS-K-7-68 strain was significantly different from the parent or that the SLS-K-7-68 strain resulted in a dramatic improvement in yield were incorrect. Kelber, Tr. 1932.

FF E 56. Mr. Kelber knew during the reissue prosecution that the SLS-K-7-68 strain was not deposited in any public depository. Kelber, Tr. 1926, 1930, 1935.

FF E 57. Mr. Kelber knew during the reissue prosecution that Kaken considered the SLS-K-7-68 strain to be Kaken's property, although he also testified that there was some question as to whether it was properly considered a trade secret. RX 875C, Kelber Dep. Tr. 19.

FF E 58. Mr. Kelber knew during the reissue prosecution that the SLS-K-7-68 strain was developed prior to the time the first Japanese foreign

priority application to the '942 patent was filed. RX 875C, Kelber Dep. Tr. 15, 24-25; RX 57C.

FF E 59. Mr. Kelber did not disclose the above information to the PTO. RX 875C, Kelber Dep. Tr. 120-125.

FF E 60. Mr. Kelber knew during the reissue prosecution that the SLS-K-7-68 strain was used in the reissue Patent Example 3. Order No. 16, Established Fact No. 7.

FF E 61. The substantive facts, set forth in Established Fact Nos. 6 and 7 of Order No. 16 were not disclosed to the Patent Examiner, even though they are inconsistent with Complainant's argument made in response to the Examiner's rejection on the ground that the strains used in the Examples were not properly deposited. Witherspoon, Tr. 1850; Order No. 16, Established Fact Nos. 6 and 7.

FF E 62. Mr. Kelber knew during the reissue prosecution about the chronological chart in the articles by the inventor shown in Fig. 6 of RX 57, for example, which shows the time line and the period of years involved in the development of the invention. Kelber, Tr. 1923-1924; RX 57.

FF E 63. Mr. Kelber changed his testimony at trial in numerous material respects from that given at his deposition. See, e.g., Kelber, Tr. 1953-1955.

FF E 64. Mr. Kelber testified that he became aware, some time between the deposition itself and the beginning of June 1995, that his deposition testimony was not accurate. Kelber, Tr. 1955.

FF E 65. Mr. Kelber testified that his recollection regarding when he learned about the strain used in Example 3 changed after he reviewed the transcript of his deposition, his records of the litigation, the papers that

were reviewed, the reissue file, and the papers contained in it. Kelber, Tr. 1957.

FF E 66. Mr. Kelber had been litigating this case for at least 4½ months prior to his deposition and had been involved in preparation for the case for a substantial period of time prior to that. By the time of his deposition he had already worked on his prehearing brief. Kelber, Tr. 1955-1956.

FF E 67. Mr. Kelber's trial testimony also establishes inequitable conduct, because the '698 reissue patent did not issue until August 16, 1994 (RX 901). The reissue prosecution therefore continued well past April 1994, the date Mr. Kelber testified at trial that he acquired knowledge concerning the strain used in Patent Example 3. Kelber, Tr. 1916, 1955.

FF E 68. Regardless of whether Mr. Kelber credibly changed his earlier deposition testimony, at the very least Mr. Kelber admitted at the hearing that he heard about the SLS-K-7-68 strain during meetings in April 1994 with Kaken. Kelber, Tr. 1916.

FF E 69. Regardless of whether Mr. Kelber credibly changed his earlier deposition testimony, at the very least Mr. Kelber admitted at the hearing that when he learned in April 1994 that Example 3 was actually performed with a strain that was not deposited he did not provide that information to the Examiner. Kelber, Tr. 1938.

FF E 70. According to Mr. Kelber's trial testimony, before he learned of the information regarding Example 3 in April 1994, he believed Example 3 was performed with the deposited 80614 strain. Kelber, Tr. 1951-1952, 1973. Nevertheless, Mr. Kelber admitted at the hearing that when he learned in April 1994 that the data reflected in Example 3 did not indeed reflect work with the deposited strain, he did not suggest to Mr. Kudo or others at the meeting in

April 1994 that they test the deposited strain with the claimed invention. Kelber, Tr. 1973.

FF E 71. Regardless of whether he acquired the information in 1993 as he described in his deposition or in 1994 as he stated at the trial, Mr. Kelber did not tell the PTO that the SLS-K-7-68 stain was used in the work reported in Example 3. Kelber, Tr. 1953-1953.

FF E 72. Mr. Kelber also knew at least as early as April 1994 about the translation of the Miyazaki and Hara article that was produced from Kaken's files (RX 57), which was given to Mr. Kelber in April of 1994. RX 57; Kelber, Tr. 1921-1922.

FF E 73. Mr. Kelber did not disclose the Miyazaki and Hara article (RX 57) or its contents to the PTO, even though the reissue prosecution continued after April 1994. RX 901.

FF E 74. Even if Mr. Kelber credibly changed his testimony at the hearing to say that he did not know about the October 1976 Kaken technical report (RX 48C) until the April 1994 meetings with Kaken in Japan, Mr. Kelber at the very least knew about this report by April 1994. RX 48C; Kelber, Tr. 1913-1915.

FF E 75. Mr. Kelber did not disclose the October 1976 technical report (RX 48C) or its contents to the PTO, even though the reissue prosecution continued after April 1994. RX 901.

FF E 76. Mr. Kelber indicated at his deposition that he knew of another Kaken know-how report (RX 50C) prior to filing the reissue application. However, later he testified at the hearing that he was not aware of it prior to the filing of the reissue application and only became aware of it prior to the issuance of the reissue patent. RX 50C; Kelber, Tr. 1915-1916.

FF E 77. Mr. Kelber did not disclose any Kaken technical reports or their contents to the PTO, even though the reissue prosecution continued after April 1994. RX 901.

FF E 78. At the hearing, Mr. Kelber alleged for the first time that he was told at a meeting in Japan in April 1994 that it was Kaken's understanding that the SLS-K-7-68 strain was not a mutant. Kelber, Tr. 1917. However, at his deposition, Mr. Kelber testified that Kaken merely told him that it was "probably inaccurate" to characterize the SLS-K-7-68 strain as a mutant. Kelber, Tr. 1918.

FF E 79. Mr. Kelber said at his deposition that he was informed that Example 3 was not carried out with the 80614 strain as deposited. Later at the hearing, Mr. Kelber testified that it was explained to him at the April 1994 Kaken meeting that the 80614 strain as deposited is a wild type deposit and has a diverse population of microorganisms and one of the microorganisms drawn from that population was SLS-K-7-68, so SLS-K-7-68 was not deposited. Kelber, Tr. 1926.

FF E 80. Mr. Kelber testified at the hearing that although Kaken no longer considered SLS-K-7-68 a trade secret in April of 1994 because its existence had been known for more than ten years, Kaken still considered it their property. Kelber, Tr. 1930-1931.

FF E 81. Kaken introduced no documents indicating that the SLS-K-7-68 had become publicly available by April 1994. As of 1990 Kaken had proffered a draft license agreement to Hoechst wherein strict restrictions were maintained prohibiting distribution of the SLS-K-7-68 strain. RX 474C at Articles 10 and 12; Hori, Tr. 905-906; Kelber, Tr. 1931-1932.

FF E 82. Mr. Kelber testified at the hearing that he learned in April 1994 that Example 3 was not performed with the 80614 strain as deposited, and that even though it was after he submitted the Inaba Declaration, he did not alert the PTO to that fact because he believed that the Inaba Declaration does not rely on the Examples in the specification. Kelber, Tr. 1971-1972.

FF E 83. Mr. Kelber instructed Mr. Kudo in May 1992 not to test the 80614 strain because Kaken had already tested that strain in the patent Examples. RX 875C, Kelber Dep. Tr. 57-58; Kelber, Tr. 1972.

FF E 84. The PTO specifically focused on the Examples in the patent in its June 30, 1993 Office Action in which it rejected claims 1-4 under 35 U.S.C. § 112, first paragraph, because, among other things, "[t]he strains of Streptomyces albus used within the Examples of the specification have not been properly deposited." RX 901 at 146.

FF E 85. Mr. Kelber said that if he had known in November 1993 when he filed his response to the June 30, 1993 Office Action that it took four years to develop the strain and those of ordinary skill in the art could not obtain it through conventional methods and the four years were associated with intensive inventive efforts throughout that period to obtain the strain, then he would have passed the information along to the PTO. Kelber, Tr. 1959-1960.

FF E 86. Mr. Kelber was responsible for preparing the TEO motion in this investigation. Kelber, Tr. 1926-1927.

FF E 87. In the revised TEO Memorandum, Mr. Kelber indicated that, "[i]t is of course true that different yields, per se, will be obtained with different strains of *Streptomyces* and that Kaken had developed strains not deposited or reported that gave yields higher than those reported." RX 664; Kelber, Tr. 1927.

FF E 88. The undeposited and unreported strains referred to by Mr. Kelber in the revised TEO Memorandum included the SLS-K-7-68 strain. RX 664C; Kelber, Tr. 1927.

FF E 89. Mr. Kelber's statement in the TEO Memorandum was submitted in December 1994. RX 664C; Kelber, Tr. 1927.

FF E 90. After Mr. Kelber's statement in the TEO Memorandum, Respondents submitted a request for admission asking Kaken to admit to the statement made in the revised TEO Memorandum. Kaken refused to admit and stated "it is admitted that the revised memorandum contains the quoted phrase which was believed to be true when made. However, recently discovered documents and interviews with Mr. M. Hara, who is no longer a Kaken employee, have revealed that the strains believed not to have been deposited were, in fact, strains deposited at FERM-P. 419. The strains were selected for the experiments by standard selection procedures." RX 673C; Kelber, Tr. 1927-1928.

FF E 91. Mr. Kelber was unable to explain the inherent contradiction in his testimony that he believed in April 1994 that the SLS-K-7-68 strain was actually deposited, believed in December 1994 that the SLS-K-7-68 strain was not deposited, and indicated in response to a request for admission that he first learned that the SLS-K-7-68 strain was deposited as part of the 80614 strain in meetings with Mr. M. Hara in 1995. Kelber, Tr. 1927-1930.

D. Kaken's Attorney's Concealment Of The Falsity Of Patent Example 3 Furthered The False Impression That The High Yields Were Independent Of Strain

FF E 92. In the first official action, the Examiner rejected all of the claims under 35 U.S.C. § 112, first paragraph. The basis for this rejection was that the strains used within the Examples were not deposited. In this regard, the Examiner specifically stated:

> Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objections to the specification. The strains of Streptomyces albus used within the examples of the specification have not been properly deposited.

RX 901 at 146; Witherspoon, Tr. 1846-1847.

FF E 93. The microorganism is essential to the claimed invention and thus the Examiner required deposit of the strain used within the Examples of the specification. In this regard, the examiner stated:

> Since the microorganism is essential to the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, the requirements of 35 U.S.C. § 112, first paragraph may be satisfied by deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public.

RX 901 at 144 (emphasis added); Witherspoon, Tr. 1847.

FF E 94. Mr. Kelber in response to the official action did not contest the Examiner's holding that "the microorganism is essential to the claimed invention." RX 901. See Witherspoon, Tr. 1847-1848.

FF E 95. Mr. Kelber responded that 80614 strain had been deposited and thus was publicly available. There was no mention in Mr. Kelber's response that the SLS-K-7-68 strain was used in any of the patent Examples. RX 901 at 151-156; Witherspoon, Tr. 1849.

FF E 96. In responding to the Examiner's requirement that the strain used within the Examples of the specification be deposited, Mr. Kelber specifically stated:

> The claims stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the referenced microorganism, Streptomyces albus 80,614 has not been guaranteed as available. It should be noted that this microorganism has been deposited, with all restrictions or conditions on access thereto long irrevocably waived under ATCC Deposit 21,838. This deposit is referenced in U.S. Patent 3,857,948, and the deposit continues to be available

> to members of the public without restriction, which access will continue upon issuance of this patent. Enclosed herewith is the Promise of Unrestricted Distribution filed in connection with prosecution of the '948 patent. It should be noted that this strain is widely available.

RX 901 at 152-153.

FF E 97. Mr. Kelber knew during the reissue prosecution that at least one of the named inventors regarded the SLS-K-7-68 strain as a mutant strain and that this strain had not been deposited. The SLS-K-7-68 strain produced substantially higher yields in the claimed process than prior strains. Order No. 16, Finding Nos. 1, 5, 6 and 7; RX 8/5C, Kelber Dep. Tr. 123.

FF E 98. Mr. Kelber testified at trial that he believed that the PTO would look at the Inaba Declaration and at the Examples in the reissue application as further evidence that various strains worked in connection with the claimed method. Kelber, Tr. 1968.

FF E 99. Patent Example 3 of the '698 reissue patent states that "[t]he production amount of salinomycin at the end of cultivation is 60,000 μ/ml (salinomycin only)." CX 1 (RX 5) at col. 7, lines 39-41.

FF E 100. Kaken asserted to the PTO that the claimed invention gave particularly high yields of salinomycin. Example 3 was among the data that was asserted to the PTO as showing the high yields achieved by the claimed invention. Kelber, Tr. 1969-1970.

FF E 101. When Mr. Kelber learned during the reissue prosecution that the data reflected in Example 3 did not reflect that of the deposited strain, he did not suggest to Mr. Kudo or others at the meeting in April 1994 that they go back and test the deposited strain. Kelber, Tr. 1973.

FF E 102. Where a different strain was used than the strain disclosed to the PTO as having been used, Kaken's own expert, Dr. Demain admitted at his

deposition that he felt that such a practice was misleading. In his own patents, Dr. Demain consistently deposited those strains actually used in the Examples. RX 407; Demain, Tr. 2195-2198; RX 408; Demain, Tr. 2198-2199; Demain, Tr. 2210-2216.

FF E 103. In one of Dr. Demain's patents, U.S. Patent No. 3,681,198, he deposited the wild-type strain, as well as the sub-isolates that were probably the result of subsequent work using monospore isolation. RX 407; Demain, Tr. 2195-2196.

FF E 104. The Examples in Demain's U.S. Patent No. 3,681,198 specifically refer to the use of the deposited strains. When the patent indicates that the deposited strain was used, it was in fact the strain used in the Examples, although there was a reference to mutants elsewhere in the specification. RX 407; Demain, Tr. 2196-2198.

FF E 105. Another of Dr. Demain's patents, U.S. Patent No. 3,410,753, describes various mutant strains in the Examples. Dr. Demain deposited those mutants. RX 408; Demain, Tr. 2198-2199.

FF E 106. Dr. Demain admitted that in his own practice, he would not feel comfortable disclosing in his own patents that the deposited strain was used when in fact another strain had been used. Demain, Tr. 2210-2210.

FF E 107. Dr. Demain testified that if he were writing the patent he would tell the public what strains were used, because to do it any other way would be misleading. Demain, Tr. 2215-2216.

FF E 108. Dr. Demain testified that, no matter how long it took him to develop a strain like the non-deposited SLS-K strain yielding 60,000, he would not ever apply for a patent and tell the PTO that he got such yields with the deposited strain. Demain, Tr. 2212-2214.

FF E 109. Dr. Hutchinson would not be comfortable applying for a patent that did not accurately describe the strain used in the Examples. Hutchinson, Tr. 1508.

FF E 110. Dr. Hutchinson agrees with Dr. Demain's deposition testimony that he would tell the public in his own patents the identity of the strain he used in the patent Examples. Hutchinson, Tr. 1509-1510.

FF E 111. Dr. Demain admitted at the hearing that if he had developed, by whatever means, a strain that was different from the deposited strain, he would not feel comfortable indicating in his patents that the deposited strain was used when in fact the strain that he had developed was used. Demain, Tr. 2210-2210.

FF E 112. Dr. Demain testified that he would either deposit the strain or provide instructions in the patent on how to obtain the mutant. Demain, Tr. 2211-2212.

FF E 113. Dr. Demain admitted that no matter how long it took him to develop the SLS-K strain yielding 60,000 μg/ml, which could not be obtained with the deposited strain, he would not ever apply for a patent and tell the PTO that he got such yields with the deposited strain. Demain, Tr. 2212-2214.

FF E 114. Dr. Hutchinson agrees with Dr. Demain's deposition testimony that if he were the developer of a strain used in a patent example, he would put the strain number in the patent example, no matter how long it took him to develop the strain. Hutchinson, Tr. 1510-1511.

FF E 115. Dr. Demain said that if he were writing the patent he would tell the public what strains were used, because to do it any other way would be misleading. Demain, Tr. 2215-2216.

FF E 116. Dr. Hutchinson agrees with Dr. Demain's deposition testimony that to fail to disclose the strain that was used in the patent examples would be misleading. Hutchinson, Tr. 1510.

E. The Kaken Reissue Application And The Inaba Declaration Were Filed To Avoid The Berg Patent

FF E 117. According to the papers submitted with the application to reissue the '942 parent patent, Kaken filed the reissue application because it was "possible to interpret the claims of the . . . '942 patent as embracing subject matter described in U.S. Patent 4,035,481 [the Berg patent]." RX 901 at 16, ¶ 3.

FF E 118. A preliminary amendment submitted with the reissue application reaffirmed that Kaken filed the reissue application "to resolve any question of patentability" over the Berg patent. RX 901 at 61.

FF E 119. In the Preliminary Amendment, Kaken amended the claims of its original '942 patent to require the presence of at least 12% fatty acid or its precursor. Kaken relied on the Inaba Declaration to avoid a rejection over the Berg patent by arguing that the claimed method, as amended, produced yields unexpectedly greater than the amount of oil used in the Berg patent. RX 901 at 61-62; Witherspoon, Tr. 1844-1845.

FF E 120. Relying on the Inaba Declaration to argue patentability of the claimed process over the Berg patent, Kaken's attorney stated in the preliminary amendment that:

> Applicants have endeavored, through comparative testing, reflected in the Declaration of Inaba, to demonstrate the patentable distinction between the claims as amended above and the teaching of the prior art. Thus, the addition of such a minor amount as 0.46% of refined soy bean oil does not influence the production of salinomycin in any respect. In contrast, more substantial amounts, including the 12% by weight herein, confers on the process a dramatic increase in yield, that could not be predicted by those of skill in the art. This enhanced yield not only could

> not have been predicted by those of skill in the art based [sic, on] the prior art, see paragraph 5 of the Inaba Declaration, but is of substantial commercial significance, see paragraph 4. Accordingly, the Reissue claims, as presented, are believed to patentably define over all prior art of which Applicants are aware, and are in condition for examination.

RX 901 at 61-62.

FF E 121. Mr. Kelber alerted Kaken of the desirability to demonstrate a sharp improvement in yield when operating within the claimed range of at least 12% fatty acid or its precursor. RX 124C; Kelber, Tr. 1962-1963.

FF E 122. Mr. Kelber anticipated that absent such a showing of a sharp improvement within the claimed range, the reissue claims would be rejected. Kelber, Tr. 1963.

FF E 123. Mr. Kelber knew in May 1992 that to get broad claims, Kaken would have to test more than one strain and more than one fatty acid or its precursor. Kelber, Tr. 1966.

FF E 124. When Mr. Kelber met with Mr. Kudo on May 12, 1992, he recommended conducting additional testing in connection with the reissue application for the purpose of getting quick allowance of the case. RX 121C; Kelber, Tr. 1965-1966; Kelber, Tr. 1963.

FF E 125. The Berg Example 21 discloses other carbon sources (other food sources) which were not included in the testing submitted to the PTO by Mr. Inaba. Inaba, Tr. 1172, 1260-1263.

FF E 126. The culture medium for antibiotic production shown in Example 21 of Berg includes 0.46% oil as well as 9.5% carbohydrate. Moreover, the Berg patent discloses various carbohydrates which can be used in a culture medium for antibiotic production. Fructose is included among those carbohydrates. RX 95, col. 16, lines 55-59, col. 33, line 56 to col. 34, line 8; Inaba, Tr. 1310; Inaba, Tr. 1265.

FF E 127. However, Mr. Inaba testified that, even though Example 21 of the Berg patent also uses a significant amount of carbohydrate as an additional carbon source, the test run in his declaration that was intended to represent the Berg patent did not have such an additional carbon source. Inaba, Tr. 1263; RX 793C, Inaba Dep. Tr. 250, 591-595.

FF E 128. Mr. Inaba first said Kaken's old data (CX 147C) caused him to exclude the carbohydrate, but he later admitted on cross-examination that this old data (CX 147C) formed no basis whatsoever for his decision not to include a carbohydrate source. CX 147C; Inaba, Tr. 1225-1229.

FF E 129. For a microorganism to produce salinomycin, it needs a carbon source as food. Within a certain range, the more carbon source (food) provided, the more salinomycin production. Inaba, Tr. 1262; Hara, Tr. 140; Hara, Tr. 155; Hutchinson, Tr. 1680.

FF E 130. Since the carbon source is food for the microorganism, the test that the Inaba Declaration told the PTO was representative of the Berg reference effectively starved the microorganism. Mr. Inaba admitted at trial that in his testing said to be representative of Berg, the microorganism was starved in that test. Inaba, Tr. 1263, 1266; RX 793C, Inaba Dep. Tr. 249-250; Hutchinson, Tr. 1601.

FF E 131. It came as no surprise to Mr. Inaba that the microorganism would not produce much salinomycin since it was only provided with 0.5 percent soybean oil in the experiment which was said to be representative of Berg. Inaba, Tr. 1263; Hutchinson, Tr. 1602-1603.

FF E 132. Mr. Inaba admitted that if an additional carbohydrate carbon source was added as described in Berg, the salinomycin yield would be higher. Inaba, Tr. 1263-1264.

FF E 133. In tests using such an additional carbohydrate carbon source disclosed in Berg (i.e., fructose), Kaken, using one of the same strains tested in the Inaba Declaration (91-2-57), obtained a yield of about 5,000 μg/ml. This should be compared to 210 μg/ml reported in the Inaba Declaration for the test run said to be representative of Berg. RX 793C, Inaba Dep. Tr. 600-603; RX 96 at 21812; Inaba Tr. 1306-1310.

FF E 134. Mr. Inaba did not tell the Examiner that Kaken starved the microorganism in the experiment said to be representative of Berg. Inaba, Tr. 1305-1306.

FF E 135. In rejecting the claimed process directed to at least 12% fatty acid or its precursor as prima facie obvious over the Berg patent, the Examiner stated:

> It would have been obvious to one of ordinary skill in the art to use the method as taught by Berg et al. to enhance the production of antibiotics given that the antibiotics were being produced by bacteria of the same genus. It has not been shown that the amount of fatty acid being added to the medium would greatly affects [sic] the enhancement of the antibiotic production. Applicants have not demonstrated the criticality of adding at least 12% fatty acid.

RX 901 at 148-149.

FF E 136. The Examiner did not consider the Inaba Declaration when she made the statement in the first Office Action of June 30, 1993 that it had not been shown that the amount of fatty acid being added to the medium would greatly affect the enhancement of antibiotic production. Kelber, Tr. 1978-1979.

FF E 137. In response to the Examiner's obviousness rejection, Kaken's attorneys argued that:

> The Declaration of Inaba adequately demonstrates that when culturing at values typical of Berg, that is well below 12%, inferior results are obtained. Contrast the maximum production

> obtained at values of 1%, 0.5% and 0%, which are insignificant in terms of microgram/gram, whereas an increase to 12% results in an increase of two orders of magnitude. This is nowhere predicted in the art, and wholly unobvious, see the Declaration of Inaba . . . . Clearly, the claimed invention has been demonstrated to be unobvious over Berg, and withdrawal of the rejection based thereon is respectfully requested.

RX 901 at 155-156.

FF E 138. Kaken clearly relied on the alleged unexpected differences in yield between, on the one hand, the claimed process and, on the other, the amount of oil used in the Berg process. RX 901 at 155.

FF E 139. The Patent Examiner also rejected the reissue claims because the disclosure was not enabling for all strains and all fatty acids. The rejection stated:

> Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited [to] the specific strain of *Streptomyces albus* exemplified within [the] specification and a fatty acid content of 12-20%. See M.P.E.P. §§ 706.03(n) and 706.03(z).
>
> It is not clear that all strains of *Streptomyces albus* have been adequately enabled since not all strains found to carry out the same activity with regard to salinomycin production.

RX 901 at 146-147 (emphasis added).

FF E 140. In response to the Examiner's rejection that the disclosure did not enable all strains, Kaken relied on the Inaba Declaration to contend that the extraordinary high yield achieved by the claimed process could be obtained with all microorganisms. RX 901 at 153-154.

FF E 141. In this regard, Kaken contended that:

> The claims also stand rejected for lack of enablement, as the claims are not limited to the specific strain reflected in the examples. With respect to this issue, attention is respectfully directed to the Inaba Declaration, in particular paragraphs 3 and 4, and report no. 4 of the attachment to the Inaba Declaration, which specifically concludes that all microorganism strains capable of producing salinomycin are effective in the invention.

> The invention is not strain speciric, provided a salinomycin-producing streptomyces microorganism is employed.

RX 901 at 153-154 (emphasis added).

FF E 142. The Inaba Declaration also alleged that the "startling and unobvious improvements" were independent of strain and independent of the source of fatty acid or its precursor:

> In each of tests 1-4, substantial improvements in yield are obtained where the fatty acid or its precursor content in the medium is at least 12%, as contrasted with the prior art process of U.S. Patent 4,035,481 [the Berg patent], using less than 1% fatty acid or its precursor. Thus, independent of microorganism strain, the source of fatty acid or its precursor, ammonium substance employed, culturing Streptomyces microorganisms capable of producing salinomycin in a medium containing at least 12% fatty acid or its precursor gives rise to startling and unobvious improvements in yield of the salinomycin obtained.

RX 901 at 28, ¶ 4 (emphasis added).

FF E 143. Kaken clearly relied on the evidence of the Inaba Declaration to allege a wide disparity between the claimed process and the prior art process. Kaken also clearly relied on the Inaba Declaration to show that such unexpected increases in yield over the prior art were independent of both strain and fatty acid or fatty acid precursor used. In this regard, Kaken stated that:

> Applicants have demonstrated that the claims are enabled across their entire breadth, by Declarative evidence, and have similarly shown, by direct comparison, that the claimed invention is unobvious over the teachings of the prior art.

RX 901 at 156.

FF E 144. The large disparity in yield between the prior art process and the claimed process was a result of starving the microorganism in testing said to be representative of the Berg process, and using the best strains with the best oils for the claimed process. Inaba, Tr. 1262-1264; Hutchinson,

Tr. 1601-1602; Hutchinson, Tr. 1614-1615; Hutchinson, Tr. 1624-1625; Hutchinson, Tr. 1601-1602.

FF E 145. Mr. Inaba made no attempt in his comparison test to optimize the yield achieved by the Berg patent process. Indeed, Mr. Inaba's test is not fairly representative of the Berg patent. Inaba, Tr. 1269-1270; Hutchinson, Tr. 1599-1602; Inaba, Tr. 1268-1270.

FF E 146. Mr. Inaba knew there was not much meaning to directly compare the claimed invention to a fermentation where only .5% carbon source was used. Tr. 1613-1614.

FF E 147. In the testing submitted to the PTO, Mr. Inaba selected conditions to maximize the differences in salinomycin production between the prior art Berg process and Kaken's claimed process. The tests were designed to be as "appealing" as possible in terms of showing a "large difference" between the prior art process and the claimed process, and to obtain a result that was "clear-cut". Inaba, Tr. 1269-1270; Tr. 1267-1268; RX 793C, Inaba Dep. Tr. 247-249.

FF E 148. Mr. Inaba's failure to duplicate the Berg patent Example dramatically increased the difference in yield reported for the claimed invention as compared to the yield reported for the Berg patent Example. Hutchinson, Tr. 1614-1615.

FF E 149. Kaken utilized a trade secret [C] in the tests that were supposed to address the Berg patent. The use of [C] [C] in the Inaba Declaration further magnified the differences in yield reported between the Berg patent Example and the claimed invention because the addition of [C] could not increase the yield of a starving microorganism. Hutchinson, Tr. 1609-1611.

FF E 150. Although [C] was used in the Inaba Declaration testing, the Inaba Declaration does not indicate that [C] [C] because Kaken considered the substance a trade secret. Thus, the patent examiner was not aware that cobalt sulfate was used. Inaba, Tr. 1180; RX 793C, Inaba Dep. Tr. 251-261; Hutchinson, Tr. 1611-1612; Hutchinson, Tr. 1616-1617; Hutchinson, Tr. 1611.

FF E 151. Mr. Inaba testified that [C] is used at Kaken's Shizuoka facility because the water in that area, unlike the water in other locations, lacks [C] . Inaba, Tr. 1181-1182.

FF E 152. Contrary to Kaken's representations to the PTO, high yields of salinomycin cannot be achieved independent of strain and fatty acid or its precursor. If other strains or other fatty acids or fatty acid precursors had been used in the Inaba Declaration testing as representative of the claimed invention, far lower antibiotic yields would have resulted. Hutchinson, Tr. 1524-1525, 1623.

FF E 153. High yielding industrial production strains are necessary to achieve the yields reported in the Inaba Declaration and in the '698 reissue patent. A specific high-yielding salinomycin-producing strain, such as the SLS-K-7-68 strain, is necessary to give rise to the high salinomycin yields reported in the '698 reissue patent and the Inaba Declaration. Hutchinson, Tr. 1525; Hutchinson, Tr. 1624.

FF E 154. The tests reported in the Inaba Declaration do not represent the yields that would be achieved by using different fatty acids that fall within the language of claim 2 of the '698 patent such as, for example, stearic acid or other animal fats that harden easily. Hutchinson, Tr. 1624-1625.

FF E 155. The tests reported in the Inaba Declaration do not represent the yields that would have been achieved using different strains falling within the language of claim 2 of the '698 patent, for example, strain 80614. Hutchinson, Tr. 1624-1625.

F. The False And Misleading Representations In Connection With The Inaba Declaration Were Material To The Prosecution Of The Kaken Reissue Patent

FF E 156. The Inaba Declaration was used for two purposes: (1) to submit purported comparative testing to argue patentability over the prior art Berg patent; and (2) as a basis to support an argument to overcome a rejection under 35 U.S.C. § 112, first paragraph. RX 901. See Witherspoon, Tr. 1832-1833.

FF E 157. The Office Action of June 30, 1993, rejected all of the claims as containing obvious subject matter over the teachings of the Berg patent. RX 901 at 148-49.

FF E 158. The Patent Examiner also rejected the reissue claims because the disclosure was not enabling for all strains. The rejection stated:

> Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited [to] the specific strain of *Streptomyces albus* exemplified within [the] specification and a fatty acid content of 12-20%. See M.P.E.P. §§ 706.03(n) and 706.03(z).
>
> It is not clear that all strains of *Streptomyces albus* have been adequately enabled since not all strains found to carry out the same activity with regard to salinomycin production.

RX 901 at 146-147 (emphasis added).

FF E 159. Kaken relied on the Inaba Declaration to overcome the Examiner's rejections for obviousness and lack of enablement. In this regard, Kaken stated that:

> Applicants have demonstrated that the claims are enabled across their entire breadth, by Declarative evidence, and have similarly

shown, by direct comparison, that the claimed invention is unobvious over the teachings of the prior art.

RX 901 at 156.

FF E 160. The Patent Examiner thereafter withdrew his rejections of the claims and allowed the '698 reissue patent. RX 901 at 160.

G. Kaken Suppressed Material Prior Art

FF E 161. Osamu Kudo has worked in Kaken's Legal Affairs Department (previously called the Patent Department) since 1976. Kudo, Tr. 1314.

FF E 162. Mr. Kudo was involved in the prosecution of the U.S. patent application that issued as the '942 patent and its foreign counterparts, including its European counterpart patent application. Kudo, Tr. 1315.

FF E 163. During the prosecution of the European counterpart patent application, the European Patent Office cited references labeled "NL-A-75 08629" and "NL-A-75 03905," corresponding to U.S. Patent No. 3,992,263 to Dietrich et al. (RX 115) ("the Dietrich patent") and British Patent No. 1,500,965 (RX 148) ("the British '965 patent") respectively, in a search report issued in 1978. RX 892 at 52-53; RX 520; RX 837 at 174; Shimada, Tr. 698-699.

FF E 164. The Dietrich patent discloses the use of up to 16% oil as a carbon source and an ammonium salt in the fermentation of the antibiotic moenomycin. Hutchinson, Tr. 1558-1560, 17; RX 115 at col. 2, lines 24-32; col. 2, line 64 to col. 3, line 5.

FF E 165. The 1978 European Search Report listed both the Dietrich patent and the British '965 patent as falling within category "X", meaning that it was "particularly relevant." Shimada, Tr. 683-685, 698-699; Kudo, Tr. 1315-1317.

FF E 166. The '965 British patent states that the complete specification was published on February 15, 1978. RX 148.

FF E 167. Mr. Kudo did not provide the Dietrich patent to the United States Patent and Trademark Office during the pendency of the '942 application, which did not issue until July 15, 1980. Kudo, Tr. 1316-1317; RX 901 at 14.

FF E 168. Mr. Kudo also was the person at Kaken primarily responsible for the reissue prosecution for the '698 reissue patent and was involved in almost all the substantial aspects of the prosecution for that reissue application. Kudo, Tr. 1326, 1368; RPX 120C, Ikemoto Dep. Tr. 54-55, 80-81.

FF E 169. T.S. International Corporation, headed by Yukiyasu Shimada, is a company that files and prosecutes foreign patent applications for Kaken Pharmaceutical Company. Shimada, Tr. 634.

FF E 170. The law firm of Oblon, Spivak, McClelland, Maier and Neustadt ("the Oblon firm") is a U.S. associate of T.S. International. Shimada, Tr. 634.

FF E 171. T.S. International also was involved, along with the Oblon firm, in prosecuting the reissue application that resulted in the '698 reissue patent. Shimada, Tr. 634.

FF E 172. Since at least 1982, it has been the general practice of T.S. International to immediately send to Kaken's United States patent attorneys, the Oblon firm, prior art cited by the European Patent Office in foreign counterparts to the United States patent applications because of the duty of disclosure in the U.S. PTO. Shimada, Tr. 682-685, 690, 694-695, 734.

FF E 173. In late 1991 or early 1992, before the filing of the reissue application for the '698 patent, Mr. Kudo sent the Dietrich patent (as well as

other prior art references that Hoechst had provided to Kaken) to T.S. International, which then sent the prior art references to the Oblon firm for citation to the U.S. PTO. RX 114C; RX 112C; Kudo, Tr. 1320-1321.

FF E 174. Therefore, by late 1991 or early 1992, the Dietrich patent and the other references cited by Hoechst were provided to the Oblon firm and Mr. Kudo expected the Oblon firm to cite those references to the U.S. PTO when the reissue application was filed. Kudo, Tr. 1319-1321, 1377.

FF E 175. In addition, Mr. Kelber was aware in early 1992 of a letter from Mr. Shibuya to Mr. Shimada that referred both to meetings between Kaken and Hoechst and certain prior art, including the Dietrich patent, that had been provided by Hoechst to Kaken. RX 112C; Kelber, Tr. 1979; RX 113C.

FF E 176. Thus, by January 1992, roughly a year before he filed the reissue application, Mr. Kelber already had the Dietrich patent. Kelber, Tr. 1980.

FF E 177. When the reissue application was filed, the Oblon firm was aware of the importance of early disclosure of any known prior art. RX 145C; Shimada, Tr. 686.

FF E 178. The Oblon firm sent a letter to Mr. Shimada in March 1993 reminding him of the importance of early disclosure of any known prior art. RX 145C; Shimada, Tr. 686.

FF E 179. Mr. Shimada forwarded to Kaken instructions that he got from the Oblon firm in July 1993 regarding the citation of prior art. RX 146C; Shimada, Tr. 686-688.

FF E 180. Page 16323 of RX 146 represents the policy of the Oblon firm concerning the submission of prior art. That policy noted that relevant prior art includes prior art cited in foreign search reports, such as the European

Patent Office search report, discussed above. Kelber, Tr. 1981-1982; RX 146 at 16323.

FF E 181. Nevertheless, the Oblon firm did not cite the Dietrich patent to the U.S. PTO when the reissue application and first Information Disclosure Statement were filed. Kudo, Tr. 1321; RX 901 at 63-64. The first Information Disclosure Statement filed during the prosecution of the '698 patent disclosed the Berg U.S. patent (and its Japanese counterpart), for consideration by the U.S. PTO. RX 901 at 63-64; Kelber, Tr. 1979-1980.

FF E 182. The undisclosed prior art known to Kaken at the time of filing the first Information Disclosure Statement included the Dietrich patent deemed by the European Patent Office, in a European Search Report dated August 31, 1978, to be "particularly relevant." Witherspoon, Tr. 1838-1839; RX 901 at 174, 241.

FF E 183. Mr. Kudo did not realize that the Oblon firm had not cited the Dietrich patent to the U.S. PTO until after a January 12, 1994 Notice of Allowance in the reissue application had issued. Kudo, Tr. 1321.

FF E 184. After issuance of the January 12, 1994 Notice of Allowance and at Mr. Kudo's instructions, T.S. International sent a letter to the Oblon firm, dated February 28, 1994, that instructed the Oblon firm to submit additional prior art references to the U.S. PTO either by filing a file wrapper continuation application or by requesting reexamination after permitting the reissue application to issue as a reissue patent. RX 144C; Kudo Tr. 1321; RX 354C.

FF E 185. Thus, as of February 28, 1994, Kaken wanted to submit a number of prior art references, including the Dietrich patent, to the U.S. PTO so

that the Examiner would consider the references. RX 354C; Hori, Tr. 913-914; RX 144C.

FF E 186. Kaken initially contemplated that the U.S. PTO would substantively consider these references, and Kaken's attorneys provided advice as to the best way to achieve such review. RX 144C; RX 149C; Shimada, Tr. 698-699, 705-710.

FF E 187. A March 4, 1994 letter from Mr. Kelber to Mr. Shimada indicates that "I have spoken with Mr. Oblon on this matter, and understand the desire to have the references secured," which reflects Mr. Shimada's desire to have the references in his February 28, 1994 letter put before the U.S. PTO so they could be substantively considered. RX 144C; RX 149C; Shimada, Tr. 705-707.

FF E 188. In his March 4, 1994 letter, Mr. Kelber recommended procedures for submitting the prior art that would have ensured its substantive review by the U.S. PTO. RX 149C; RPX 130C, Kelber Dep. Tr. 159-160.

FF E 189. Specifically, Mr. Kelber's letter to Mr. Shimada identified three ways of getting the cited art before the U.S. PTO for consideration. RX 149C; Shimada, Tr. 707-709.

FF E 190. The first option was to let the reissue application issue and then file a request for a reexamination proceeding to put the art before the U.S. PTO. RX 149C; Shimada, Tr. 709; Kelber, Tr. 1987.

FF E 191. Kaken never filed for reexamination. Kelber, Tr. 1987.

FF E 192. The second option described in Mr. Kelber's letter was not to let the reissue application issue, but file a file wrapper continuation application so the U.S. PTO would have time to consider substantively the prior art. RX 149C; Shimada, Tr. 709.

FF E 193. The third option described in Mr. Kelber's letter to Mr. Shimada was, while the reissue application was pending, to fail to submit the supplemental declaration required by the U.S. Patent Examiner so he would issue a rejection and the art could then be placed before the Examiner. RX 149C; Shimada, Tr. 709.

FF E 194. All of the options expressed by Mr. Kelber in his letter of March 4, 1994 to Mr. Shimada regarding submission of the prior art to the U.S. PTO would have resulted in the Examiner substantively considering the prior art. Kelber, Tr. 1984; RX 149C.

FF E 195. Mr. Kelber's letter to Mr. Shimada recommended pursuing the third option. RX 149C; Shimada, Tr. 710.

FF E 196. On deposition, Mr. Kelber testified that he believed he had read the prior art before making his recommendation in his March 4, 1994 letter to Mr. Shimada. However, at the hearing, Mr. Kelber testified that he was uncertain as to whether he had reviewed all of the references cited before making his recommendation in the letter to Mr. Shimada. RX 144C; RX 149C; Kelber Tr. 1982-1984.

FF E 197. On March 8, 1994, Mr. Shimada responded to Mr. Kelber's letter by instructing him to proceed with the third option so that the art could be considered by the U.S. PTO. RX 150C; Shimada, Tr. 710-711.

FF E 198. Thus, Kaken initially chose an option, recommended by Mr. Kelber, to have the prior art references substantively considered by letting the Examiner issue a rejection. Shimada, Tr. 709-711; RX 149C; RX 150C.

FF E 199. By mid-March of 1994, however, Kaken had changed its plan and instead took action to ensure that the reissue patent would be issued as soon as possible. Shimada, Tr. 711; RX 834C.

FF E 200. Kaken did not attempt to submit any additional prior art references for substantive consideration by the U.S. PTO. RX 153C; RX 154C.

FF E 201. Specifically, a second Information Disclosure Statement, filed on March 18, 1994, disclosed several prior art references, including the Dietrich patent and the British '965 patent, that were known to Kaken and its attorneys prior to the filing of the first Information Disclosure Statement. RX 901 at 173-268; Witherspoon, Tr. 1837-1838.

FF E 202. Thus, Kaken could not make the certification required by the U.S. PTO that it did not have the prior art more than three months before its submission with the second Information Disclosure Statement. Kelber, Tr. 1988.

FF E 203. As a result, when Mr. Kelber submitted the prior art references to the U.S. PTO, he and Kaken had "the foreknowledge that they . . . [would] not be considered in the ordinary course of events." RX 153C; RX 154C; Kelber, Tr. 1988; Hori, Tr. 932.

FF E 204. The U.S. Patent Examiner did, in fact, refuse to consider the untimely submitted references. RX 901 at 285; RPX 130C, Kelber Dep. Tr. 177-178.

H. The Suppressed Prior Art Was Material

FF E 205. Mr. Kudo's involvement in the prosecution of the reissue application included involvement in devising the tests for the Inaba Declaration. Kudo, Tr. 1326.

FF E 206. At Mr. Kudo's instructions, another reference forwarded to the Oblon firm in the February 28, 1994 letter from T.S. International for submission to the U.S. PTO was D. Boeck et al. "Narasin, A New Polyether Antibiotic: Discovery and Fermentation Studies," 18 Developments In

Industrial Microbiology, 471-485 (1976) ("the Boeck article"). RX 144C; RX 62; CX 82; Kudo, Tr. 1321, 1323; RX 354C.

FF E 207. The Boeck article reports on 4-methylsalinomycin (also known as narasin), which is within the term "salinomycins" used in the claims of the '698 reissue patent. RX 62; Kudo, Tr. 1378.

FF E 208. As of February 28, 1994, Kaken wanted to submit the Boeck article to the U.S. PTO in a manner so that the Examiner would substantively consider that reference. RX 354C; RX 144C; RX 149C; Shimada, Tr. 705-711; RX 150C.

FF E 209. By mid-March of 1994, however, Kaken had changed its plan and instead took action to ensure that the '698 reissue patent would be issued as soon as possible. Shimada, Tr. 711; RX 834C.

FF E 210. As a result, Kaken did not attempt to submit the Boeck article for substantive consideration by the U.S. PTO. RX 153C; RX 154C.

FF E 211. Specifically, Kaken disclosed the Boeck article to the U.S. PTO after the Notice of Allowance had issued in a second Information Disclosure Statement filed on March 18, 1994. RX 901 at 162, 173-268.

FF E 212. However, Mr. Kelber and Kaken knew that the Boeck article, submitted after the Notice of Allowance, would not be substantively considered by the U.S. Patent Examiner. RX 153C; RX 154C; Kelber, Tr. 1987-1988; Hori, Tr. 932.

FF E 213. The U.S. Patent Examiner did, in fact, refuse to consider the Boeck article. RX 901 at 285.

FF E 214. Mr. Inaba intended his testing using 0.5 percent soybean oil as the sole carbon source in Report 1 of the Inaba Declaration to be representative of Example 21 of the Berg patent. The Berg patent, like the

Boeck article, discloses production of 4-methylsalinomycin. Inaba, Tr. 1260-1262; Hutchinson, Tr. 1598; RX 95; RX 901 at 26-36.

FF E 215. However, Example 21 of the Berg patent contained approximately 10% of a carbon source in the fermentation medium; specifically, 8% dextrin, 1.5% blackstrap molasses, and .46% soybean oil. Hutchinson, Tr. 1598-1599; RX 95; RPX 114C, Inaba Dep. Tr. 607-608.

FF E 216. The use of 0.5% of soybean oil is far too small an amount as a sole carbon source to permit a significant amount of antibiotic production. Hutchinson, Tr. 1599-1600; RPX 114C, Inaba Dep. Tr. 250.

FF E 217 As admitted by Mr. Inaba, because the carbon source is analogous to food for the microorganism, the test said to be representative of the Berg patent effectively starved the microorganism, resulting in low antibiotic yields. Mr. Inaba failed to tell the U.S. Patent Examiner that the microorganism was starved. Inaba, Tr. 1263, 1266, 1305-1306; RPX 114C, Inaba Dep. Tr. 249-250; Hutchinson, Tr. 1601-1602.

FF E 218. The Boeck article teaches that omitting carbohydrates from a fermentation medium containing 2% oil results in a reduced yield of 4-methylsalinomycin. RX 62 at 06521 (Tables 6 and 7); Hutchinson, Tr. 1578-1580.

FF E 219. The Examiner was neither apprised by Kaken that in the test run alleged to be representative of Example 21 of the Berg patent, the microorganism was being starved, nor provided with the Boeck article (as a result of its untimely submission by Kaken) when he evaluated Kaken's alleged "unexpected" results in the Inaba Declaration. RX 901 at 285; Inaba, Tr. 1305-1306.

FF E 220. Numerous fatty acids are described in the specification as within the scope of the '698 patent claims, including saturated or unsaturated fatty acids, acetic acid, propionic acid, caproic acid, capric acid, palmitic acid, stearic acid, methacrylic acid, undecylic acid, linolic acid, linolenic acid and oleic acid. RX 5 at col. 2, lines 13-18.

FF E 221. Numerous fatty acid precursors are described in the specification as within the scope of the '698 patent claims, including soybean oil, safflower oil, cotton seed oil, sesame oil, olive oil, rape oil, peanut oil, corn oil, sunflower oil, and like vegetable oils, cod oil and like fish oils, and lard and like animal fat and oils, esters of fatty acids and salts of fatty acids. RX 5 at col. 2, lines 18-31.

FF E 222. The Boeck article indicates that fatty acid esters and fatty salts inhibited or blocked 4-methylsalinomycin production and that fatty acids containing less than twelve or more than eighteen carbon atoms blocked 4-methylsalinomycin production. Fatty acid salts such as acetate, propionate and butyrate also were reported to inhibit 4-methylsalinomycin production. Hutchinson, Tr. 1627-1629; RX 62 at 478, 481-483.

FF E 223. Mr. Hara admitted at the hearing that saturated fatty acids produce poor yields of salinomycin, that stearic acid and palmitic acid are examples of saturated fatty acids that are poor, and that stearic acid and palmitic acid are disclosed in the '698 reissue patent as acids that could be used in the claimed invention. Hara, Tr. 420-422.

FF E 224. Mr. Inaba admitted during this investigation that stearic acid or palmitic acid are saturated fatty acids and therefore use of them results in low productivity. Inaba, Tr. 1257-1260.

FF E 225. For testing in his declaration, Mr. Inaba was instructed, in effect, to use only high yielding oils. RX 96C at 21874; RX 97C; RX 99; RX 817C; RPX 114C, Inaba Dep. Tr. 120-121; Inaba, Tr. 1217, 1219-1220.

FF E 226. Kaken's own experimentation shows that certain acids listed in its patent specification do not result in high yields of salinomycin. Saturated fatty acids are poor, as are fats and waxes that harden easily such as coconut oil, palm oil and whale oil. Hutchinson, Tr. 1629-1630.

FF E 227. If other fatty acids or fatty acid precursors had been used in the Inaba Declaration testing as representative of the claimed invention as described in the '698 patent, far lower antibiotic yields would have resulted. Hutchinson, Tr. 1623.

FF E 228. The U.S. Patent Examiner was without the Boeck article when he evaluated Kaken's alleged "unexpected" results in the Inaba Declaration. RX 901 at 285.

FF E 229. The criteria for determining "material information" that should be disclosed to the U.S. PTO is set forth in 37 C.F.R. § 1.56(b). RX 743. See Witherspoon, Tr. 1861-1862.

FF E 230. 37 C.F.R. § 1.56 indicates that information is material, inter alia, if it "establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim." A "prima facie case of unpatentability" is defined as "when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability." 37 C.F.R. § 1.56(b) (1994); RX 743.

FF E 231. 37 C.F.R. § 1.56 of the PTO regulations in effect at the time Kaken filed its reissue application, dealing with disclosure of material references, encourages patent applicants to carefully examine prior art cited in a foreign counterpart application and cite to the U.S. PTO all such material prior art. RX 743, 37 C.F.R. § 1.56; Witherspoon, Tr. 1840-1841.

FF E 232. The Dietrich patent was supplied to Kaken by Hoechst, was cited in the nullification suit in Italy, and was listed as "particularly relevant" in the European search report for the European counterpart patent application. RX 115; RX 144C; RX 520; Shimada, Tr. 691-692, 697-699; Witherspoon, Tr. 1839-1840.

FF E 233. It is the general practice at T.S. International to forward search reports and all prior art references cited in foreign counterpart applications to a United States patent application to the United States attorneys prosecuting the U.S. patent application. Shimada, Tr. 682-683.

FF E 234. Mr. Shimada automatically sends prior art cited by the European Patent Office to the Oblon firm to make sure he satisfies the duty of disclosure to the U.S. PTO. Shimada, Tr. 690, 695.

FF E 235. Oblon's letter to Mr. Shimada informed him that "U.S. Patent Law and the Rules of the U.S. Patent and Trademark Office require inventors, patent attorneys and agents to submit copies of any known prior art which might have an adverse effect on the patentability of the claims in a pending patent application. Please send us copies of any such prior art for filing at the U.S. Patent and Trademark Office." RX 146C at AC 16323; Shimada, Tr. 688-689.

FF E 236. The Oblon firm's letter to Mr. Shimada states that "[r]elevant prior art includes information cited in search reports or official actions

issued by all government patent offices and the search reports and official actions themselves, as well as prior art the inventor may have been trying to avoid in his research." RX 146C at AC 16323; Shimada, Tr. 689.

FF E 237. 37 C.F.R. §§ 1.56 and 1.97 also encourage early submission of prior art. Specifically, § 1.56 provides:

> The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability.

Section 1.97 deals with timing and requirements for filing Information Disclosure Statements. The substantive requirements and conditions for filing an Information Disclosure Statement increase as the various stages of patent prosecution occur. RX 743; Witherspoon, Tr. 1841-1844.

FF E 238. It was Mr. Shimada's practice to make sure that if there was prior art available, such as prior art cited by the EPO, to get it before the U.S. PTO early so that the Office would have an opportunity to consider it. Shimada, Tr. 686.

FF E 239. The U.S. Patent Examiner provided a Statement of Reasons for Allowance as follows:

> The following is an Examiner's Statement of Reasons for Allowance: the amended claims narrow the scope of the invention to recite a method wherein the fermentation medium contains 12-25% fatty acid or its precursor. The limitation of 12-25% fatty acid or its precursor limits the claim so that the art neither anticipates nor makes obvious the claimed invention, because the art of record teaches similar processes using substantially less fatty acid and fails to provide any reasons or motivation to increase the concentration of the fatty acid in the fermentation medium.

RX 901 at 285-286.

FF E 240. The Examiner's Reasons for Allowance show that prior art that would provide reasons or motivation to one of ordinary skill in the art to increase the concentration of fatty acid or precursor would be material prior

art because it would make out a prima facie case of unpatentability. Witherspoon, Tr. 1862.

FF E 241. The prior art references which were not of record, however, directly provided the precise "motivation to increase the concentration of the fatty acid [precursor] in the fermentation medium" which the U.S. Patent Examiner felt was lacking in the record before the U.S. PTO. RX 115; RX 147; RX 148.

FF E 242. For example, the Dietrich patent discloses the use of soybean oil in amounts up to 16%, which is well within the 12-25% range claimed by Kaken. RX 115 at col. 3, lines 3-5; RX 5.

FF E 243. British patent 1,083,546, cited in the second Information Disclosure Statement, teaches that the yield of moenomycin by *Streptomyces* can be "increased considerably" by replacing carbohydrate with vegetable fats (e.g., soybean oil) as a carbon source and discloses the successful use of up to 10% fat. RX 147 at col. 1, lines 29-33, col. 2, lines 44-50, 53-55; RX 901 at 175.

FF E 244. Mr. Kelber alleged that the Dietrich patent was not filed with the reissue application because of an accident in file construction that occurred at his offices. Kelber, Tr. 1980.

FF E 245. Were it not for the accident in file construction at the Oblon firm, Mr. Kelber admitted he would have submitted the Dietrich patent when he originally filed the reissue application in January 1993. Kelber, Tr. 1980-1981.

FF E 246. Paragraph 6 of Mr. Kelber's Declaration states: "As reflected by the Notice of Allowance, I have caused to be made a careful and thorough

search of the prior art, and I have a good knowledge of the pertinent prior art." RX 901 at 276A.

FF E 247. Mr. Kelber structured his computer search so that it would be broad enough to include antibiotics other than salinomycin, such as non-polyether antibiotics like the one disclosed in the Dietrich patent, indicating that he believed nonpolyether antibiotic prior art was relevant. Kelber, Tr. 1992-1993.

FF E 248. In February 1994, Mr. Shimada concluded that all of the references cited in his February 28, 1994 letter to the Oblon firm should be put before the U.S. PTO in the reissue prosecution. RX 144C; Shimada, Tr. 699.

FF E 249. Mr. Shimada's letter to the Oblon firm includes a category of documents that Hoechst sent Kaken on October 31, 1991. RX 144C; Shimada, Tr. 695-696.

FF E 250. Mr. Shimada's letter to the Oblon firm includes a second category of document that were received from Hoechst on November 3, 1992. RX 144C; Shimada, Tr. 696.

FF E 251. Mr. Shimada's letter to the Oblon firm includes a third category of references submitted to the Italian court in a nullification proceeding regarding Kaken's Italian patent corresponding to the '698 reissue patent. RX 144C; Shimada, Tr. 696-697.

FF E 252. Mr. Shimada's letter to the Oblon firm includes a fourth category of documents, which were cited in the search report of Kaken's European patent application that corresponds to the '698 reissue patent. RX 144C; Shimada, Tr. 697.

FF E 253. Though Mr. Shimada's letter to the Oblon firm indicates he does not consider the prior art references to affect the patentability of the claims, he believed the art was sufficiently relevant to make sure it was cited to the U.S. PTO. RX 144C; Shimada, Tr. 701.

FF E 254. Mr. Shimada's belief that the prior art listed in his letter to the Oblon firm did not affect patentability of the claims was based on the assumption that the U.S. Patent Examiner had already considered the art during the prosecution of the original '942 patent. RX 144C; Shimada, Tr. 702, 713, 726. Mr. Shimada's assumption was not correct. RX 901 at 14.

FF E 255. If the file of the original patent prosecution showed that the U.S. PTO did not consider the prior art cited in Mr. Shimada's letter to the Oblon firm, his conclusion that it does not affect the patentability of the '698 patent would change. RX 144C; Shimada, Tr. 704-705.

FF E 256. If all the prior art cited in Mr. Shimada's letter to the Oblon firm had never been considered by the U.S. PTO, he would have wanted to make sure that the art was placed before the PTO. RX 144C; Shimada, Tr. 702-703.

FF E 257. In fact, the art had never been considered by the PTO. RX 901 at 14.

I. The Prior Art Was Suppressed With An Intent To Deceive -- Kaken's Desire Was To Expedite Issuance Of The Reissue Patent And Block Hoechst's Entry Into The U.S. Market, With An Intent To Deceive

FF E 258. Mr. Wakiyama, the president of Kaken, signed the English language reissue declaration found in the prosecution history of the reissue patent. Mr. Wakiyama does not read or understand the English language and no one read him his declaration in Japanese before he signed it. Before

executing his declaration, Mr. Wakiyama did not read it. RX 901 at 15-20; RX 895C, Wakiyama Dep. Tr. 16, 56-57, 77.

FF E 259. In 1994, after it was decided to file a complaint at the Commission against the Hoechst respondents to prevent them from entering the United States market, a "countermeasures" project team was formed at Kaken for the sole purpose of winning this case. Members of the team included Mr. Inaba, Dr. Hori, Mr. Kudo, and a Mr. Nakamura. Inaba, Tr. 1199-1200, 1303; RX 874C at 35483-83.

FF E 260. The Notice of Allowance's issuance in January 1994 did not prevent the prior art that Mr. Shimada provided to Mr. Kelber in February of 1994 from being substantively considered by the U.S. PTO. RX 149C; Shimada, Tr. 742; RPX 130C, Kelber Dep. Tr. 159-160.

FF E 261. As of February 28, 1994, Kaken wanted to submit a number of prior art references, including the Dietrich patent, the British '965 patent, the British patent 1,083,546, and the Boeck article, to the U.S. PTO so that the Examiner would substantively review the references. RX 354C; RX 144C; Hori, Tr. 913-914.

FF E 262. However, in early March 1994, Kaken became aware that Hoechst had received FDA approval to sell salinomycin in the United States. This became a matter of urgent concern to Dr. Hori. Hori, Tr. 914.

FF E 263. March of 1994 was a very sensitive time in Kaken's negotiations concerning a supply agreement with American Home Products because Kaken was committed to an expensive plant expansion and needed a Supply Agreement. Hori, Tr. 918-919.

FF E 264. American Home Products, the target for Kaken's supply agreement, told Kaken, through Mr. Becze, to take quick legal action against Hoechst. RX 736C; Hori, Tr. 919.

FF E 265. Specifically, Mr. Becze, a consultant to Kaken, sent a facsimile message to Kaken on March 2, 1994, suggesting that a prompt patent infringement action be filed against Hoechst. RX 736C; Hori, Tr. 914-916.

FF E 266. Mr. Becze's letter raised the question:

> AHP is willing to tell the breeders that Hoechst material may not be available due to a patent suit with Kaken, but they must know if Kaken can support such an action. They believe that if they can instill doubt about Hoechst's ability to supply, that it would greatly assist AHP in retaining market share. What is Kaken's response to this?

RX 736C at 1.

FF E 267. As a result of Mr. Becze's letter (RX 736C), Kaken tried to arrange a meeting with its patent attorneys as soon as possible. Hori, Tr. 917.

FF E 268. The meeting on March 15-16, 1994 resulted from the FDA approval of Hoechst's salinomycin product. Dr. Hori made notes of the March 15, 1994 meeting that form part of RX 893C. RX 893C, 17854 et seq.; Hori, Tr. 920-921.

FF E 269. The meeting on March 15-16, 1994, was held in the United States. Mr. Eguchi (Executive Managing Director of Kaken), Mr. Hori (Director, R & D Agrochemicals and Animal Health of Kaken), Mr. Ikemoto (General Manager, Patent Division of Kaken), Mr. Kudo (Staff Patent Attorney of Kaken), Mr. Kelber, Mr. Becze (President, Princeton Regulatory Associates, Consultant to Kaken), Mr. Corcoran (Vice President, Specialty Pharmaceuticals of American Home Products Corporation), Mr. Alice (Corporate Licensing Counsel of American Home Products Corporation), an interpreter, and Mr. James Heinle

(Hoffmann LaRoche) attended the March 16, 1994 meeting. RX 399C at AC 17873; Kelber, Tr. 1985; RX 154C; RX 398C.

FF E 270. The major subject of the March 15, 1994 meeting was how to proceed with reissue of Kaken's patent. Hori, Tr. 922.

FF E 271. During the meeting on March 15, 1994, there was a discussion of how long it would take to obtain a reissued patent if the existing application were refiled. Refiling was decided to involve too long a time period, because Kaken needed to have a reissued patent as soon as possible to sue Hoechst, and did not want to waste time. RX 893C at 17856; Hori, Tr. 924-925, 930; RX 154C; Shimada, Tr. 711, 729-730; RPX 120C, Ikemoto Dep. Tr. 145-146.

FF E 272. Kaken's attorneys at the March 15, 1994 meeting told Kaken it was not a good idea to send a warning letter to Hoechst at that time because the '942 patent was invalid and the reissue patent application had not yet issued. RX 893 at 17857; Hori, Tr. 926.

FF E 273. In Dr. Hori's notes, the following notations appears:

> problems
> reissue
> risky
> prior art.

RX 893C at 17859.

FF E 274. Mr. Hori explained his notes at 17859 as reflecting the fact that Kaken didn't know what the U.S. Patent Examiner would think. RX 893C at 17859; Hori, Tr. 931-932.

FF E 275. Dr. Hori's notes on page 17859 of RX 893 are notations that reflect comments by Mr. Oblon who stated in words or substance that Kaken was in a position of obtaining a reissue patent in one week if Kaken didn't worry about the prior art references. Hori, Tr. 932-933; RX 893C at 17859.

FF E 276. The desire of obtaining quick allowance to sue Hoechst was discussed at the March 16, 1994 meeting. Specifically, Mr. Corcoran expressed the interest of American Home Products Corporation, the licensee at the time, of obtaining quick issuance, and Mr. James Heinle from Hoffmann LaRoche made a presentation at the end of the meeting regarding their desire to obtain quick issuance of the patent. Kelber, Tr. 1986.

FF E 277. Mr. Kelber's recommendations in his March 4, 1994 letter concerning the submission of the prior art changed when Kaken informed him at the meetings of the need to secure prompt issuance of the reissue patent. Kelber, Tr. 1986-1987; RPX 130C, Kelber Dep. Tr. 174-176.

FF E 278. Mr. Kelber testified similarly at his deposition:

> Q. After the March 15, 1995 meeting, did you change your recommendation to Kaken concerning how to deal with the prior art which was identified in RDX-145?
>
> A. I offered a new alternative to proceed on an expedited time basis, yes.
>
> Q. What caused you to change your recommendation?
>
> A. The need expressed at the meetings on March 15 and 16 to secure prompt issuance of the reissue patent.
>
> Q. And what caused that desire to obtain issuance of the reissue patent?
>
> A. One of the factors that was involved was the report that I had not previously heard of the imminent issuance of an NADA to Hoechst for salinomycin. Another factor was the interest in Hoffmann-La Roche in the progress of the patent and issuance and the value it attached to that. The third factor was the interest that American Home Products representatives expressed in securing prompt issuance.
>
> Q. . . . Prior to learning of those three factors at the March 16th meeting, the only recommendations that you had provided to Kaken concerning the prior art which is identified in RDX-145 would have permitted that art to have been substantively considered by the Patent Office either in connection with the reissue application or in connection with

a continuation application or in connection with a reexamination application, is that correct?

A. Prior to that time, the only alternative committed in writing as a recommendation to Kaken, that's an accurate characterization, yes.

RPX 130C, Kelber Dep. Tr. at 174-176.

FF E 279. Kaken wanted the reissue patent to issue quickly so it could bring an action. Shimada, Tr. 712.

FF E 280. The decision in March 1994 to submit the prior art in a manner in which it would not be considered by the U.S. Patent Examiner was made by Kaken at a board meeting. Kudo, Tr. 1388; Hori, Tr. 936.

FF E 281. Mr. Kudo attended the board meeting. Kudo, Tr. 1388.

FF E 282. In Mr. Shimada's letter of March 17, 1994 to Mr. Kelber, he instructed Mr. Kelber to change plans and file the supplemental declaration mentioned in option number three so the patent could issue as soon as possible. RX 834C; Shimada, Tr. 711.

FF E 283. Mr. Kelber's letter of March 17, 1994 to Mr. Shimada states that Hoechst is planning to enter the market and therefore things are changing, which is a reference to why Kaken wanted to get the reissue patent to issue quickly. RX 154C; Shimada, Tr. 728-730.

FF E 284. Mr. Kelber submitted a declaration to the PTO to secure expeditious issuance of the case. RX 901 at 276-278; Kelber, Tr. 1989.

FF E 285. Kaken submitted the prior art references with the Supplemental Reissue Declaration in an attempt to limit the impact of charges of inequitable conduct that Kaken expected to be leveled by Hoechst. RX 154C at AC 16068, 16070; RX 901 at 170-175; RX 153C.

FF E 286. Mr. Kelber knew that two of the references submitted in the Information Disclosure Statement were cited as "particularly relevant" in a

search report issued by the European Patent Office in 1978 in a European application that corresponded to the '698 reissue patent. Kelber, Tr. 1909.

FF E 287. Mr. Kelber knew that certain of the references he was submitting in the Information Disclosure Statement had been cited in the Italian lawsuit against the Italian counterpart of the '698 reissue patent. He testified that he knew certain of the references cited in the Italian lawsuit were "nullified." Kelber, Tr. 1909.

FF E 288. After receipt of a Notice of Allowance, Kaken could not file an Information Disclosure Statement and meet the requirements that are set forth in 37 C.F.R. § 1.97. RX 743, § 1.97; Witherspoon, Tr. 1856-1858.

FF E 289. Nevertheless, Kaken eventually simply submitted the prior art references in the second Information Disclosure Statement "with the foreknowledge that they . . . [would] not be considered." RX 153C; RX 154C at AC 16068 and AC 16070.

FF E 290. Kaken could have submitted the prior art using a procedure under which the U.S. Patent Examiner would consider it. For example, it could have refiled the application as a continuation application. The existing reissue application would have been abandoned, and that could have been handled very simply by not paying the issue fee. As to that refiled application, Subparagraph B of Section 1.97 would have applied, and the art clearly would have been considered without any certification or fee or anything else accompanying it, if an Information Disclosure Statement had been filed within three months of the filing date of that new application. Witherspoon, Tr. 1858-1859.

FF E 291. Kaken chose to follow a procedure that Kaken and its attorneys knew would result in the PTO refusing to consider the prior art it had not yet

cited. Hori, Tr. 923-925; RX 154C; RX 893C at 17855-56. Eleven prior art references were submitted as part of the Information Disclosure Statement filed on March 18, 1993. RX 901 at 173-175. The U.S. Patent Examiner, as expected, refused to consider these prior art references because the Information Disclosure Statement failed to comply with the rules set forth in 37 C.F.R. § 1.97. RX 901 at 285.

FF E 292. In the March 18, 1994, Statement of Relevancy filed with the untimely submitted prior art after the Notice of Allowance, Kaken represented to the PTO that the references were not material, but that they were being submitted "in the interest of completeness." RX 901 at 270; Kelber, Tr. 1907, 1910. Yet, in Mr. Kelber's letter of March 17, 1994, to Mr. Shimada, Mr. Kelber indicated that the art discussed in the meeting on March 16 was being submitted "only to diffuse any possible charge of inequitable conduct that might arise." RX 153C.

FF E 293. The Statement of Relevancy indicates that the references cited in the Information Disclosure Statement have been provided by a number of sources, primarily third parties. Kelber, Tr. 1907. The Statement of Relevancy did not, however, indicate that, in fact, the third parties thought the references invalidated the '698 reissue patent. Kelber, Tr. 1907-1908.

FF E 294. Dr. Hori's notes from the March 15, 1994 meeting contain the statement "it is only inagdable [sic inequitable] conduct." RX 893C at 17859.

FF E 295. At the March 15, 1994 meeting, the statement "it is only inequitable conduct" was discussed in connection with the idea of submitting the prior art to the U.S. Patent Examiner in a way that the Examiner would not actually review it. Hori, Tr. 933-934; RX 893C at 17859.

FF E 296. Dr. Hori understood from the March 15, 1994 meeting that there was "essentially no risk" in submitting the prior art to the U.S. PTO in a manner such that the Examiner would not review it. RX 893C at 17860; Hori, Tr. 935.

FF E 297. Dr. Hori understood from the March 15, 1994 discussion that 90% of U.S. litigation gets settled, and Mr. Oblon's policy is to settle litigation. RX 893C at 17860; Hori, Tr. at 935-936.

VI. CLAIM 2 OF THE '698 REISSUE PATENT IS NOT OBVIOUS

A. The Level Of Ordinary Skill In The Art

FF F 1. A person of ordinary skill in the art as of 1977 would have had a Bachelor's Degree and at least two years of experience in antibiotic fermentation and biosynthesis. Hutchinson, Tr. 1552; Demain, Tr. 2115-2116. One would still have ordinary skill in the art if one had more experience, which could compensate for a lack of formal education, or vice versa. Hutchinson, Tr. 1553.

B. The Prior Art Relevant To The Claimed Invention

FF F 1. The prior art most closely related to claim 2 of the '698 reissue patent is that directed to polyether antibiotics. Demain, Tr. 2119-2120; Hutchinson, Tr. 1761-1762.

FF F 2. Dr. Demain testified as follows:

> Q. Let's consider the backdrop for the patent in suit, the prior art. Now before turning to specific prior art, what prior art would someone of ordinary skill in the art consult if faced with the problem of how to increase salinomycin titer through fermentation?
>
> A. The first thing you look for are articles dealing with salinomycin. If you don't find those, you look for articles dealing with polyethers. If you don't find those or after you find those and react to the finding, you

would then look at all, broadly, in the whole fermentation field concerning that aspect that you're interested in.

Demain, Tr. 2119-2120.

FF F 3. The invention of the '698 reissue patent as first disclosed in the '942 original patent was highly relevant to those working in the general field of polyether fermentation. The patent is a teaching patent in the fermentation industry with respect to polyether fermentation technology. It directed the field to the extensive use of oils in polyether fermentations. Demain, Tr. 2146-2147.

FF F 4. The '698 reissue patent teaches the use of large amounts of oil in fermentation in order to raise the titer of polyether antibiotics, and salinomycin in particular. Demain, Tr. 2146-2147, 2191.

FF F 5. Dr. Hutchinson testified as follows:

Q. And that's because polyether antibiotics, as a class, have a common biosynthetic pathway?

A. They do.

Q. And you've written on that several times, correct?

A. Yes, of course.

Q. And, in fact, within the general class of antibiotics, you can carve out the biosynthetic pathway of polyether antibiotics because of their homologous structure, correct?

A. Yes, you can.

Q. And you've characterized that as a novel pathway, correct?

A. Novel pathway? I imagine I might have said that at one time but it's -- novel is no more novel than some other pathway that has some intriguing characteristics. It doesn't mean that as compared with all pathways, it's remarkably different or unusual.

Q. It's just plain different, right?

A. Well, it's different than other antibiotics, of course.

Q. And narasin is just about as close as you can get to the structure of salinomycin without being salinomycin, right?

A. True.

Q. So if you were trying to develop an idea of how a microorganism would react in terms of the biosynthesis of an antibiotic to a particular nutrient or group of nutrients, you would turn to, in this case, polyether antibiotic literature to develop that understanding, correct?

A. As to how they're put together, yes.

Hutchinson, Tr. 1760-1762.

FF F 6. There are many species of Streptomyces, and there are differences in their preferred carbon sources for production of their secondary metabolites which includes antibiotics. One can obtain only a certain amount of guidance by comparing the results obtained with various Streptomyces. Demain, Tr. 2134-2135.

FF F 7. However, one of ordinary skill in the art would not look only to polyether antibiotics when reading prior art. One would need a broad perspective based on more than polyether references. Hutchinson, Tr. 1815.

C. The Prior Art Relied On By Respondents In This Investigation

U.S. Patent No. 4,035,481 to Berg et al. (RX 95)

FF F 8. One of the co-inventors of the Berg patent, Marvin M. Hoehn, was a co-author of the Boeck reference. RX 95, RX 358; RX 62 at 471.

FF F 9. Berg discloses the use of an A-28086-producing streptomyces. RX 95, col. 2, lines 53-57.

FF F 10. Berg reports on the polyether antibiotic, A-28086, to be used as an anticoccidial. RX 95, col. 2, lines 9-10.

FF F 11. Polyether antibiotic A-28086 is narasin, which is a methyl derivative of salinomycin, specifically 4-methyl salinomycin. Hutchinson Tr.

1555; Demain Tr. 2137, 2139; RX 62 (Boeck article) at 471-472; CX 1, col. 20-21.

FF F 12. Berg teaches that the streptomyces culture changes color depending upon the culture characteristics. RX 95, col. 12, line 30 to col. 16, line 40.

FF F 13. Berg teaches the use of ammonia or an ammonium salt. RX 95, Example 21, col. 33, line 68.

FF F 14. Berg teaches that the culture medium can be any one of a number of media. However, for economy of production, optimal yield, and ease of isolation, the preferred media contains preferred carbohydrate sources, such as tapioca dextrin and sucrose, although glucose, corn starch, fructose, magnesia, maltose, lactose, and the like can also be employed. Corn oil, peanut oil, soybean oil and fish oil are also described as useful. RX 95, col. 16, lines 50-60.

FF F 15. In Example 21, Berg teaches the use of 9.96% carbon sources, specifically: tapioca dextrin (tapioca starch) at 8.0%, black strap molasses at 1.5%, and a fatty acid precursor (refined soybean oil) in the amount of 0.46%. RX 95, Example 21, col. 34, line 4.

FF F 16. Berg teaches that the use of a small amount of oil, such as soybean oil is not essential, but can enhance production. RX 95, col. 17, lines 11-14. A small amount of oil in the Berg reference is .46% or somewhat more than this amount. Hutchinson Tr. 1732.

FF F 17. The art as of 1977 described small amounts or low levels of fatty acid to be .46%. 0.5%, and 2%. Hutchinson Tr. 1732; RX 95, Example 21, col. 34, line 4; RX 62 at 478.

British Patent 1,374,414 to Miyazaki et al. (RX 443)

FF F 18. Recovery of salinomycin together with the mycelial mass is disclosed in Kaken's British '414 patent to Miyazaki. RX 443 at H031 00007, lines 1-7; Hutchinson, Tr. 1586.

The Boeck Article (RX 62)

FF F 19. The reference to Boeck et al. teaches away from the invention of claim 2 of the '698 patent. Demain, Tr. 2143-2144.

FF F 20. With respect to the Boeck article, Dr. Demain testified in part, as follows:

> Q. Do you see the discussion with respect to myristate, oleate and linolate methyl esters?
>
> A. One second. Yes, growth equivalent to the control in the case of these fatty acids.
>
> Q. How about antibiotic titer?
>
> A. Low.
>
> Q. And what does that suggest to those of ordinary skill in the art with respect to using a fatty acid or precursor as a major carbon source for the fermentation to produce salinomycin?
>
> A. Indicate that that would be a poor move.
>
> Q. And by poor move, Doctor, do you mean that titer would not be expected to be high?
>
> A. That's correct.
>
> Q. Is it your testimony, then that Boeck teaches away from the use of the conditions recited in claims 2 of CX-2?
>
> A. That's correct.

Demain, Tr. 2142-2144.

FF F 21. Boeck et al. is the type of reference one of skill in the art might turn to if faced with the problem of how to increase levels of salinomycin through fermentation. Demain, Tr. 2139.

FF F 22. Dr. Demain testified that:

Q. In connection with your earlier testimony, Doctor, is this the type of reference that one of skill in the art might turn to if faced with the problem faced by the '698 Patent inventors; how to increase the levels of salinomycin through fermentation?

A. Yes.

Demain, Tr. 2139.

FF F 23. Dr. Demain testified that:

Q. Is the experience of Boeck a predictor of the experience reported in example 4 of the patent?

A. No.

Q. Does it teach away from those results?

A. Yes.

Demain, Tr. 2144.

FF F 24. Boeck et al. teaches that when using 2 percent oil, there is a reduced yield of antibiotic as compared to the use of starch. This might indicate to one of ordinary skill in the art that the use of oil, e.g. 6 percent oil, might inhibit the culture, although the results reported in Boeck could indicate that there simply was not enough carbon source for the microorganism. The Boeck article is at best inconclusive as to what would happen if one relied on a higher percentage of oil as a carbon source for a microorganism which produced polyether antibiotic. Hutchinson, Tr. 1580-1581; Demain, Tr. 2140-2141.

FF F 25. Dr. Demain testified that:

Q. Does table 6 and the text associated with it provide any teaching to those of skill in the art about what will happen if oil is used as the principal carbon source for fermentation of a polyether antibiotic?

A. Well, for the production of narasin, it certainly is poor compared to carbohydrates. Oils are poor carbon sources.

Demain, Tr. 2140.

FF F 26. With respect to the effect of Boeck's teachings, Dr. Demain testified that:

> [A]bove table 6 it says these low antibiotic levels were not improved by higher levels of oil. And my guess would be that if you went up to 6 percent oil, you would start inhibiting this culture.
>
> Q. Do you see to see the data on which that statement with respect to higher levels of oil is based to come to that conclusion?
>
> A. No, I mean, there is a certain amount of trust in the scientific literature. Every statement is not documented by figures and tables.

Demain, Tr. 2140-2141.

FF F 27. Boeck et al. shows at table 7 that while small additions in the amount of fatty acid precursor (soybean oil) of the magnitude taught in the Berg patent, give mild increases in antibiotic titer, increases as much as 2 percent do not substantially improve titer. Demain, Tr. 2142.

FF F 28. Dr. Demain testified with respect to Boeck et al.:

> Q. How much oil did the authors recommend as an addition or a supplement to the carbohydrate carbon source?
>
> A. Well, they test 2 percent and a half percent. And in most cases the 2 percent has very little effect and I think in one case it actually -- in the case of fish oil -- has an inhibitory effect. And in the case of medium 2, even refined soybean oil and moving from a half to 2 percent is inhibitory.
>
> Q. Does that suggest to those of ordinary skill in the art that higher titers of polyether antibiotics of this type, salinomycins, can be obtained using high levels of oil?
>
> A. No.

Demain, Tr. 2142.

FF F 29. In at least half of the cases investigated by Boeck et al., the addition of as much as 2.0 percent soybean oil resulted in a decrease in antibiotic titer. Demain, Tr. 2142.

FF F 30. Boeck et al. teaches that the use of methyl esters of fatty acids resulted in no antibiotic production, but normal microorganism growth. Demain, Tr. 2144.

FF F 31. Dr. Demain testified that with respect to Boeck:

> Q. Would you turn to page 478 and in particular, the discussion with respect to methyl esters just above the title Effect of Various Proteins, et cetera.
>
> A. Yes.
>
> Q. Do you see the discussion with respect to myristate, oleate and linolate methyl esters?
>
> A. One second. Yes, growth was equivalent to the control in the case of these fatty acids.
>
> Q. How about antibiotic titer?
>
> A. Low.

Demain, Tr. 2142.

U.S. Patent 3,992,263 to Dietrich et al., (RX 115)

FF F 32. U.S. Patent No. 3,992,263 to Dietrich et al. discloses the use of up to 16% oil as a carbon source and an ammonium salt in the fermentation of Streptomyces which produce the antibiotic moenomycin. Hutchinson, Tr. 1558-1560; RX 115 at col. 2, lines 24-32; col. 2, line 64 to col. 3, line 5.

FF F 33 Dietrich, however, contains teachings which would also discourage one from using high amounts of oil to give an increase in antibiotic titer. Demain, Tr. 2123.

FF F 34. The Dietrich patent states in pertinent part, as follows:

> All fats are used in concentration of from 0.1 to 16% by weight, preferable from 2 to 5% by weight.

RX 115, col. 3, lines 3-5.

FF F 35. Dr. Demain testified with respect to the Dietrich Patent:

Q. And specifically, the sentence that begins about line 4. "All fats are used." Do you see that sentence?

A. Yes.

Q. Does that sentence reflect a teaching that the use of increasing amounts of oil leads to an increased antibiotic titer?

A. Only between 2 and 5 percent, additional oil would have a negative effect on production.

Q. What's your basis for that statement?

A. Because the range is a tenth percent to 16 percent but they mention a preferable range, which is 2 to 5 percent. That means anything above 5, between 5 and 16, you're going to have a lower performance.

Demain, Tr. 2123 (emphasis added).

FF F 36. It is not easy to move from one antibiotic to another when trying to make predictions about the titer of antibiotic that will be obtained from fermentation. It makes a difference whether the antibiotic is structurally related or distant in terms of chemical structure. Demain, Tr. 2122.

FF F 37. Moenomycin, as discussed in Dietrich, is not a similar chemical structure to salinomycin. Demain, Tr. 2122.

FF F 38. The Dietrich UK publication does not teach those of ordinary skill in the art that use of large amounts of oil will lead to an increase of antibiotic titer. Demain, Tr. 2124.

FF F 39. Dr. Demain testified with respect to the Dietrich UK patent publication:

Q. Let me hand you up another patent or publication from the same group on moenomycin, which is RX-147. Doctor, does RX-147 add in any way to the teaching of the Dietrich patent in terms of what those of skill in the art might expect from the fermentation of the salinomycins-producing microorganism using 12 to 25 percent oil?

A. No.

Q. Why do you say that?

A. Well, in fact this patent even has a lower limit. Instead of I think it was 16 percent was the highest limit, I think this is 10 percent. So -- and the preferable is again up to 5 percent. So again, anything over 5 percent would be detrimental to the process.

Q. Do these references reflect an awareness of the art of a linear relationship between the addition of oil and antibiotic titer?

A. No.

Q. Let me ask you to turn, Doctor -- well, don't they indicate the use of high amounts of oil, for instance, in the document we're looking at, RX-147; they indicate 10 percent fat in this particular case?

A. That's the limit. The preferable is a half to 5 percent. That means between 5 and 10 percent you're not only going to fail to get increased production, you're going to get a decrease in production.

Demain, Tr. 2123-2124.

U.S. Patent No. 3,869,346 to Vezina et al. (RX 249)

FF F 40. The Vezina patent teaches the fermentation of an antimycin-producing Streptomyces, Streptomyces antibioticus, with the use of oil. Demain, Tr. 2126.

FF F 41. The amount of oil used in the Vezina patent does not approach 12 percent. In fact, it states a preferred amount of oil which is substantially below the amount used in the '698 reissue patent, and thus indicates to one of ordinary skill in the art that larger amounts of oil would have a negative effect on fermentation. Demain, Tr. 2125.

FF F 42. The Vezina patent does not teach a linear relationship between the amount of fatty acid precursor used and the amount of antibiotic obtained. Demain, Tr. 2124-25.

FF F 43. Dr. Demain testified with respect to the Vezina patent:

Q. Does this patent teach a linear relationship between the use of oil and antibiotic titer?

A. No.

Q. Why do you say that?

A. Well, I not finding it right off the bat but they're talking about -- here it is -- a range of .5 to 2 percent per day but they have a preferable value of 1.25. That means anything between 1.25 per day and 2 percent per day is going to have a negative effect on the fermentation.

Q. And is that teaching --

A. In terms of comparing it to the optimum performance. It's going to go down if you add over 1.25 percent by day.

Q. And is the teaching you're referring to the teaching that appears at column 9, beginning about line 3 and continuing to the third sentence there?

A. Yes.

Demain, Tr. 2124-2125.

FF F 44. Dr. Hutchinson's conclusion as to the fact that Vezina teaches a linear relationship between soybean oil and antibiotic titer was based at least in part on a misunderstanding of the reference. Dr. Hutchinson understood the reference to teach the use of a total of 24 percent soybean oil, beginning with a starting amount of 10 percent. Hutchinson, Tr. 1571; Demain, Tr. 2125-2126.

FF F 45. Dr. Demain testified with respect to Vezina:

Q. Do you recall hearing Dr. Hutchinson testify that this patent taught up to 24 percent soybean oil?

A. I've heard the figure 24 percent. I don't know if it's example 2 because to get up -- you can't get up to 24 percent. I mean, that was a miscalculation on the part of Dr. Hutchinson. The 10 percent to start out with was not soybean oil but soybean meal.

Demain, Tr. 2125-2126.

FF F 46. Dr. Hutchinson acknowledged on cross examination that the total amount of soybean oil used in the examples of Vezina did not reach 12 percent. Hutchinson, Tr. 1655.

FF F 47. Dr. Hutchinson testified with respect to Vezina:

> Q. So the Vezina example, your interpretation is it shows a total addition of 7.5 percent soybean oil?
>
> A. I would calculate the added amount as five times 1.25, which is 6.25 plus the amount we began with.
>
> Q. Which is something under 1 percent, correct?
>
> A. Yes.

Hutchinson, Tr. 1655.

FF F 48. Dr. Hutchinson acknowledged on cross-examination that the total amount of soybean oil used in the examples of Vezina was 7.5% or roughly one-half of the minimum required by claim 2 of the '698 patent. Hutchinson, Tr. 1655.

FF F 49. Dr. Hutchinson testified further with respect to Vezina:

> Q. So the Vezina example, your interpretation is it shows a total addition of 7.5 percent soybean oil?
>
> A. I would calculate the added amount as five times 1.25, which is 6.25 plus the amount we began with.
> Q. Which is something under 1 percent, correct?
>
> A. Yes.
>
> Q. Now, that's roughly half of the 12 percent recited in the patent, correct?
>
> A. Yes.

Hutchinson, Tr. 1655.

U.S. Patent No. 3,892,850 to Struyk et al. (RX 440)

FF F 50. The Struyk patent concerns the fermentation of Streptopimaricin, a polyene, and not related to polyethers. It does not allow

one to draw any conclusions about what to expect when fermenting a salinomycins-producing Streptomyces microorganism in 12-25% oil. Demain, Tr, 2130.

FF F 51. The Struyk patent teaches the possibility of using small amounts of oils and fats to enhance fermentation run on other carbon sources. It does not teach that high levels of oils will result in high titers, especially of salinomycin. Demain, Tr. 2131.

FF F 52. Dr. Demain testified:

> Q. Now, this patent directed to pimaricin does teach the possibility of using oils and fats, doesn't it? And I would direct you to column 6, beginning at about line 30.
>
> A. Yes, I would like to read a little before that.
>
> Q. Of course.
>
> A. This paragraph in column 6 talks about materials which are added in small amounts that enhance the fermentation being run on other carbon sources. So that has nothing to do with what we're talking about in salinomycin fermentation.
>
> Q. It doesn't suggest to one of skill in the art that high levels of oil will be rewarded with high levels of salinomycin?
>
> A. Does not.

Demain, Tr. 2130-2131.

U.S. Patent No. 3,989,820 to Florent (RX 441)

FF F 53. Respondents' expert witness testified that the Florent patent concerns an anticoccidial substance, the structure of which is undertermined from the patent. He testified further that Florent taught that one could replace the carbohydrate carbon source with oil as the main carbon source, and the use of ammonium salts. Hutchinson, Tr. 1575, 1585-1586.

British Patent 1,083,546 (RX 147 RX 250)

FF F 54. The British '546 patent discloses the use of a moenomycin-producing Streptomyces. RX 250.

FF F 55. The British '546 patent teaches the use of ammonia or an ammonium salt. RX 147, page 1, line 23.

FF F 56. The British '546 patent teaches the doubling in the formation of moenomycin by the use of fats as the sole source of carbon in the range of 0.1 to 10%, preferably 0.5 to 5%. RX 250, page 1, lines 46-50; Hutchinson Tr. 1562-1563. A person of ordinary skill in the art would know from the preferred low range that the production would be detrimentally affected as the amount of fat increased above 5%. Demain Tr. 2123-2124.

FF F 57. As with the Dietrich patent, there is not an awareness of a linear relationship between the addition of oil and antibiotic titer. Demain, Tr. 2124.

FF F 58. The British '546 patent does not add to the teaching of Dietrich with respect to the effect that an addition of oil in the 12-25% range might have on the fermentation of a salinomycins-producing microorganism. Demain, Tr. 2123.

The Ratledge Article (RX 413)

FF F 59. The Ratledge article discusses, among other things, the addition of fats and oils to media containing carbohydrates. Demain, Tr. 2127.

FF F 60. The Ratledge article does not indicate that an increase in antibiotic titer can be obtained by using 12 percent or more oils (fatty acid precursor) in fermentation. Demain, Tr. 2127, 2129.

British Patent 1,500,965 (RX 148)

FF F 61. The British '965 patent states that the complete specification was published on February 15, 1978. RX 148.

FF F 62. The British '965 patent reports on polyether antibiotics, homologues of Lasalocid A. RX 148, page 3, lines 1-24.

FF F 63. The British '965 patent uses a Streptomyces. RX 148, page 1, lines 21-24.

FF F 64. The British '965 patent teaches that the streptomyces culture changes color depending upon the culture characteristics. RX 148, page 2, lines 10-14.

FF F 65. The British '965 patent does not teach the use of ammonia or an ammonium salt. RX 148.

FF F 66. The British '965 patent teaches the use of carbohydrate such as sugar or molasses, with brown sugar being most preferred, and an addition of an oil such as soybean oil or lard oil as a carbon and surfactant (to control foam) and to improve yields. The British '965 patent does not teach yields or oil amounts. RX 148, page 3, line 25 to page 4, line 1.

U.S. Patent No. 4,366,147 to Hamill et al. (RX 442)

FF F 67. The Hamill patent reports on a non-polyether, sulphur containing antibiotic, Antibiotic A-7413. The RX 442, col. 1, line 45 to col. 2, line 13; Boeck, RX 62 at 471. Respondents admit that the Hamill patent does not disclose the structure of the antibiotic A-7413. See Respondents' Comments on OUII's Proposed Findings, Section V, p. 28.

FF F 68. The Hamill patent discloses the use of Actinoplanes which produces A-7413. It does not teach the use of a Streptomyces. RX 442, col. 2, lines 14-17.

FF F 69. The Hamill patent teaches that the culture changes color depending upon the culture characteristics. RX 442, col. 7, line 46 to col. 8, line 40.

FF F 70. The Hamill patent teaches the use of ammonia or an ammonium salt (ammonium sulfate). RX 442, col. 8, line 67 to col. 9, line 3.

FF F 71. The Hamill patent teaches that dextrose, glucose, fructose, maltose, sucrose, and the like can be used as carbon sources. Hamill also teaches that, "[a]lthough not essential for growth, an oil such as corn oil improves antibiotic titer. Other useful sources of carbon include peanut oil, soybean oil, fish oil, and the like." RX 442, col. 8, lines 55-63.

The Stark Articles (RX 454 and RX 446)

FF F 72. The 1967 Stark article, Monensin, A New Biologically Active Compound, II. Fermentation Studies, in Antimicrobial Agent and Chemotherapy, 353-358, teaches that the addition of oils to the fermentation medium "markedly increased" monensin production, with soybean oil being the best tested. Monensin is a polyether antibiotic produced by a Streptomyces microorganism. The 1967 Stark article states that several factors influencing the biosynthesis of monensin were discovered in the study reported therein. The article listed several factors as "most important," including "strains of the culture," "concentration of selected minerals in the medium," and last on the list, "supplementation of the medium with oils." RX 446 at H031 00327, abstract, lines 1-2, H031 00330, col. 2, lines 5-9, H031 00332, col. 1, lines 19-24; RX 468 at 27.

FF F 73. There was no testimony at the hearing concerning the 1967 Stark article. See Complainant's Comments on Respondents' Proposed Findings of Fact at 2; Respondents' Proposed Finding of Fact VIII 22.

FF F 74. The 1969 Stark article, Monensin, A Biologically Active Compound Produced by a Fermentation Process, Fermentation Advances, pp. 517-40, describes a culture medium for monensin production which contains up to 4% of a fatty acid and a fatty acid precursor. Monensin is a polyether antibiotic produced by a Streptomyces microorganism. RX 454 at 524, 531; RX 468 at 27. See Kudo, Tr. 1318-1319.

FF F 75. The 1969 article was considered by the Examiner during the reissue prosecution, while the 1967 article was not. CX 1; RX 901.

FF F 76. The data in the 1967 Stark article in Table 4 is identical to the data in the 1969 Stark article in Table 1. RX 446 at 355 (H031 00329), RX 454 at 531 (H031 00042).

Canadian Patent 823,631 (RX 63)

FF F 77. The kasugamycin addressed by the Canadian Patent is of a structure which is unrelated to salinomycin. Kasugamycin is an aminoglycoside, which denotes a sugar structure; it looks like a small oligosaccharide with two or three sugars. It has a structure that is extremely unlike that of salinomycin. Demain, Tr. 2131.

FF F 78. The Canadian '631 patent teaches the use of small amount of oil, i.e., around 5%. The Canadian '631 patent would not teach one of ordinary skill in the art the use of oil in the 12-25% range, especially in connection with a Streptomyces microorganism like that used in the '698 reissue patent. Demain, Tr. 2134-2135.

FF F 79. One of ordinary skill in the art would not be able to obtain a value of 10,000 micrograms/ml of Kasugamycin based on the disclosure of the Kasugamycin patent. Hutchinson, Tr. 1720; Demain, Tr. 2131.

FF F 80. Dr. Hutchinson testified with respect to the Canadian Patent:

Q. Well, does this patent, the Canadian patent, allow one of skill in the art to obtain those 10,000 micrograms per milliliter? Is there enough teaching there to get one skilled in the art to the 10,000 level?

A. If we assume -- no, I would say that if we assume that this is a strain derived from, and however that was done, there is no direct statement of how that was done or how one could reproduce it . . .

Hutchinson, Tr. 2131.

D. Unexpected Results From The Claimed Invention

FF F 81. The Berg patent discloses a culture medium containing 0.46% soybean oil in combination with ammonium sulfate, while the Stark article describes a culture medium containing at most 4% of a fatty acid and fatty acid precursor. Both disclosures taught the use of substantially less fatty acids and fatty acid precursor (4%) than claimed by Kaken (12-25%). RX 95 at col. 33, line 57 to col. 34, line 8; RX 454 at 531; RX 5 at col. 8, lines 54-59. See Respondents' Proposed Finding of Fact VIII 114.

FF F 82. The art directed to polyether antibiotics available as of May 31, 1977, as a whole, would lead one of ordinary skill in the art to predict that use of 12-25 percent oils would not be a good concentration to use to make salinomycin. Demain, Tr. 2144.

FF F 83. Dr. Demain testified that:

Q. Reviewing the art we've discussed as a whole, including Boeck and Berg and the non-polyether prior art that we've discussed, what does the art taken collectively teach those of skill in the art as of May 31, 1977 as to the use of 12 to 25 percent fatty acid or fatty acid precursor and ammonia or an ammonium salt in a fermentation media to produce salinomycin from streptomyces?

A. Well, none of them address salinomycin production by streptomyces albus but if you took the teachings of all of those, you would predict that in fact 12 to 25 percent would not be a good concentration of oil to use to make salinomycin by streptomyces albus. That would be a prediction.

Q. And the basis for your opinion is?

A. Because none of them use high levels without showing that those high levels are less useful than lower levels.

Q. And by high levels, do you mean like 12 percent?

A. I mean 12 percent.

Demain, Tr. 2144.

FF F 84. The Berg patent does not enable one of skill in the art to predict the impact of large amounts of oil on salinomycin titer. Demain, Tr. 2138.

FF F 85. Dr. Demain testified with respect to Berg:

Q. Is there any teaching in this patent that you're aware of that would enable one of skill in the art to predict what larger values of oil, what impact that would have on titer?

A. No, there is nothing in here. The claims are all based on structures and out of all the examples, I think that's the only example that has oil in it.

Demain, Tr. 2138.

FF F 86. It is not a general principle in the fermentation of antibiotics that if a little oil is good, a lot of oil is going to be better. As seen in some of the prior art relied on by Respondents, there is a preferred range stated which is even lower than the larger amounts of oil which had been tested. Demain, Tr. 2138.

FF F 87. One of ordinary skill in the art cannot make a prediction, based on art directed to the fermentation of antibiotic of an unrelated structure, as to the titer of salinomycin that might be obtained. Hutchinson, Tr. 1678-1679; Demain, Tr. 2122.

FF F 88. One of skill in the art cannot predict the result of fermentation of a microorganism to produce salinomycin on the basis of art

directed to a structurally different antibiotic produced by a different microorganism. Demain, Tr. 2122.

FF F 89. Dr. Demain testified that:

> Q. Doctor, what is the basis for your opinion that one of skill in the art reviewing the Dietrich patent could not develop an expectation of the salinomycin titer to be obtained using oil as a fermentation base?
>
> A. Well, I've already said that the antibiotic is totally unrelated and the organism is different.
>
> Q. Is it not possible to move from one antibiotic to another in terms of prediction in fermentation?
>
> A. Not easily, no.
>
> Q. Does it make a difference whether the antibiotic is structurally related or distant in terms of chemical structure?
>
> A. It makes a difference.

Demain, Tr. 2122.

FF F 90. One of skill in the art cannot make a prediction, based on art directed to the fermentation of an antibiotic using a non-salinomycins producing microorganism, as to the titer of Salinomycin that might be obtained. Hutchinson, Tr. 1684.

FF F 91. Dr. Hutchinson admitted that the relationship between the use of increased oil and antibitic titer is uncertain. Hutchinson, Tr. 1664-1667, 1678-1679, 1682-1684.

FF F 92. Both Dietrich references, the Vezina reference, Florent, the Canadian Patent 821,823 and Struyk are directed to the fermentation of antibiotics unrelated to salinomycin, using microorganisms different from those that produce salinomycins. Demain, Tr. 2134-2135.

FF F 93. Dr. Demain testified with respect to the prior art:

Q. Isn't that sufficient to teach one of ordinary skill in the art relatively high levels of salinomycin can be obtained through using even higher levels of fatty acid precursor?

A. Well, I don't think the 5 percent, we've seen it before. It's not new. We've gone over some patents here dealing with other structural antibiotics and other species. We've seen 5 percent before so it's nothing approaching the 12 to 25 percent in the Kaken patent.

Q. And is it sufficiently closely related to develop a prediction based on what is reported, the 5 percent, what you could get with salinomycin?

A. No.

Q. No, you mentioned different species. These are all streptomyces that we've been dealing with, correct?

A. So far, yes.

Q. Isn't that a sufficient relationship to allow one of ordinary skill in the art to say, if it worked here, it will work with streptomyces albus or another streptomyces?

A. No, there are many, many species of streptomyces and there are differences in their preferred carbon sources for production of their secondary metabolites. You can only take some guidance from these but if you have no guidance based on the level of carbohydrate and you have no guidance based on the organism or the product, then you will not be taught how to make salinomycin at the levels in this patent.

Q. And when you say this patent, do you mean the patent involved in litigation?

A. The patent involved, streptomyces albus growing on high levels of oil.

Demain, Tr. 2133-2135.

FF F 94. Prior art to the '698 reissue patent (e.g. Vezina, Florent, the Ratledge article, the Dietrich patent, the Struyk patent) indicated that carbohydrates could be substituted for oils, and at least in some cases the prior art taught that carbohydrates would perform as a carbon source in a fashion parallel to that of fatty acids and fatty acid precursors. Hutchinson

Tr. 1717-1718, 1727-1728, 1733-1734, 1821. See Hutchinson, Tr. 1739-1740, 1750.

FF F 95. On the question of whether the prior art taught the interchangeability of carbohydrates and oils, Dr. Hutchinson testified with respect to the Dietrich patent, as follows:

> Q. With respect to the Dietrich reference, Dietrich teaches the combined use of carbohydrates together with animal fats or oils as a carbon source, correct? And I would refer you, sir, to column 2, the paragraph beginning at line 24.
>
> A. Yes, it's true. If you recall my testimony yesterday, I made a specific reference to the predecessor of this Dietrich patent on moenomycin where the express statement was made that carbohydrates may be replaced with oils. And consequently, a person reading both together would have the impression that one could in fact replace the carbohydrate with the oil.

Hutchinson, Tr. 1734-1735.

FF F 96. Oil and carbohydrate are not interchangeable in the production of salinomycin, at least with respect to the titer obtained. Hutchinson, Tr. 1749.

FF F 97. Upon issuance of the '698 reissue patent, Hoechst began a series of tests designed to find a non-fatty acid precursor substrate for fermentation of salinomycin. Rathscheck Dep. (CX-874C) Tr. 70, 84, 89-90.

FF F 98. Hoechst was unable to find any substrate other than a fatty acid or fatty acid precursors suitable for the production of salinomycin through fermentation. Rathscheck Dep. (CX 874C) Tr. 75-76, 84-89.

FF F 99. At no time in Hoechst's experiments did it run a fermentation, either production or shake flask culture, in which the salinomycin titer obtained from glucose was higher than the salinomycin titer obtained from soybean oil as the major carbon source in an otherwise similar process. Rathscheck Dep. (CX 874C) Tr. 89-90.

FF F 100. [C]

[C]

[C]

FF F 101. When using carbohydrate, even amounts as high as 24 percent total carbon source failed to give results as high as 2 or 4 percent of soybean oil. Hutchinson, Tr. 1752-1753.

FF F 102. Dr. Hutchinson testified:

> Q. That's run J but as a general matter, in the fermentation of streptomyces albus, to produce salinomycin, is a total level of 24 percent carbon source starving the microorganism?
>
> A It's not starving it but my interpretation is that the carbohydrate simply is not a good carbon source vis-a-vis antibiotic production. So it's different than having insufficient amount of carbon source. Here we have something that even though there is a lot of it around, streptomyces albus is simply ignoring it with respect to antibiotic production.

Hutchinson, Tr. 1753

FF F 103. Demain testified notwithstanding the role played by improved microorganism strains, such as the withheld SLS-K-7-68 strain, the value of the patent is that it will tell the public the extremely high titers that can be obtained using an oil medium with one or more of these cultures." Demain, Tr. 2191.

FF F 104. Dr. Demain testified with respect to the '698 Patent:

> Q. Do you have any expectation sir, that the 80614 strain as deposited could achieve the yield of 60,000?
>
> A. I do not have any expectation that with current technology 80614 could reach 60,000 micrograms per milliliter. On the other hand, I do consider that 80614, under present technology, could achieve over 20,000 micrograms per milliliter.

Demain, Tr. 2216.

FF F 105. The reissue '698 patent teaches yields of 20,000 micrograms/ml can be obtained using the 80614 strain as deposited. Demain, Tr. 2216.

FF F 106. If ammonia or an ammonium salt was used in conjunction with Example 1 of the '698 reissue patent, those of skill in the art would expect an increase in titer beyond 20,000 micrograms/ml. Demain, Tr. 2243.

FF F 107. With respect to the method taught in the '698 reissue patent, and use of the 80614 strain, Dr. Demain testified:

> Q. In discussing the patent involved in this investigation, and that's RX-5, the '698 reissue patent, you I believe indicated that it was your feeling that titers of 20,000 micrograms per milliliter of salinomycin could be obtained from the 80614 strain and you were particularly referring to Example 1. Do you recall that?
>
> A. Yes.
>
> Q. And you observed that Example 1 does not employ either ammonia or an ammonium salt, correct?
>
> A. Not added as that, that's correct.
>
> Q. Do you have an opinion as to whether the titer that could be obtained would increase or decrease if you practiced Example 1 and added ammonia or ammonium salt?
>
> A. I think it probably would increase to a certain extent, a small amount, probably, if this is as it's stated in Example 1, 80614.

Demain, Tr. 2242-2243.

E. Secondary Considerations (Objective Indicia of Nonobviousness)

FF F 108. Kaken uses the process recited in claim 2 of the '698 reissue patent to prepare salinomycin. Kaken uses soybean oil with a final concentration of 24 to 27 percent. Kaken uses ammonium tartrate and urea. Kaken recovers salinomycin from the mycelial mass. Nakamura, Tr. 956-958.

FF F 109. Salinomycin is the leading coccidiostat in the United States. Salinomycin accounts for about 30% to 35% of all domestic coccidiostat sales. Hori, Tr. 857.

FF F 110. Pfizer International is licensed under the '698 reissue patent from Kaken. Tr. 1700-1701; CX-250C.

FF F 111. [C]

[C]

[C]

[C]

FF F 112. A.H. Robbins, and the successor-in-interest thereto, American Home Products, had a license under the '698 reissue patent. Hori, Tr. 858.

FF F 113. Hoffmann-LaRoche took a license under the '698 patent. Hoffman-LaRoche continues to pay royalties under its license in addition to payments for product. Hori, Tr. 867; CX 322C.

FF F 114. The invention of the '698 reissue patent as first disclosed in the '942 original patent, has had what Complainant's expert termed a "revolutionary impact" on the field of polyether antibiotic fermentation. The disclosure of the invention directed the field to the extensive use of oils in polyether fermentations. Demain, Tr. 2146.

FF F 115. The importance of the invention disclosed in the '698 reissue patent is recognized in the fermentation industry. Complainant's expert characterized the '698 reissue patent as "the gold standard of polyether antibiotic fermentation patents." Demain, Tr. 2147.

FF F 116. The teachings of the '698 reissue patent have been widely followed throughout the polyether antibiotic industry and changed the way people develop polyether antibiotic fermentations. Demain, Tr. 2146-2147.

FF F 117. Dr. Demain testified that:

> Q. Do you feel that this patent, and by this patent I mean the '942 patent and the reissue patent which is based thereon, has contributed a substantial teaching to the industry in polyether fermentation technology?
>
> A. Yes, it's a real teaching patent in which the field has been generally impressed by this patent. I've seen a number, even in Dr. Hutchinson's publications, he points out the unique nature of the subject matter of this patent and it has changed the way people develop fermentations in the polyether field. I mean, the public, as far as companies are concerned, have benefitted from this patent.

Demain, Tr. 2146-2147.

FF F 118. Dr. Demain has successfully employed the teachings of the '698 reissue patent to use large amounts of oils in the fermentation of an antibiotic. Demain, Tr. 2146.

VII. ALLEGED MISUSE

FF G 1. Preparations containing salinomycin account for about 30% to 35% of all domestic coccidiostat sales. Hori, Tr. 857.

FF G 2. Salinomycin premixes compete with several other coccidiostats. Hori, Tr. 857, 887-889; Heinle, Tr. 1036-1037; CX 630.

FF G 3. Mr. E. Thomas Corcoran, American Home Products ("AHP"), Corporate Vice President, Specialty Pharmaceuticals, wrote to Mr. H. Shibuya, Kaken's Executive Managing Director, International Operations and Licensing Department in a letter dated and sent by facsimile on December 29, 1993. The letter discussed previous negotiations with Kaken and a possible sale of Agri-Bio, a subsidiary of A.H. Robins ("Robins") which used salinomycin, to American Cyanamid ("ACC"). Robins is a subsidiary of AHP. CX 315C. See RX 920C, Joint Stip. of Facts, Nos. 13-18. The letter from Mr. Corcoran stated in part as follows:

ACC is willing to enter into a long-term exclusive supply agreement with Kaken. It is my understanding that ACC fulfills the conditions desired by Kaken.

However, unless we have your consent as previously requested, it is going to be very difficult for us not to pursue a long-term supply contract with Hoechst. We also would be forced to cancel our salinomycin orders recently placed with Kaken, which have a value of over $3.2MM. This would not be in the best long-term interests of all concerned.

We are trying to accommodate the needs of Kaken. You must understand that we are under time pressures from Hoechst. If you would like us to continue with Hoechst please respond immediately. If not, we need your consent with no monetary transfer fees.

The continuing royalty, the exclusive supply agreement for salinomycin, and a strong partner like ACC provide excellent long term returns for Kaken. Let's proceed on that basis.

CX 315C (emphasis added).

FF G 4. Mr. Shibuya responded to Mr. Corcoran, in a letter sent by facsimile on January 6, 1994, on the subject: "Request for Consent to Transfer of License from A.H. Robins to American Cyanamid Company." He stated in part, as follows:

As we mentioned in our fax of December 29 and over the phone on December 31, the most important conditions to us with regard to the requested consent are,

* * *

(3) Guarantee that the Supply Agreement acceptable to ACC and Kaken will be executed.

* * *

We are going to have meetings with ACC on January 10 and 11 to discuss terms and conditions of the Supply Agreement. If the result of the discussion is satisfactory to both parties we would like to discuss the conditions with regard to the consent to the Transfer in more detail to reach a final agreement with you as soon as possible.

CX 316C (emphasis added).

VIII. DOMESTIC INDUSTRY

A. Complainant Kaken Practices Claim 2 Of The '698 Reissue Patent

FF H 1. Kaken uses the process recited in claim 2 of the '698 reissue patent to prepare salinomycin. Kaken uses soybean oil with a final concentration of approximately 24 to approximately 27 percent. Kaken uses ammonium tartrate and urea. Kaken recovers salinomycin from the mycelial mass. Hori, Tr. 900; Nakamura, Tr. 956-958, 969-970.

FF H 2. The Kaken 1994 Drug Master File shows that the medium used by Kaken contains a fatty acid, soybean oil and an ammonium salt, ammonium tartrate. CX 891 at 13330.

FF H 3. Kaken adds a total of approximately 13,500 liters of soybean oil over the course of fermentation (CX 891 at 13330) and the total fermentation volume at hour 36 is approximately 55,000 liters (CX 891 at 13325). The calculated percentage based upon Kaken's DMF is 24.8%. Hori, Tr. 900; CX 891.

FF H 4. Mr. Nakamura of Kaken calculated the actual percentage of soybean oil based upon Kaken's production records for 12 recent lots. The percentage ranged from a high of 28.67 to a low of 24.6%. Nakamura, Tr. 969-970; CX 1170.

FF H 5. Mr. Nakamura made his calculations by adding together the total amount of soybean oil added to the fermentation tank, including the initial charge and all subsequent additions during the process; and dividing that total cumulative amount by the total amount of all components added to the fermentation tank during the process, except for the amount of caustic soda added at the end of the process after completion of the culturing. Nakamura, Tr. 966, 968.

FF H 6. Mr. Nakamura works in the fermentation of antibiotics on an industrial scale. Mr. Nakamura's calculations of oil percentage use a denominator which is based on the total culture solution. Such a calculation is by one working in the fermentation of antibiotics on an industrial scale. It is consistent with the claim language of the '698 reissue patent, and is how one of ordinary skill in the art would therefore read the patent claims. Nakamura, Tr. 964, 968, 991-993; Hori, Tr. 880-881; CX 1.

FF H 7. Ten of the twelve runs for which Mr. Nakamura made calculations show a total cumulative percentage of oil greater than 25 percent. Nakamura, Tr. 990; CX-1170.

B. The Domestic Activities And Investments Of Kaken's Licensee

FF H 8. Kaken has a consultant in the United States that it uses in connection with FDA matters related to salinomycin. Hori, Tr. 873-874.

FF H 9. Hoffmann-LaRoche, Inc. ("HLR") is principally involved in the human health care field, and it has a division that manufactures and markets vitamins for human and animal consumption. Heinle, Tr. 1035.

FF H 10. Hoffman-LaRoche took a license under the '698 patent. Hoffman-LaRoche continues to pay royalties under its license in addition to payments for product. Hori, Tr. 867; CX 322C.

FF H 11. HLR's animal health group is associated with the animal nutrition business. The animal nutrition business comprises the manufacture and sale of vitamins and animal feed. The animal feed made and sold by HLR includes Bio-Cox, which contain's salinomycin from Kaken. Heinle, Tr. 1035-1036.

FF H 12. The parties have entered into numerous joint stipulations of fact with respect to HLR's investments and activities. See RX920, Joint Stip of Fact.

FF H 13. Bio-Cox is used for poultry. RX 920C, Joint Stip. of Fact No. 20.

FF H 14. Under current FDA registrations, bulk salinomycin biomass must be formulated into premix forms and the premix then mixed with animal feed before it can be administered, for example, to broiler chickens. RX 920C, Joint Stip. of Fact No. 28.

FF H 15. Production and sale of Bio-Cox was AgriBio's only business prior to its acquisition by HLR. Heinle, Tr. 1042.

FF H 16. HLR purchased AgriBio Corp. as a going concern for approximately [C] . Heinle, Tr. 1048-1049; CX 550.

FF H 17. HLR acquired tangible and intangible assets. Tangible assets included plant and equipment and inventories. Intangible assets included trademarks, patents, licenses. There were also new drug applications ("NADAs"). Heinle, Tr. 1049.

FF H 18. HLR also manufactures and sells two other anticoccidial products, Avatec and Rofenaid. Heinle, Tr. 1036.

FF H 19. The active ingredient in each of the three products is salinomycin in Bio-Cox, lasalocid in Avatec, and a combination of sulfa di methoxine and ormetoprim in Rofenaid. Heinle, Tr. 1037.

FF H 20. Bio-Cox is the most widely sold anticoccidial in the United States. Heinle, Tr. 1037.

FF H 21. HLR purchases bulk salinomycin biomass, warehouses it, blends it, tests it for quality, bags it, ships it, invoices and services its customers. Heinle, Tr. 1056.

FF H 22. HLR converts bulk salinomycin into a lower-potency form acceptable for inclusion in finished poultry feeds by mixing the bulk salinomycin with inert ingredients. RX 920C, Joint Stip. of Fact No. 39.

FF H 23. Salinomycin as sold to the end users consists of salinomycin biomass and inert materials. Hori, Tr. 855. FDA regulations require that salinomycin be sold only in a premix form. SX 57, Response to Interrogatory No. 41; SX 57, Responses to Interrogatories Nos. 46-48; RX 920C, Joint Stip. of Fact No. 28.

FF H 24. All the inert materials with which the bulk salinomycin is blended to form Bio-Cox salinomycin premix are purchased in the United States. RX 920C, Joint Stip. of Fact No. 54.

FF H 25. The only use of Kaken's salinomycin biomass is in the production of Bio-Cox premix as a veterinary pharmaceutical product. See Klett, Tr. 1108-1109.

FF H 26. HLR began selling Bio-Cox in May 1994, when HLR acquired the AgriBio Corp. from American Home Products. Heinle, Tr. 1037-1038.

FF H 27. It is typical in the broiler industry to rotate anticoccidial products, using one product for several months and then changing to another product. This is known as a "shuttle program." Heinle, Tr. 1037.

FF H 28. HLR assigned a value of [C] as of September 1994 to the intangible assets it had acquired. All of this value is attributed to salinomycin. Heinle, Tr. 1053; CX 591C.

FF H 29. The FDA-approved VanBuren, Arkansas blending plant occupies [C] square feet of space, of which [C] square feet is used for office space, [C] square feet is used for blending and bagging, and [C] square feet is used for warehousing. CX 920C, Joint Stip. of Fact No. 42.

FF H 30. HLR assigned a value of [C] as of September 1994 to the equipment located at the VanBuren blending plant and testing equipment at the Gainesville facility. All of this value is attributed to salinomycin. Heinle, Tr. 1054; CX 591C.

FF H 31. Subsequent to acquiring the VanBuren blending facility, HLR has invested approximately [C] to improve the facility, including the purchase of a new air compressor and loading dock leveller. RX 920C, Joint Stip. of Fact No. 46.

FF H 32. The total payroll for the VanBuren plant for 1995 is budgeted to be approximately [C] in salary and benefits. RX 920C, Joint Stip. of Fact No. 51.

FF H 33. HLR sold and now leases the VanBuren plant. Klett, Tr. 1149-1150; CX 550.

FF H 34. HLR conducts quality control at both its VanBuren facility and its facility located at Gainesville, Georgia. RX 920C, Joint Stip. of Fact No. 57.

FF H 35. The Gainesville, Ga. facility is the Salinomycin Analytical Laboratory, which is a salinomycin quality control and customer services laboratory. RX 920C, Joint Stip. of Fact No. 59.

FF H 36. HLR has [C] full-time employees at the Gainesville facility who devote their full time to salinomycin premix production quality control

and to conducting assay tests of finished feed containing salinomycin premix for customers. RX 920C, Joint Stip. of Fact No. 60.

FF H 37. The total 1995 budgeted salaries and benefits for the employees at the Gainesville facility is [C] . RX 920C, Joint Stip. of Fact No. 61.

FF H 38. The total 1995 budgeted amount for conducting production quality control and customer service activities for salinomycin premix at HLR's Gainesville facility is [C] . RX 920C, Joint Stip. of Fact No. 62.

FF H 39. Over[C] HLR employees perform activities related to salinomycin. Heinle, Tr. 1056-1058.

FF H 40. Approximately [C]of these employees are employed in performing production and distribution activities. Heinle, Tr. 1057.

FF H 41. Approximately[C]of these employees are employed in performing quality control and quality assurance activities. Heinle, Tr. 1057.

FF H 42. HLR employs approximately [C]employees who spend at least part of their time on research and development, and regulatory activities. Heinle, Tr. 1057-1058.

FF H 43. HLR currently employs the equivalent of approximately [C] person-years of labor annually in the United States to perform research, development, regulatory, production, promotion, and sales activities related to HLR's salinomycin premix products. RX 920C, Joint Stip. No. 36.

FF H 44. HLR has invested additional resources to assure the success of salinomycin in the United States. Heinle, Tr. 1056.

FF H 45. HLR has invested a substantial amount of time, resources and money to develop additional uses for salinomycin in swine and cattle. Heinle, Tr. 1056; RX 920C, Joint Stip. of Fact No. 22.

FF H 46. HLR has plans to submit elements of the package seeking FDA approval for use of salinomycin with swine as part of a phased-submission, and may have already so by the time of the hearing. Heinle, Tr. 1065; RX 920C, Joint Stip. of Fact No. 116.

FF H 47. HLR has begun to plan for the expiration of an outstanding court order prohibiting actual physical developmental activities related to cattle by reviewing the NADA documentation, and registration work that had been done previously. Heinle, Tr. 1065.

FF H 48. A conservative calculation of the domestic value added by HLR, (which excludes profits and royalties, and the amortization of intangibles) is 30 percent. Klett, Tr. 1161.

FF H 49. Respondents contend that the value added by HLR domestically amounts to 28 percent. See Respondents' Proposed Finding of Fact FF I XII 35.

FF H 50. A calculation of domestic value added by HLR which includes amortization of intangibles, and profits and royalties is 51.7 percent. Klett, Tr. 1135.

CONCLUSIONS OF LAW

1. The '698 reissue patent would be infringed if it were valid and enforceable. Op. at 44-45.

2. The '698 reissue patent is invalid under 35 U.S.C. § 112 for failure to disclose the best mode. Op. at 76.

3. The '698 reissue patent is unenforceable due to inequitable conduct. Op. at 100-101.

4. The '698 reissue is not invalid under 35 U.S.C. § 103 due to obviousness. Op. at 117.

5. The '698 patent reissue is not indefinite under 35 U.S.C. § 112. Op. at 118.

6. The '698 reissue patent is not unenforceable due to patent misuse. Op. at 120.

7. There is a domestic industry as required by section 337. Op. at 128.

Based on the foregoing opinion, findings of fact, conclusions of law, the evidence, and the record as a whole, and having considered all pleadings and arguments as well as proposed findings of fact and conclusions of law, it is the Administrative Law Judge's INITIAL DETERMINATION ("ID") that no violation of § 337 exists in the importation of certain salinomycin biomass and preparations containing same, or in their sale, by reason of infringement of claim 2 of U.S. Letters Patent Re. 34,698.

The Administrative Law Judge hereby CERTIFIES to the Commission this ID, together with the record of the hearing in this investigation consisting of the following:

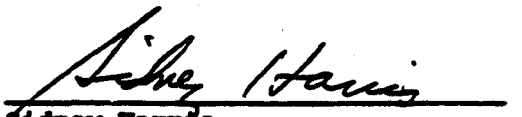
1. The transcript of the hearing, with appropriate corrections as may hereafter be ordered by the Administrative Law Judge; and further

2. The exhibits accepted into evidence in this investigation as listed in the attached exhibit lists.

In accordance with 19 C.F.R. § 210.39(c), all material found to be confidential by the Administrative Law Judge under 19 C.F.R. § 210.5 is to be given in camera treatment.

The Secretary shall serve a public version of this ID upon all parties of record and the confidential version upon counsel who are signatories to the protective order issued by the Administrative Law Judge in this investigation, and the Commission Investigative Attorney. To expedite service of the public version, counsel are hereby ordered to serve on the Administrative Law Judge by no later than November 15, 1995, a copy of this ID with those sections considered by the party to be confidential bracketed in red.

This ID shall become the determination of the Commission 45 days after its date of service unless the Commission within those 45 days shall have ordered review of this ID, or certain issues herein, pursuant to 19 C.F.R. § 210.43(d) or § 210.44.



Sidney Harris
Administrative Law Judge

Issued: November 6, 1995