CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE for:

APPLICATION NUMBER: 019971

TRADE NAME: Dextrose Injection USP 5% in Flexible Plastic Container

GENERIC NAME: Dextrose Injection USP 5% in Flexible Plastic Container

SPONSOR: DHL Laboratories

APPROVAL DATE: 09/28/95

NDA 19-971

SEP 28 1995

DHL Laboratories
155 Medical Sciences Drive
P.O. Box 805
Union, South Carolina 29379

Attention: Douglas G. Braun
Vice President

Dear Mr. Braun:

Please refer to your April 18, 1989, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dextrose Injection USP 5% in Flexible Plastic Container.

We acknowledge receipt of your amendments and correspondence dated January 3, February 7, April 24, May 4, 9, and 11, and November 5, 1990; July 7, 1993; March 10, June 28, and September 28 and 29, 1994; and March 20, May 11, July 13, August 17, and September 15, 1995. Additionally, we refer to our not approvable letters dated December 29, 1989; October 31, 1990; and June 23, 1994; and to our approvable letter dated July 6, 1995.

This new drug application provides a source of water and carbohydrate when administered intravenously.

We have completed the review of this application including the submitted draft labeling and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling in the submission dated September 15, 1995. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft labeling submitted on September 15, 1995. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit fifteen copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved NDA 19-971. Approval of this labeling by FDA is not required before it is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and
Communications, HFD-240
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any deficiencies that may occur.

Please submit one market package of the drug when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Steve McCort
Consumer Safety Officer
(301) 443-7515

Sincerely yours,

Patricia Y. Love, M.D., M.B.A.
Director, Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:

Original NDA 19-971*
HFD-160/Div. files*
HFD-160/DivDir/Love
HFD-2/M.Lumpkin
HFD-100
HFD-130/DISTRICT OFFICE
HF-2/medwatch
HFD-80
HFD-244
HFD-613
HFD-735
HFD-160/SChem/Sheinin
HFD-160/Chem/Koch
HFD-160/Pharm/See
HFD-160/Micro/Vincent
HFD-16/CSO/McCort*

* with labeling

drafted: jr/September 14, 1995/ 19971.ap
r/d Initials:Cheever 9-19-95/Koch 9-20-95/Sheinin 9-21-95/See 9-21-95/Vincent 9-21-95/Cooney 9-21-95
F/T by: Rhee 9-21-95

APPROVAL

6 Page(s) Redacted

Rhee

RECORD OF TELEPHONE CONVERSATION/MEETING	**Date:** September 12, 1995
Re: 8-17-95 submission I called Mr. Braun to request the following: 1. Bag labeling: The NDC number should not immediately follow the product name as it appears the NDC number is a part of a product name. I asked him to move the NDC number to the top and to allow enough space between the NDC number and the product name. Mr. Braun said because of the small bag size, he was not sure how much space he will have between the NDC # and the name. I mentioned that that takes care of my next requests which were going to be: **a**. Separate line for "Recommended Storage" statement, **b**. Add a space between "CAUTION" and "Single dose....nonpyrogenic." statement. Also, add a space between "Single dose.....nonpyrogenic." and "Additives may.....Do not store." statement. Mr. Braun agreed to move the NDC number to the top. 2. Overpouch labeling: I asked him to add a comma after between "overwrap" and "check" on line 8, and between "found" and "discard" on line 10. He agreed. 3. Package Insert: Add NDC number at the end of the How Supplied section. Mr. Braun agreed. He is going to make these changes using his computer and fax me a copy. If the fax is acceptable, he'll follow with a hard copy. cc. Orig NDA HFD-160/Div File HFD-160/Koch HFD-161/Rhee Julie Rhee --- **Name: Julie Rhee**	**NDA/IND#:** NDA 19-971 **Telecon/Meeting initiated by:** ○ Applicant/Sponsor ● FDA **By:** Telephone **Product Name:** 5% Dextrose Injection USP **Firm Name:** DHL Laboratories Union, SC **Name and Title of Person with whom conversation was held:** Douglas G. Braun Vice President **Phone:** (803) 427-6293

ADMINISTRATIVE REVIEW OF NDA 19-971

Dextrose Injection USP 5% in Flexible Plastic Container

Our approvable letter dated July 6, 1995 included only labeling recommendations.

STATUS OF OUTSTANDING ISSUES:

1. The sponsor, DHL Laboratories, responded to our labeling recommendations on August 17, 1995. However, this submission needed the following 3 corrections:

   a. Location of NDC number on the bag label,
   b. Placement of commas after the word "overwrap" and "found" in the first paragraph of the overpouch, and
   c. Placement of NDC number under HOW SUPPLIED section of package insert--the company was informed that this is not required but we recommended that they use the NDC number under HOW SUPPLIED section.

2. On September 15, 1995, the company re-submitted their revised labeling and it is acceptable.

ACTION TO BE TAKEN:

The NDA is now ready for approval and approval letter have been drafted.

Julie Rhee
Consumer Safety Officer
September 22, 1995

cc:OrigNDA
HFD-160/DivFile

ADMINISTRATIVE REVIEW

Labeling Review

NDA 19-971 Dextrose Injection USP 5% in Flexible Plastic Container

Sponsor: DHL Laboratories

Submissions Date: August 17 and September 15, 1995

Review Date: September 18, 1995

Reviewer: Julie Rhee, CSO

August 17, 1995 submission incorporates our labeling recommendations which were included in our July 6, 1995 approvable letter. The sponsor submitted a minor amendment, which deals with the location of NDC number on the container, placement of commas on the overpouch, and including NDC number under the HOW SUPPLIED section of package insert, on September 15, 1995.

Container Label: Acceptable.

Overpouch: Acceptable

Package Insert:

DESCRIPTION:	Acceptable
CLINICAL PHARMACOLOGY:	Acceptable
INDICATIONS AND USAGE:	Acceptable
CONTRAINDICATIONS:	Acceptable
WARNINGS:	Acceptable
PRECAUTIONS:	Acceptable
ADVERSE REACTIONS:	Acceptable
OVERDOSAGE:	Acceptable
DOSAGE AND ADMINISTRATION:	Acceptable
HOW SUPPLIED:	Acceptable
Directions for Use:	Acceptable

Recommendation:

The labeling as submitted on August 17 and September 15, 1995, is acceptable for an approval of this NDA.

Julie Rhee, CSO

Concurred by:

Stan Koch
Reviewing Chemist

Norman See, Ph.D. 9/18/95
Reviewing Pharmacologist

Eric Sheinin 9-20-95
Eric Sheinin, Ph.D.
Supervisory Chemist

David Bailey 9/18/95
David Bailey, Ph.D.
Acting Supervisory Pharmacologist

DHL Laboratories Inc.
155 Medical Sciences Drive • P.O. Box 805 • Union S.C. 29379
803 427-6293 • Fax 803 427-1668

September 15, 1995

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I.
DATE

By United Parcel Service

Food and Drug Administration
Office of Drug Evaluation I
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

Attn: Patricia Love, M.D., M.B.A.
Director
Division of Medical Imaging, Surgical
& Dental Drug Products
(Room 18B-06)

Dear Dr. Love:

RE: NDA #19-971 for 5% Dextrose Injection USP / DHL Laboratories, Inc Amendment No. 8

The contents of this amendment consist of changes to draft labeling as recommended by your office as follow:

1) The NDC number on the bag imprint has been moved to the upper left corner to set it off from the product name.

2) Two commas have been inserted into the first paragraph of the overpouch labeling for clarity.

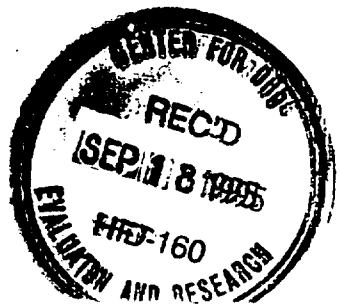
3) The "How Supplied" portion of the package insert has a sentence added at the end declaring the number of overpouches per shipper and NDC number.

A complete set of all draft labeling is attached.

Sincerely,

D. G. Braun

Douglas G. Braun



7 Page(s) Redacted

Labeling Review Meeting Minutes

Date: June 15, 1995

NDA 19-971 Dextrose Injection USP 5% In Flexible Plastic Container

Attendees:

Mr. Stan Koch, Chemist, DMISDDP
Norman See, Ph.D., Pharmacologist, DMISDDP
Susan Cusack, Consumer Safety Officer, DMISDDP
Julie Rhee, Consumer Safety Officer, DMISDDP

The following recommendations were made during the meeting:

~~Delete~~
Add

Bag labeling:

1. The recommend storage statement should be included on the immediate container label.

2. Move NDC number to the top, i.e, next to the 100 ml.

3. The font of the concentration (5%) should be as large as "Dextrose Injection USP".

4. "~~Approximate~~ pH 4.1 (specify the pH range) ~~Calculated~~ Osmolarity ~~approximately~~ 252 mOsm/L (calc.)".

5. Replace "~~Some additives may be incompatible, consult pharmacist.~~" with "Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic techniques. Mix thoroughly. Do not store.".

Over pouch labeling:

1. 3 ~~UNITS~~ BAGS.

2. "DO NOT REMOVE ~~UNITS~~ BAGS FROM OVERWRAP UNTIL READY FOR USE. USE ALL ~~UNITS~~ BAGS PROMPTLY WHEN OVERPOUCH IS OPENED.".

Package insert:

DESCRIPTION:

1. Add "5%" on the following statement:

   "Each 100 ml of Dextrose Injection USP 5% contains 5.0 grams of Dextrose Monohydrate (D-glucose monohydrate) which has the following structural formula:"

2. "The pH of the solution is ~~approximately~~ 4.1 (specify the pH range) and the ~~calculated~~ osmolarity is ~~approximately~~ 252 mOsmol (calc.) per liter."

3. Between the third and the fourth paragraph, insert "Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period."

4. Replace the following statement "~~Dextrose Injection USP inside the plastic container can leach out very small amounts of the chemicals used to manufacture the plastic container. The safety of the plastic used to fabricate the container has been evaluated in both *in vitro* and *in vivo* studies according to USP requirements for Biological Tests for plastic containers.~~" with "Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts within the expiration dating period; however, biological testing was supportive of the safety of the plastic container materials.".

~~W~~ARNINGS:

1. Add the following statement at the beginning of this section:

   "Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic techniques. Mix thoroughly. Do not store.

   Because of the potential for life-threatening events, caution should be taken to ensure that precipitates have not formed in any parenteral nutrient admixture."

PRECAUTIONS:

1. Add the following statement after the third paragraph "Do not administer unless solution is clear.....":

"Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term animal studies with Dextrose Injection USP 5% have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility."

2. Change the Pregnancy Category subsection as follow:

Pregnancy: *Teratogenic Effects.*
Pregnancy Category C: Animal reproduction studies have not been conducted with ~~d~~Dextrose Injection USP 5%. It is also not known whether ~~d~~Dextrose Injection USP 5% can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Dextrose ~~by injection~~ Injection USP 5% should ~~only~~ be given to a pregnant woman only if ~~it is definitely~~ clearly needed.

3. Add the following subsection following the Pregnancy Category:

"Nursing Mothers: Caution should be exercised when Dextrose Injection USP 5% is administered to a nursing woman."

OVERDOSAGE:

Revise the following statement:

"In the event of ~~overhydration or solute overload~~ fluid overload during parenteral therapy, reevaluate the ~~patient~~ patient's condition and institute appropriate corrective ~~measures~~ treatment.

HOW SUPPLIED:

Revise the following statement:

Delete comma

"Dextrose Injection~~,~~ USP 5% is supplied ~~as a three pack providing 100 ml~~ in a partial fill bag containing 100 mL. Three partial filled bags are packaged in an overpouch.".

To Open the Flexible Container:

Replace the word "outer wrap" with either overwrap or overpouch in this section.

To Add Medication:

"~~WARNING: Some additives may be incompatible. Use aseptic technique when introducing additives~~."

"Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic techniques. Mix thoroughly. Do not store."

Julie Rhee

cc:OrigNDA 19-971
HFD-160/DivFile
R/D by: Rhee 6-16-95 win6.0c:19971lab.min
Acknowledgements:Koch 6-23-95
F/T by:Rhee 7-6-95

Internal meeting minutes

19 Page(s) Redacted

ELLIS PHARMACEUTICAL CONSULTING, INC.
913 STATE ROAD
PRINCETON, NEW JERSEY 08540-1484

April 10, 1989

Food and Drug Administration
Center for Drugs and Biologics
5600 Fishers Lane
Rockville, MD 20857

Dear Sir:

We are authorized by DHL Laboratories, Inc. to provide the following Patent Certification Statement pursuant to Section 505(b)(2)(A)(i) of the Federal Food, Drug and Cosmetic Act. We hereby certify that in our opinion and to the the best of our knowledge that no patent information has been filed on the drug that is the subject of this application.

Sincerely yours,

ELLIS PHARMACEUTICAL
CONSULTING, INC.

Hanni Levi Ellis
For DHL Laboratories, Inc.

HLE:pf

9-1-95

EXCLUSIVITY SUMMARY for NDA # 19-971 SUPPL # —

Trade Name Dextrose Injection **Generic Name** Dextrose

Applicant Name DHL Labs **HFD-** 160

Approval Date 9-28-95

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

   a) Is it an original NDA?

   YES /✓/ NO /___/

   b) Is it an effectiveness supplement?

   YES /___/ NO /✓/

   If yes, what type? (SE1, SE2, etc.) _____

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

   YES /___/ NO /✓/

   If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

   _____

   _____

   If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   _____

   _____

d) Did the applicant request exclusivity?

YES /___/ NO /✓/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

_____

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?

YES /✓/ NO /___/

If yes, NDA # 16-673 Drug Name Dextrose in plastic Container

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

   For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

   (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

   YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # _____ YES /___/ ! NO /___/ Explain: _____

! _____

Investigation #2

IND # _____ YES /___/ ! NO /___/ Explain: _____

! _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

Investigation #2

YES /___/ Explain _____

_____

_____

NO /___/ Explain _____

_____

_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

_____

Julie Phee
Signature
Title: CSO

9-18-95
Date

Signature of Division Director

9/19/95
Date

cc: Original NDA Division File HFD-85 Mary Ann Holovac

ORIGINAL

Medical Officer Review of Original NDA

MAY 10 1989

NDA 19-971 Completed: 5/10/89

Sponsor: DHL Laboratories Inc.
200 Medical Science Drive
P.O. Box 805
Union, SC 29379

Drug: 5% Dextrose Injection USP in DRG Flexpak plastic container

Category: Fluid replenisher and caloric source

Classification: 5C

Dosage Form: Sterile, non-pyrogenic aqueous solution

Route of Administration: I.V. Infusion

Proposed Indication: Water and calorie source

Submitted: 4/18/89
Received: 4/20/89
Assigned: 5/5/89

Type of Submission: Original NDA

General Comment:

This NDA is filed by DHL Laboratories, a firm unknown to the Agency heretofore as far as can be determined. According to the discussion during a pre-NDA meeting in November of 1987, they are a new company who intend to manufacture and distribute a line of LVP solutions in a new plastic container that is made in the U.K. and sold to a number of LVP distributors abroad.

The drug product is not new. No clinical studies have been performed and none are required. The central issue of this NDA is the new flexible plastic container.

The primary focus of the drug approval process will be on manufacturing and control issues and on sterility and stability issues. These will be addressed in the Chemistry and Microbiology reviews.

A draft of the proposed package insert is submitted.

Description:

The composition and specifications are presented in a table appearing at the end of the insert. The pH range is not specified. This problem and the location of this table will be addressed in the Chemistry review.

Clinical Pharmacology: Satisfactory

Indications and Usage: Satisfactory

Contraindications: Satisfactory

Warnings: Satisfactory

Precautions: Satisfactory

Adverse Reactions: Satisfactory

Overdosage:

There is no overdosage section as required by 21 CFR 201.57. This heading should be included and should read as follows: "In the event of fluid overload during parenteral therapy, reevaluate the patient's condition and initiate appropriate corrective therapy."

Unsatisfactory

Dosage and Administration: Satisfactory

How Supplied: Satisfactory

Directions for Use: Satisfactory

Conclusion and Recommendations

1. This NDA is clinically approvable.

2. The sponsor should be requested to make the following revision in proposed package insert:
   Following the Adverse Reactions section, add a new section entitled Overdosage. This section should read as follows: In the event of fluid overload during parenteral therapy, reevaluate the patient's condition and institute appropriate corrective treatment.

J.C. Kenealy, M.D.

cc:
NDA 19-971
HFD-160/Division File
HFD-160/JCKenealy
HFD-160/JLewis
R/D Init by: PGWalters/5-10-89
F/T by: SDavis/5-11-89
Wang 4097N

12-26-89

NDA 19-971 Dextrose Injection USP 5% In Flexible Plastic Container

Statistical review on this submission was not done

OCT 28 1993

5% DEXTROSE
NDA 19-971
Reviewer: M. Daniel Gordin, Ph.D.

DHL LABS
UNION, SC
Submission Date
JULY 7, 1993

REVIEW OF A WAIVER REQUEST

BACKGROUND:

In this submission, the firm has submitted a request for a waiver of *in vivo* bioavailability testing for this product. It is the same concentration as approved dextrose solution, and it is intended for intraveneous administration.

RECOMMENDATION:

The bio-waiver requested under NDA 19-971 is found to be acceptable under 21 CFR 320(b)(i) by the Division of Biopharmaceutics

Please convey the Recommendation to the firm.

M. Daniel Gordin 10/27/93

M. Daniel Gordin, Ph.D.
Pharmacokinetics Evaluation Branch

RD/FT Initialed by John P. Hunt October 27, 1993

cc: NDA 19-971, HFD-160, HFD-426 (Gordin), Drug, Chron, and HFD-19 (FOI).

\160\N19-971\Wai

NDA# 19-971

FEB - 1 1995

9.1

Review and Evaluation of Pharmacology and Toxicology Data

Norman A. See, Ph.D., R.Ph.
Draft Completed 9/9/93

Supplement AZ
Submission Date: 7/7/93
Center Receipt Date: 7/22/93

Sponsor: DHL Laboratories, Inc.

Drug: 5% Dextrose Injection, USP

Formulation: Sterile solution for IV administration

Indication: As a source of water and calories, and as a diluent and delivery system for compatible drug additives.

Maximum recommended human dose: Not applicable

Labelling: The following modifications in the labeling of NDA 19-971 are recommended. These comments should be communicated to the sponsor.

1. In the second paragraph of the "Description" section, please delete the sentences that read "Solutions in contact with..." and "However, the safety of...". Please replace these sentences with the following:

Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials.

2. Please add the following to the "Precautions" section of the draft label:

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term animal studies with dextrose injection USP have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

3. **Pregnancy.** Please change this section to read:

Pregnancy: ***Teratogenic Effects.***
Pregnancy Category C. Animal reproduction studies have not been conducted with dextrose injection USP. It is also not known whether dextrose injection USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Dextrose injection USP should be administered to a pregnant woman only if clearly needed.

4. Please add the following to the "Precautions" section of the draft label:

Nursing Mothers: Caution should be exercised when dextrose injection USP is administered to a nursing woman.

9/9/93

Norman A. See, Ph.D., R.Ph.
Reviewing Pharmacologist

Concur
Lorraine L. Meyers
2-1-95

cc: NDA 19-971
HFD-160 Div. File
HFD-160/Pharm/NSee
HFD-160/MO/PLove
hfd-160/Chem/SKoch
HFD-160/CSO/AWeikel

JUN 14 1995

DIVISION OF RADIOPHARMACEUTICAL, SURGICAL AND DENTAL DRUG PRODUCTS
(HFD-160)

CHEMISTRY REVIEW # 4

NDA#: 19-971 DATED: 9-28-94 (AC) 9-29-94 (BC) 5-11-95 (BC) CDER DATE: 9-29-94 9-30-94 5-12-95

SUBMISSION TYPE: NDA Original Amendments REVIEWER: Stan Koch

APPLICANT/SPONSOR:
DHL Laboratories, Inc.
200 Medical Sciences Dr.
Union, S.C. 29379

Agent:
Ellis Pharmaceutical Consulting, Inc.
913 State Road
Princeton, N.J. 08540

ASSIGNED DATE: 10-6-94

COMPLETED DATE: 5-31-95

ROUTE/ADMIN: Injection

DOSAGE FORMS: Parenteral Plastic Bag

PRODUCT NAME(S):

Proprietary: none

Nonproprietary: Dextrose Injection USP in Flexible Plastic Container

Code Name/Number: none

STRENGTHS: 5%

DRUG CATEGORY: LVP

INDICATIONS: caloric source 100 ml fill in 150 ml mini bag

	YES	NO	DATED
DRAFT LETTER			
TELECONS		x	

RX OR OTC: Rx

SUPPORTING DOCUMENTS:

REMARKS: The original submission dated 4-18-89 was the subject of Chemistry Review #1 on 10-25-89; the application was found to be Not Approvable from the standpoint of chemistry. An action letter issued on 12-29-89. The 4-24-90 AZ plus several minor amendments were the subject of Chemistry Review #2, completed 7-4-90. The application was once again found to be deficient from the standpoint of the chemistry manufacturing and controls. Another deficiency letter issued on 10-31-90. The 7-7-93 AC generated the 4-15-94 chemistry review followed by the 6-23-94 N/A letter, to which the 9-28-94 and 9-29-94 amendments respond.

The cover letter in this amendment is from Ellis Pharmaceutical Consulting, Inc., submitted for DHL Laboratories, Inc., and signed by Hanni L. Ellis. On 2-15-95 a conference call was held between this reviewer, Ms. Ellis, and Mr. Douglas Braun, v.p. Quality Assurance and Regulatory Compliance, DHL, for the purpose of discussing revisions needed in the analytical procedures made a part of the 9-29-94 Methods Validation package. We requested that the procedures be rewritten to be more specific and analyst-friendly, and that the rewritten procedures be validated. Refer to MEMO of telecons dated 2-15-95, 2-21-95, 2-23-95, 3-8-95, 3-10-95, and 3-15-95. The revised Methods Validation package was submitted in the 5-11-95 amendment.

The original CGMP evaluation request sent to HFD-320 on 9-5-89 found DHL Laboratories facility in Union, SC and acceptable as of 1-3-90. Another request for the plant dated 5-15-90 was returned on or about 8-2-90 with favorable results. The 1-31-94 EER was found acceptable by HFD-324 on 7-8-94. An EER update, including Dr. D. Castillo, Chief of the Chemistry Department, Wofford College, Spartenburg, SC, was sent forward on 1-17-95.

SUMMARY/CONCLUSIONS/RECOMMENDATIONS: This application is now "approvable" from the standpoint of the chemistry manufacturing and controls with the understanding that the following aspects of this review are not yet acceptable:

1. A response to the recommendations for revisions in the labeling contained in the chemistry deficiencies in the 6-23-94 N/A letter has not been received by this reviewer.

2. The Methods Validation process has been initiated but not completed.

3. The establishment inspection CGMP evaluation process has not been completed.

Orig. NDA
HFD-160/Div File
~~HFD-160/ESheinin~~
HFD-160/SKoch
HFD-161/JRhee
F/T SKoch 5/31/95
Revised 6/13/95

Stan Koch

Stan Koch

6-14-95

19 Page(s) Redacted

DIVISION OF RADIOPHARMACEUTICAL, SURGICAL AND DENTAL DRUG PRODUCTS
(HFD-160)

CHEMISTRY REVIEW # 3

MAY 18 1994

NDA#: 19-971 DATED: 7-7-93 (AC) CDER DATE: 7-22-93 REVIEW # 3

SUBMISSION TYPE: NDA Original Amendment REVIEWER: Stan Koch

APPLICANT/SPONSOR:
DHL Laboratories, Inc.
200 Medical Sciences Dr.
Union, S.C. 29379

ASSIGNED DATE: 7-30-93

COMPLETED DATE: 4-15-94

ROUTE/ADMIN: Injection

DOSAGE FORMS: Parenteral Plastic Bag

PRODUCT NAME(S):

STRENGTHS: 5%

Proprietary: none

DRUG CATEGORY: LVP

Nonproprietary: Dextrose Injection USP in Flexible Plastic Container 100 ml fill in 150 ml mini bag

INDICATIONS: caloric source

Code Name/Number: none

	YES	NO	DATED
DRAFT LETTER			
TELECONS		x	

RX OR OTC: Rx

SUPPORTING DOCUMENTS:

REMARKS: The original submission dated 4-18-89 was the subject of Chemistry Review #1 on 10-25-89; the application was found to be Not Approvable from the standpoint of chemistry. An action letter issued on 12-29-89. The 4-24-90 AZ plus several minor amendments were the subject of Chemistry Review #2, completed 7-4-90. The application was once again found to be deficient from the standpoint of the chemistry manufacturing and controls. Another voluminous deficiency letter issued on 10-31-90. This most recent 7-7-93 AC is submitted in response to the last deficiency letter and is the subject of this review.

The cover letter in this amendment is from Ellis Pharmaceutical Consulting, Inc., submitted for DHL Laboratories, Inc., and signed by Hanni L. Ellis.

The original CGMP evaluation request sent to HFD-320 on 9-5-89 found DHL Laboratories facility in Union, SC and Corn Products facility in Argo, IL acceptable as of 1-3-90. Another request for the Corn Products plant dated 5-15-90 was returned on or about 8-2-90 with favorable results. The most recent request for an evaluation of the DHL and Corn Products facilities was completed for disposition to HFD-320 on 1-31-94.

While a separate submission to this NDA solely addresses the deficiencies dealing with microbiology, information in the submission made the subject of this chemistry review also contains microbiological data. This fact was verbally pointed out to Dr. C. Vincent the week of 2-7-94, and a consult form was completed to formalize this notification on 2-14-94.

Toxicological test results discovered in this amendment on 3-16-94; a consult request was initiated on 3-17-94. Data appear sufficiently aged to have been the subject of earlier pharmacology review by J. Wilson.

The mini bag is fitted with a closed filling tube, a drug additive port, and a set port.

SUMMARY/CONCLUSIONS/RECOMMENDATIONS: Although making good progress, this application remains unacceptable from the standpoint of manufacturing and controls.

Stan Koch

Stan Koch

Orig. NDA
HFD-160/Div File
HFD-160/ESheinin
HFD-160/SKoch
HFD-161/AMWeikel
F/T SKoch 4/15/94, revised 5/18/94

ESheinin 5-18-94

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OCT - 5 1990

DIVISION OF RADIOPHARMACEUTICAL, SURGICAL AND DENTAL DRUG PRODUCTS
(HFD-160)

DATA SUMMARY SHEET

NDA#: 19-971 DATED: 4-24-90 (AZ)
5-4-90 (BC)
5-11-90 (BC)
2-7-90 (BC) - Methods Validation Package
5-9-90 (BC) - Methods Validation Update

CDER DATE: 4-25-90
5-7-90

REVIEW # 2

SUBMISSION TYPE: NDA Original Amendments

REVIEWER: Stan Koch

APPLICANT/SPONSOR:
DHL Laboratories, Inc.
200 Medical Sciences Dr.
Union, S.C. 29379

ASSIGNED DATE: 4-25-90

COMPLETED DATE: 7-4-90

ROUTE/ADMIN: Injection

DOSAGE FORMS: Parenteral Plastic Bag

PRODUCT NAME(S):

STRENGTHS: 5%

Proprietary: none

DRUG CATEGORY: LVP

Nonproprietary: Dextrose Injection USP in Flexible Plastic Container

INDICATIONS: caloric source

Code Name/Number: none

	YES	NO	DATED
DRAFT LETTER			
TELECONS		x	

RX OR OTC: Rx

SUPPORTING DOCUMENTS:

REMARKS: The original submission dated 4-18-89 was the subject of Chemistry Review #1 on 10-25-89; the application was found to be Not Approvable from the standpoint of chemistry. Our action letter issued on 12-29-89.

This review addresses material submitted in the 4-24-90 AZ original amendment as well as the minor amendments listed above. The cover letter in this AZ amendment is written under the letterhead of Ellis Pharmaceutical Consulting, Inc., continuing as the Applicant's agent when in communication with this Agency. The cover letter is signed by Hanni Ellis on behalf of DHL Laboratories.

This application calls for the use of a 150 ml container filled with approximately 100 ml of fluid (amount is adjusted due to underformulation and excess fill).

The Applicant has provided two filled and overwrapped pouches each of which contains three bags, as we requested in our N/A letter. These samples are for observation only.

The DHL inspection date remains a valid basis for acceptable CGMP evaluation.

SUMMARY/CONCLUSIONS/RECOMMENDATIONS: Although making good progress, this application remains unacceptable from the standpoint of manufacturing and controls.

Stan Koch

Stan Koch

Eric B Sheinin
10-5-90

Orig. NDA
HFD-160/Div File
HFD-160/SKoch HFD-160 Regina Joyce
R/D Init. by: ESheinin
F/T by:

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ORIGINAL

DIVISION OF MEDICAL IMAGING, SURGICAL AND DENTAL DRUG PRODUCTS (HFD-160)

CHEMISTRY REVIEW # 1

NOV 30 1989

NDA#:19-971 DATED: 4/18/89 CDER DATE: 4/19/89

Document Type: Original submission REVIEWER: Stan Koch

APPLICANT/SPONSOR: ASSIGNED DATE: 8/25/89

DHL Laboratories, Inc.
200 Medical Sciences Drive
P.O.Box 805
Union, S.C. 29379

COMPLETED DATE: 10/25/89

PRODUCT NAME(S):

Proprietary:none ROUTE/ADMIN: IV

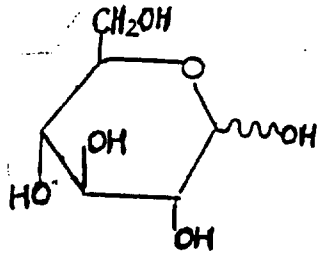
Nonproprietary: Dextrose Injection, USP in Flexible Plastic Container DOSAGE FORMS: Injection

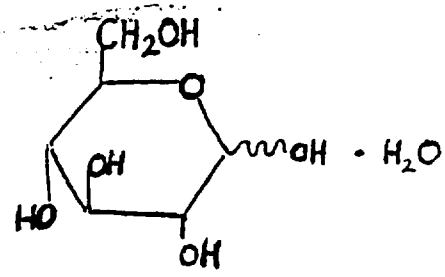
STRENGTH(S): 5% in 100 ml volume, contained in 150 ml bag

Code Name/Number:none DRUG CATEGORY:LVP

STRUCTURAL FORMULA: INDICATIONS: caloric source

Dextrose USP, both anhydrous and monohydrate





EMPIRICAL FORMULA: $C_6H_{12}O_6$
$C_6H_{12}O_6\ H_2O$

MOLECULAR WEIGHT: anhydrous, 180.16
monohydrate, 198.17

CHEMICAL NAME: D-glucopyranose monohydrate
D-glucose

Supporting Documents:

REMARKS:

This original application was initially assigned for chemistry review on 5-9-89, and reassigned to this reviewer as of 8-25-89. This review was started on 8-30-89.

DHL Laboratories has designated Ellis Pharmaceutical Consulting, Inc., 913 State Road, Princeton, N.J. 08540 to act as their agent in the submission of this NDA. According to DHL, Ellis has the authorization to "deal with any substantive matters that may arise in connection with any .... submissions" to this file. The letter from DHL expressing this position is dated 3-21-89. Mrs. Hanni Levi Ellis is the named consultant for DHL at Ellis Pharmaceutical Consulting.

Ellis Pharmaceutical Consulting has submitted a statement dated 4-10-89 which, based on authorization from DHL Laboratories, certifies that no patent information has been filed on the drug which is the subject of this application; this information is provided in response to Section 505(b)(2)(A) of the Act.

CONCLUSIONS AND RECOMMENDATIONS:

This application is not approvable from the standpoint of the manufacturing and controls.

cc:
Orig. NDA 19-971
HFD-160/Division File
HFD-160/SKoch
HFD-161/RJoyce/FStone
HFD-102/CKumkumian
R/D Init. by: EBSheinin/11-30-89

S.A.Koch 11/28

11-30-89

Wang #0252A

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wait for ... before R/D letter dt

5.1

NOV 22 1994

DIVISION OF MEDICAL IMAGING, SURGICAL, AND DENTAL DRUG PRODUCTS
MICROBIOLOGIST'S REVIEW NO. 4
November 22, 1994

A. 1. **NDA No:** 19-971

DRUG PRODUCT NAME: 5% Dextrose Injection, USP

APPLICANT: DHL Laboratories, Inc.
Union, South Carolina 24379

REVIEWER: Carol K. Vincent

2. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:**
Sterile solution for injection.

3. **METHOD(s) OF STERILIZATION:**

4. **PHARMACOLOGICAL CATEGORY AND/OR PRINCIPAL INDICATION:**
Source of water and calories.

5. **DRUG PRIORITY CLASSIFICATION:** 5 C

B. 1. **AMENDMENT:** **(AC)** dated 09-28-94, received for review 11-01-94

C. **REMARKS:** This amendment responds to chemistry and microbiology deficiencies addressed in HFD-160's June 23, 1994 Not Approvable letter to the applicant. Pages 1-12 of the applicant's 09-28-94 letter address chemistry questions. The microbiology questions and responses from the applicant are addressed in pages 12-14 of the 09-28-94 letter with attachments and are the subject of this review.

D. **CONCLUSION:** The applicant's response and additional information submitted are adequate. No microbiology issues remain outstanding.

The application is **recommended** for approval for sterility assurance and microbiological quality.

Carol K. Vincent
11-22-94

cc:
Orig. NDA 19-971
HFD-160/ CKVincent/Koch/Rhee
Drafted by: CKVincent/11-01-94/11-21-94
R/D Init by: P. H. Cooney/11-22-94

11/22/94

8 Page(s) Redacted

DIVISION OF MEDICAL IMAGING, SURGICAL, AND DENTAL DRUG PRODUCTS
MICROBIOLOGIST'S REVIEW NO. 2
March 7, 1991

MAR 15 1991

A. 1. **NDA No; Product Name:** 19-971;
5% Dextrose Injection, USP

APPLICANT: DHL Laboratories, Inc.
Union, South Carolina 24379

2. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** Sterile solution for injection.

3. **METHOD(s) OF STERILIZATION:**

4. **PHARMACOLOGICAL CATEGORY AND/OR PRINCIPAL INDICATION:** Source of water and calories.

5. **DRUG PRIORITY CLASSIFICATION:** 5 C

B. 1. **INITIAL SUBMISSIOn:** NDA document date: 4-18-89
Microbiology section submitted: 6-6-89
Assigned for review: 6-16-89
Microbiologist's Review No. 1, dated 12-4-89

2. **AMENDMENT:** 4-24-90 (Subject of this review)

RECEIVED FOR REVIEW: 4-27-90

3. **SUPPORTING DOCUMENTS:**

C. **REMARKS:** The April 24, 1990 response from the applicant answers most questions raised in Microbiologist's Review No. 1, December 4, 1989 regarding review of sterilization validation information. These questions were conveyed to the applicant in the Agency's "Not Approvable" letter of December 29, 1989.

D. **CONCLUSION:** The applicant's response and additional information submitted are inadequate. The application is not **recommended** for approval for sterility assurance and microbiological quality.

Carol K. Vincent 3-15-91

Carol K. Vincent

3/15/91

cc:
Orig. NDA 19-971
HFD-160/ C. K. Vincent
Drafted by: C. K. Vincent/11-27-90
Revised by: C. K. Vincent/ 01-06-91, 01-25-91, 03-06-91
R/D Init by: P. H. Cooney/ 3/14/91

17 Page(s) Redacted

ORIGINAL

DEC 19

Division of Medical Imaging, Surgical and Dental Drug Products
Microbiologist's Review No. 1
December 4, 1989

A. 1. Application Number: NDA 19-971

Applicant: DHL Laboratories, Inc.
Union, S.C. 24379

2. Product Name 5% Dextrose Injection, USP

3. Dosage Form: Sterile solution for injection

4. Method of Sterilization:

5. Pharmacological Category and/or Principle Indication: Scource of water and calories

6. Drug Priority Classification: 5C

B. 1. Initial Submission: Document date 4-18-89
Microbiology Section Submitted 6-6-89
Assigned for review 6-16-89

2. Amendments: None

3. Supporting Documents:

C. Remarks: Attached (page 2)

D. Conclusions: The NDA is not approvable for sterility assurance and microbiological safety of the subject drug product.

Carol K. Vincent
PNE 12/11/89

cc:
Orig. NDA 19-971
HFD-160/Division File
HFD-160/CSO/R.Joyce
drafted by: C.Vincent/11-20-89
R/D Init. by: P.H.Cooney/12-04-89
F/T by: D.Flannigan/12-18-89
Wang 4439X

13 Page(s) Redacted

ADMINISTRATIVE REVIEW OF NDA 19-971

Dextrose Injection USP 5% in Flexible Plastic Container

Our approvable letter dated July 6, 1995 included only labeling recommendations.

STATUS OF OUTSTANDING ISSUES:

1. The sponsor, DHL Laboratories, responded to our labeling recommendations on August 17, 1995. However, this submission needed the following 3 corrections:

   a. Location of NDC number on the bag label,
   b. Placement of commas after the word "overwrap" and "found" in the first paragraph of the overpouch, and
   c. Placement of NDC number under HOW SUPPLIED section of package insert--the company was informed that this is not required but we recommended that they use the NDC number under HOW SUPPLIED section.

2. On September 15, 1995, the company re-submitted their revised labeling and it is acceptable.

ACTION TO BE TAKEN:

The NDA is now ready for approval and approval letter have been drafted.

Julie Rhee

Julie Rhee
Consumer Safety Officer
September 22, 1995

cc:OrigNDA
HFD-160/DivFile

ADMINISTRATIVE REVIEW

NDA 19-971

DHL Laboratories, Inc.
155 Medical Sciences Drive
P.O. Box 805
Union, South Carolina 29379

SEP - 1 1995

Attention: Douglas G. Braun
Vice President

Dear Mr. Braun:

We acknowledge receipt on August 21, 1995, of your August 17, 1995, amendment to your new drug application for 5% Dextrose Injection USP.

The amendment contains additional information submitted in response to our July 6, 1995, approvable letter.

We consider this a major amendment under 21 CFR 314.60 of the regulations and it constitutes a full response to our letter. Therefore, the due date is February 17, 1996.

Should you have any questions, please contact:

Julie Rhee
Consumer Safety Officer
Telephone: (301) 443-7515

Sincerely yours,

8/31/95

for Patricia Y. Love, M.D., M.B.A.
Director, Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

6 Page(s) Redacted

6-1

NDA 19-971

MAR 27 1995

DHL Laboratories Inc.
200 Medical Science Drive
P.O. Box 805
Union, South Carolina 29379

Attention: Robert Weinstein
President

Dear Mr. Weinstein:

Please refer to your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 5% Dextrose Injection USP.

We also refer to your communication dated March 20, 1995, confirming a mutual agreement between you and the Agency to extend the review clock for 120 days from the current due date pursuant to 21 CFR 314.100(c). The new due date is July 28, 1995. We remind you of your commitment to provide a revised methods validation package by May 15, 1995, in order for us to complete our review and take an action by the new due date.

Should you have any questions, please contact Ms. Julie Rhee, Consumer Safety Officer, at (301) 443-5818.

Sincerely yours,

3/27/95

Patricia Y. Love, M.D., M.B.A.
Director, Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:OrigNDA
HFD-160/DivFile
HFD-160/Chem/Koch
HFD-161/CSO/Rhee 3-27-95
R/D by: Rhee 3-21-95 win6.0c:19971ext.rev
Acknowledgements: Cheever, 3.24.95
F/T by: Wilson, 3.27.95

General Correspondence

167 Page(s) Redacted