Comment 37 BIO/Charles E. Ludlam

March 22, 2000

The Honorable Q. Todd Dickinson
Assistant Secretary of Commerce and
Commissioner of Patents and Trademarks
Box 8
Washington, DC 20231

ATTN: Mark Nagumo; Steven Walsh/Linda Therkorn

Dear Commissioner Dickinson:

On behalf of the Biotechnology Industry Organization (BIO), I am pleased to offer these remarks in relation to the request for comments on the interim guidelines concerning written description (64 FR 71427) and utility (64 FR 71440) published on December 21, 1999, particularly in light of the recently published training materials to accompany those interim guidelines.

A. General Remarks

BIO is a trade association representing over 900 biotechnology companies and others involved with biotechnology research. Our membership represents a complete cross-section of the industry, from small startups to large pharmaceutical and agricultural biotechnology companies. Our members share numerous core beliefs, including an unquestionable dependence on effective patent protection for their innovations.

The two sets of guidelines and their accompanying training materials have triggered extensive discussion and debate within our industry and within the academic circles in which many of our companies circulate. The guidelines also have been cited in recent articles in the press regarding patents and genetic information. Unfortunately, some of these recent articles have raised certain issues that BIO does not believe are pertinent to the guidelines and the formulation of U.S. patent examination policy.

As a consequence, before offering our views on the two sets of guidelines and their accompanying training materials, we believe it is important to make a number of general observations.

1. The availability of patent protection for the chemical compounds that are the foundation of modern biotechnology, namely proteins, polypeptides, and nucleic acids, is absolutely critical to the success of our industry. Without strong and effective patent protection, development, particularly commercial development, of new treatments, diagnostic tools, pharmaceuticals and other benefits of our nation's investment in science and technology will not be possible.

2. The genius of the U.S. patent system is that it provides a powerful incentive for private commercial firms to invest vast sums in research. It creates a race to invent because most patents are granted to the inventor who is first to file an application. Then, when the patent is granted, there is a race to develop the invention into a commercial product -- in this case of a diagnostic or a therapeutic to treat a patient -- before the term of the patent has expired. This race is fundamentally in the interests of patients who are awaiting medicine to treat or cure deadly and disabling diseases. We need the patent system to ensure that the entrepreneurs in the biotechnology industry can raise the capital to fund this research, to prevent others from free-riding on the investments needed to bring products to market, and to deliver products to patients in need.

3. There have been numerous recent public misstatements and mischaracterizations of patents in the biotechnology sector. Patents protect inventions from misappropriation by companies or universities engaged in commercial activity. Patents give no rights over people or their genes, and rights cannot, by definition, extend to products as they exist in Nature. Similarly, patents cannot be granted on uncharacterized nucleic acids or other chemical compounds or compositions. A patent only can be granted on such compounds if the inventor identifies specific functions or characteristics of the compound that correlate to an application in human health or some other commercially relevant purpose. No one can simply plug in a machine and generate a patentable invention. In short, patents are granted as the reward for the value added by the researcher, not for work performed by a machine in generating raw sequence data.

4. There is no difference of opinion among the BIO membership regarding the desirability of making available patent protection for specific chemical compounds that are adequately characterized by their chemical structure or physical characteristics. This includes compounds identified by an amino acid or nucleotide sequence, (*e.g.*, polypeptides, proteins, nucleic acids) including compounds containing nucleotide sequences that correspond to complete human or animal genes, or to portions of such genes. Stated simply, all BIO Members fully support the ability of inventors to obtain claims directed to novel compounds where all or part of the complete structure of the claimed compound is represented by nucleotide sequences corresponding to partial or complete genes. Some differences in opinion exist among BIO's membership related to the conditions that must be established by a patent applicant to obtain such claims and to the scope of protection granted in certain situations. We believe that these differences will be worked out over time in the Patent and Trademark Office (PTO) and the courts as cases framing these issues are evaluated and acted upon.

5. All BIO members recognize the importance of the tools being used in modern biotechnological research, including those being used in the private and public sector to decipher the human genome. We fully support the ability of developers of innovative research tools to obtain patent or other forms of intellectual property protection for their commercially valuable research tools, and support their right to use their intellectual property rights to succeed commercially.

6. BIO Members also fully support the work underway toward deciphering the human genome, particularly the work being conducted in the public research sector. Indeed, many of BIO's members have made immense contributions toward the objective of deciphering the human genome. Our industry, due in large part to its close relationship with the public research and academic communities, engages in practices that facilitate the rapid dissemination of information to promote the larger objectives of scientific progress. Indeed, the availability of patent protection makes it possible for many of our members to routinely publish their findings and make their research tools available to the academic community without charge so that the scientific community at large benefits. Retaining some flexibility in publicly disclosing information to allow for the preparation and filing of patent applications is the only overhead associated with our relationship to the public research community, and has not proven to be a barrier to the rapid dissemination of scientific information that our companies are developing.

7. The patent system is an unquestionably positive stimulus for research, development and commercialization of new technology in the biotechnology sector, and is entirely complementary to publicly funded research efforts, including the work on the Human Genome Project. The recent changes enacted by Congress, including the requirement of publication of patent applications 18 months after they are filed, will significantly improve the system once those changes are implemented. BIO believes that the publication system will further the goal of rapid dissemination of advances in the biotechnology sector, and represents another complementary element of this system with the goals of publicly funded research initiatives in the biotechnology sector.

In view of these points, we believe that the revised examination guidelines represent a helpful effort toward clarifying the practices of the PTO in evaluating certain types of patent applications in the field of biotechnology.

B. Comments on the Interim Guidelines on Written Description

The revised interim guidelines concerning the PTO's application of the written description requirement are a significant improvement over the original interim guidelines. We appreciate the exhaustive effort that the PTO has engaged in to review, consider and respond to comments that many BIO Members presented in response to the first version of these guidelines. As a general matter, we believe the guidelines represent a solid foundation for PTO examiners to conduct their review of compliance of applications with the written description requirement. Overall, we do not recommend making significant alterations to the guidelines as they have been presented.

BIO Members have identified specific issues with regard to the written description guidelines, the response to public comment and the training materials accompanying these guidelines.

1. In paragraphs (34) and (35) preceding the revised guidelines, the PTO indicates that open-ended claims reciting a specific nucleotide sequence, regardless of the character of that sequence or what it represents, will not present deficiencies under the written description requirement, a position apparently inconsistent with Example 7 of the training materials.

    - In paragraph (34), the PTO notes that several commentators expressed the view that an open-ended generic claim to a "DNA comprising SEQ. ID. NO: 1" could raise problems under the written description requirement standard as enunciated by *Eli Lilly*, if SEQ. ID. NO:1 refers to an EST. However, the PTO states that such claims are unlikely to raise any written description issues. The PTO notes that parties that criticized this example did not explain why there would be any legitimate written description problem for the claim if the specified sequence corresponded to an EST as opposed to a gene. The PTO concludes that deficiencies of these claims, if any, would be related to compliance with the utility requirement.

    - In paragraph (35), the PTO also addresses the written description requirement for open-ended claims based on disclosure of the sequence of an EST. In this paragraph, the PTO clearly disagrees that the scope of open-ended claims encompassing a specific EST sequence are "necessarily too large to satisfy the written description requirement." Again, the PTO suggests that these types of claims may not comply with the utility and enablement requirements.

    - In contrast, Example 7 of the training materials shows an example of an open-ended claim to a nucleotide comprising a specific EST sequence where the full length cDNA is not described or otherwise characterized in the specification. The PTO concludes that this claim does not satisfy the written description requirement. If, however, the EST is described in the specification as a full length cDNA, the PTO notes that the written description problem would not exist in relation to this claim.

    BIO urges the PTO to resolve the conflict between paragraphs 34 and 35 and Example 7 of the training materials.

2. Footnote 51 makes a general comment that "in the genetics arts, it is unnecessary for an applicant to provide enough different species that the disclosure will permit one of skill to determine the nucleic acid or amino acid sequence of another species from the application alone. The stochastic nature of gene evolution would make such a predictability nearly impossible. The Federal Circuit could not have intended that representative number requires "predictability of sequences." This comment is difficult to reconcile with the Federal Circuit's holding in *Regents of University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), *cert. denied*, 118 S.Ct. 1548 (1998). In *Lilly*, the court appeared to reach the opposite conclusion to that reached in the footnote. Regardless of the stochastic nature of gene evolution, it would seem evident that a disclosure must

provide sufficient guidance to a person of ordinary skill in the art to navigate whatever impediments may exist in determining the amino acid or nucleotide sequences across species. This may include information showing the conservation of domains of the protein across species, or other data that can be used to deduce the characteristics of the class of compounds within the claimed genus.

C. Comments on Revised Utility Examination Guidelines

BIO members have the following comments regarding the revised utility examination guidelines.

1. The PTO has added a third element (i.e., "substantial utility") to the test for determining whether a claimed invention meets the utility requirement of 35 U.S.C. § 101. If the PTO is using this standard to screen for and eliminate "throw-away" utilities, BIO agrees with the PTO's use of this element in the test for utility. However, if the PTO intends to use this standard to require examiners to qualitatively assess the merit of an asserted utility so that certain legitimate types of utility will be considered "insufficient," we would strongly oppose the new requirement.

   Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966), is still an important authority with respect to the standard for what must be met to establish utility. Many BIO Members do not believe the standard specified in *Brenner* requires three discrete elements (specificity, substantiality, and credibility) for establishing utility. The relevant passage in *Brenner* states

   > [t]he basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point - where specific benefit exists in currently available form - there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

   Id. at 534-535. Thus, one reading of this passage relied on by the PTO appears to define "substantial" utility as one where a "specific benefit exists in its currently available form."

   Taking note of these observations, BIO believes that if the PTO structures the analysis to be performed by patent examiners in evaluating whether a specifically recited utility does possess "a specific benefit in currently available form" in the manner proposed in the guidelines, then BIO urges that the PTO ensure that the substantiality prong of that assessment be confined to screening for the types of utilities characterized by the PTO as "throw-away" utilities.

2. According to the guidelines, the Office will not consider a method for assaying or identifying materials to be a method capable of possessing utility if the material assayed or identified has no "specific and/or substantial utility." This example is an overbroad and inaccurate characterization of the holding of *Brenner*, and should not be retained in the

training materials, insofar as it suggests that assay methods cannot possess utility if the compound found through use of the assay does not itself possess specific, substantial and credible utility.

Assay methods, like many other tools used in research, have an immediately realizable "real world" value. For example, an assay method that can identify chemical compounds that possess a particular physical, structural or biological property clearly have "real world" value irrespective and independent from the utility that may be associated with the compounds identified using the assay method. As a consequence, a presumption that assay methods cannot possess utility if the compound isolated or identified using the assay do not have utility would be the product of a flawed analysis of *Brenner*. Such a conclusion also would suggest that processes and products can never possess utility if their utility lies in the field of research. Indeed, the application of this concept of the utility requirement as it relates to methods for assaying or identifying compounds, if taken literally, would mean that claims to methods such as NMR, infrared, x-ray crystallography, and screening for important biological properties, would be unpatentable because further research would be necessary to establish utility for the compounds identified or assayed. This certainly cannot be the result intended by the guidelines.

In *Brenner*, the claimed invention was directed to a method whose only utility was making a class of steroids. The applicant's disclosure failed to disclose a utility for the products of that method, which in turn led to a § 101 rejection because the products resulting from the method lacked utility. The applicant admitted that the products produced by the method would not be patentable if they lacked utility. 148 USPQ 696. The Court obviously felt that the method lacked utility as well, holding:

> We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product.

148 USPQ 696. Clearly in *Brenner*, the method of making the compounds, which was its only use, was inextricably bound up with the compounds themselves and, as a result, the requirement for utility could not be met until a use for the compounds was found. The Court emphasized that the utility of the claimed invention (i.e., the products) would require further research to identify and ascertain, and the compounds produced by the method would be the object of that research.

In contrast, a method for assaying or identifying compounds to ascertain if they possess a particular physical, structural or biological property stands on a very different basis. Like scales, an interferometer, or a microscope, a method for assaying or identifying compounds is a valuable scientific tool in its own right. Its utility is not inextricably tied to the compound tested, but lies in its ability to facilitate research. Unlike the compounds in *Brenner*, these methods for assaying or identifying compounds are not the objects themselves of research, but aids to research. The articulation of this standard in the original legal analysis to the utility guidelines issued by the PTO in 1995 seem to address this

scenario correctly, and should be used instead of the characterization provided in example C on page 6 of the training materials.[1] For the foregoing reasons, BIO recommends deleting example "C" on page 6 of the training materials.

3. There is a difference of opinion among BIO members as to whether different types of inventions will or will not satisfy the utility requirement. For example, some BIO members believe that utility of most proteins cannot be conclusively demonstrated until the protein has been expressed and biologically characterized. Other BIO members believe that utility can be based on a prediction of biological activity made on the basis of homology to existing classes of polypeptides and proteins. Rather than attempting to dictate one standard or the other, BIO encourages the PTO to carefully evaluate the rationale presented in support of an asserted utility, particularly with respect to the specificity of the recited utility, and the scientific credibility of the basis for that specifically recited utility. Credibility is, as the guidelines provide, to be evaluated from a scientific perspective, and ultimately, the beliefs of scientists skilled in this sector, based on effective filing date knowledge, will control whether or not one can make a valid prediction of utility for a particular compound on the basis of homology. In any case, the PTO should continue to require examiners to provide an adequate basis for any challenge made to the scientific basis of an asserted utility, including citation of relevant scientific authorities.

4. The flowchart that is designed to guide application of the requirement improperly inserts as the first step an evaluation of the invention to determine if it has a well-established utility as the first inquiry. Most patent applicants will comprehend and specifically identify the utility of their claimed invention(s) in the specification. Since the patent applicant is in the best position to comprehend why their invention is believed to be useful, the PTO should rely on the specifically recited utility as the relevant utility to be evaluated. The PTO should not direct examiners to "discover" well-established utilities for claimed inventions unless no assertion of utility has been made by the patent applicant. In other words, the inquiry for whether an invention has a well-established utility should be made only if there is no specific and substantial assertion of credible utility made by the applicant for the claimed invention(s). The flowchart, guidelines and examples in the training materials should be revised to reflect the correct sequence of evaluation.

5. BIO members have a number of particular concerns with the examples provided in the training materials as discussed below.

   - BIO members disagree with the standard in Example 1 with respect to claim 2. It is inaccurate for the PTO to conclude that the broadest *reasonable* interpretation of the term "preventing infection" means that the administered agent will prevent even one microorganism from gaining entry into one cell of a host. The broadest *reasonable* interpretation of the claim is that a clinically detectable condition of infection does

[1] The 1995 Guidelines provided that "an assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the specific invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified utility and inventions whose specific utility requires further research to identify or reasonably confirm. Labels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific utility for the invention."

not manifest itself in the host as a result of administration of X. Just as treatment of a condition does not necessarily mean that the condition has to be completely cured by the treatment, preventing a condition from occurring does not have to be 100%. Thus, with respect to claim 2, the applicant should be able to demonstrate that the utility for the claimed method of preventing infection is credible if the disclosure shows that the administration of X prevents infection in practical terms, rather than in absolute theoretical terms.

The PTO's proposed attorney response is also not realistic in so far that it does not address the PTO's stated concern. The fact that microbe X only gains entry into the cells of the host through the mucosa in the nose and mouth does not answer the question of whether a single microorganism would be able to gain entry in the face of the claimed treatment. Suppose that the standard in Example 1 was applied to Example 2? Would a method of retarding wrinkling of skin by topical administration of compound A require that there be no wrinkles at all?

- Similarly, BIO members do not believe that Example 3 is realistic. The applicant would surely have some basis or rationale for suggesting that the disclosed protein would be useful in treating Alzheimer's disease. That rationale or an example setting forth data which suggests a mechanism would certainly be described in the specification or could be supplied by the applicant on demand. The problem with this example is that it implies that because Alzheimer's disease has not been responsive to any treatment, it is impossible to invent such a treatment. This philosophy is pervasive and, if extended in a rote manner, would undercut the very purpose of the patent system to stimulate new and useful inventions. It would be equally incredible to assert that the protein was an anti-inflammatory or an antibiotic without being able to state any scientific basis for such a characteristic. We encourage the PTO to refine example 3 to reflect a more realistic case.

- Example 8 also does not present a realistic fact pattern or make useful conclusions. In this example, the applicant apparently fails to assert any specific utility for the compound (an enzyme inhibitor), which then prompts the PTO examiner to make a conclusion that the compound has a "well established" utility of controlling enzymatic reactions. The example then suggests that the deficiency of claim two is that the treatment of an unspecified disease through administration of the compound has a specific utility but that the utility is not "substantial."

  The intent of the example seems to be to demonstrate that an applicant can obtain a product claim based on the possession of the product of multiple utilities, including one that is distinct from the single utility of the therapeutic method that is the basis of claim 2, but at the same time can be denied a claim to a method of using the compound if the method does not have an adequately disclosed and defined utility.

  The example should be improved by indicating that the disclosure recites a specific utility for this tyrosine kinase inhibitor (e.g., in controlling clinical assays of mixtures to avoid the artifact of tyrosine kinase activity) which is distinct from the utility of

claim two. The example should then address the question of whether a specific utility exists for a claimed therapeutic method if the disclosure does not identify any disease to which the enzyme (or its over or under expression) may be linked.

- The most relevant example to the question of utility that is linked to homology analyses is example 10. This example provides a useful guide for the evaluation of protein claims. Because it involves some fairly unique circumstances (i.e., very high degree of homology to a class of closely homologous proteins having well-known utility, lack of homology to other proteins), it may not provide the most useful teaching example standing alone. The training materials should be supplemented by examples where the homology of the novel protein and/or the family members is not as high, where the homologies are to distinct classes of proteins that do not share a common utility, or where the prediction is based on a well established, conserved domain characteristic of a particular family.

In conclusion, BIO sincerely appreciates the efforts invested by the Commissioner and the PTO staff charged with developing and revising the guidelines and the associated training materials. The meticulous consideration of comments from the public, a large number of which came from BIO members, is sincerely appreciated. We believe both sets of guidelines represent workable approaches for examiners to follow and generally acceptable to our members. We hope the comments contained in this letter help refine these guidelines further, and look forward to working with you to implement the guidelines when they are finalized.

Sincerely,

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Vice President for Government Relations

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