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The Honorable Bruce Lehman
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ATTN: Scott A. Chambers, Associate Solicitor

RE: Comments on Interim Guidelines on the Written Description Requirement

Eli Lilly and Company wishes to thank the Commissioner for the opportunity to comment on the Interim Guidelines for examination respecting the written description requirement. While we question the need for this initiative because we are concerned that portions of the Guidelines as written contradict Federal Circuit precedent and confuse the standards of patentability respecting nucleic acids, we respectfully request consideration of the attached comments if the Guidelines are finalized.

Very truly yours,

A handwritten signature in cursive script that reads "Thomas D. Webster".

A handwritten signature in cursive script that reads "Mark J. Stewart".
Thomas D. Webster, PhD
Mark J. Stewart, PhD

**Comments on the Interim Guidelines for the Examination of Patent Applications
Under the 35 U.S.C. Section 112 ¶ 1 "Written Description" Requirement**

Initially, we question the need for Guidelines for Examination respecting the written description requirement. We are satisfied that the case law is developing in a coherent and fair fashion, as evidenced recently in the Federal Circuit decision of *University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997). In our judgment, establishing Guidelines at this juncture is unnecessary. Notwithstanding, we offer the following comments on the proposed Interim Guidelines.

I. Section IID:

Section IID of the proposed Guidelines addresses generic nucleic acid claims. Sanction of description by hybridization is troubling for at least three reasons: 1) it contradicts CAFC precedent, as well as specific requirements for patentability under 35 U.S.C. Section 112, 2) it establishes a bifurcated standard of patentability for nucleic acid species and genus claims that is illogical and unnecessary, and 3) it promotes a policy that unjustly rewards the patentee.

A. Description by Hybridization Contradicts CAFC Precedent and Statutory Requirements

The proposed Guidelines advocate hybridization as a basis for describing a genus of nucleic acids. For example, the claim provided in Section D(1) reads, "An isolated DNA probe for detecting HIV-X, wherein said DNA probe hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under the following conditions: hybridization in 7% sodium dodecyl sulfate (SDS), 0.5M NaPO₄ pH 7.0, 1mM EDTA at 50° C; and washing with 1% SDS at 42° C."

This type of claim and description fails to comport with the requirements laid out by the CAFC for conception of a nucleic acid claimed as a product. Conception of a process for making an invention is inadequate to claim a product. A patentee must conceive the structure of the claimed nucleic acid, and in most cases this requires

disclosure of the nucleic acid sequence. For example, in *Fiers*, the Court held, "Before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, can at most constitute a conception of the substance claimed as a process." *Fiers v. Sugano*, 25 USPQ2d 1601, 1605, (Fed. Cir. 1993).

Description of a nucleic acid genus by specifying a process - namely hybridization to a specified nucleic acid sequence, is in direct conflict with the rule laid out in *Fiers*. Hybridization simply does not provide structural information on specific members of the genus. While structure plays an important role in hybridization, it is an undefined role. The phenomenon itself does not describe the underlying structures involved. For this reason, hybridization does not provide a declarative description sufficient to show conception of a genus of nucleic acids. Logically, therefore, "[O]ne cannot describe what one has not conceived." *Id.* at 1606.

The written description requirement respecting nucleic acids has recently been addressed by the Federal Circuit in *University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997). The Guidelines correctly state that the "written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species . . ." Two important issues raised by the Court relate to what constitutes a "sufficient description," and what constitutes a "representative number."

The Guidelines correctly state that a "sufficient description" could be met in multiple ways including structure, physical and/or chemical characteristics, and by functional characteristics when coupled with a known or disclosed correlation between structure and function. *Lilly* and predecessor cases state clearly that the standard for the written description requirement with respect to nucleic acids and proteins in most instances rests in *describing the sequence(s)* themselves. While a plurality of means for describing nucleic acids are theoretically possible, for example, based on chemical or physical properties, in practice a description of a nucleic acid for the most part requires specification of the nucleotide sequence. The reason for this is clear. Nucleic acid molecules simply do not possess the sort of chemical or physical diversity sufficient to

draw adequate distinctions. On the contrary, nucleic acids are quite similar chemically and physically, their distinctions emerging at the level of sequence differences, i.e. in the information they encode. Thus, describing a nucleic acid generally “requires a kind of specificity usually achieved by means of recitation of the sequence of nucleotides” (*Lilly* at 1406, citing *Fiers*).

What standard of description has been sanctioned by the Court? Essentially this, that a fully described genus enables a skilled artisan to “visualize or recognize the identity of the members of a genus.” (*Lilly* at 1406). We submit that hybridization fails to meet this standard. Hybridization is a phenomenon that cannot accurately describe the structure of species that could “hybridize” to a given nucleic acid sequence. Thus, the skilled artisan cannot “visualize or recognize” species falling within a genus described by hybridization. On the contrary, the skilled artisan would have to experiment in order to ascertain whether a species fell within the claimed genus. This is not an adequate description for a claimed product.

B. Description by Hybridization Would Establish an Unnecessary and Illogical Bifurcated System of Patentability of Nucleic Acid Species and Genus

Sanctioning description by hybridization would effectively establish a bifurcated system of patentability respecting written description and obviousness, that is both illogical and unnecessary. We urge the Patent Office to avoid the inevitable confusion and complication that would result.

CAPC decisions addressing both obviousness and written description issues make clear that a higher standard of disclosure is required in order to describe an invention for Section 112 purposes than for rendering a claimed invention obvious. For example, in *Lilly* the Court stated “a description that does not render a claimed invention obvious does not sufficiently describe that invention for purposes of § 112, ¶ 1.” 119 F.3d at 1567. This principle is highly significant in the present context because of the Court’s emphatic conclusion that if no basis exists to conclude obviousness, then there is not a sufficient description to meet the requirements of 35 U.S.C. Section 112.

The *Lilly* Court was in effect saying that disclosure of the rat insulin gene sequence along with the rat and human insulin protein sequences does not make the human gene obvious. Had the Court determined that U.C.'s disclosure adequately described the human insulin gene, thus making it obvious as well, all other researchers who might subsequently clone an insulin gene and corresponding protein from any other species would be effectively blocked from obtaining patents on these molecules.

Thus, to avoid such a profound effect on the patentability of such a broad number of potential compounds, the Court could not reasonably find that the U.C. specification satisfied the written description requirement for claims to the human gene. Explicit in the Court's reasoning is that hybridization methods generally do not provide a basis to conclude that a given sequence is obvious over a known homolog, even when the two might be expected to hybridize. If a description based on hybridization is inadequate for rendering a claimed nucleic acid obvious then *a fortiori* it is inadequate to describe it for the purposes of the written description requirement.

We urge the Patent Office to consider that allowing description by hybridization carries several troubling implications:

- A conflict with the Federal Circuit's stance on obviousness, away from a structural basis and toward a methodological basis;
- Creation of an unnecessary bifurcated system for patentability and examination of nucleic acid species and genus claims.

In addressing the issue of the obviousness of a nucleic acid molecule the Federal Circuit rejected a methodological focus and has emphasized a structural basis. For example, in *In re Deuel*, the Patent Office rejected a claim to a specific gene sequence based on knowledge in the art of amino acid sequence information and hybridization methods that might have been used to isolate the claimed gene sequence. *In re Deuel*, 34 USPQ2d 1211 (Fed. Cir. 1995). The Patent Office focused on the simplicity of gene isolation methods to formulate an obviousness argument. In rejecting the Patent Office position, the Court emphasized that *Deuel*'s gene, claimed as a product, would not have been obvious based on the Office's position, because the claimed sequence was just one among an enormously large genus of sequences that theoretically could have encoded

Deuel's protein. The Court emphasized that the correct analysis rested on a structural basis, and not on a methodological basis. This holding was vital for at least two important reasons: 1) it complied with the specific language of Section 103 that stipulates that an invention not be negated by the manner in which it is made, and 2) it helped to ensure the survival of the biotech industry by preserving the patentability of nucleic acid inventions.

A central question that must be asked is this, Since hybridization is inadequate to describe a species, how is it adequate to describe a genus? Fundamentally there is no difference between a nucleic acid species and a nucleic acid genus, except in degree. Both relate to nucleic acid molecules, the former respecting a single sequence, the latter a plurality of sequences. Generic descriptions should differ in degree perhaps, but not kind. Indeed, the Court has explicitly held that the written description requirement of a genus and a species be similar in kind. "A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula or chemical name . . ." (*Lilly* at 1405, citing *Fiers* at 1606, emphasis added). That species and genus descriptions should be similar finds additional support in *Deuel*. At issue in *Deuel* were generic claims to nucleic acids that could theoretically encode a protein that was the subject of Deuel's invention. The Court noted that the genetic code would have allowed specification of the members of this genus by nucleic acid sequence; in other words description of specific members by structure. *In re Deuel* at 1216.

In view of the Court's position on obviousness and written description respecting nucleic acids, we urge the Patent Office not to sanction in the Guidelines description by hybridization.

C. Description by Hybridization Would Promote Bad Policy

On logical grounds, if hybridization is sufficient to describe a nucleic acid genus then so is it sufficient to render such a genus obvious. This would imply that hybridization of at least one species in a genus to at least one other species in another genus would render the latter unpatentable. On the other hand, maintaining a structure-

based system would avert obviousness by hybridization and maintain a strong patent system that provides an incentive to public disclosure of new inventions.

An important purpose served by the patent system is to encourage full disclosure of inventions to the public so that the public derives the greatest benefit. Description by hybridization does not demonstrate that an inventor had possession of the claimed genus. Hybridization does not provide a declarative description; at most it provides a procedural description.

We urge that description by hybridization places an unfair burden on the public and unjustifiably rewards the patentee in view of the benefit provided the public. Allowing hybridization claims would, in effect, allow a patentee to possibly control totally unrelated proteins, just because of nucleic acid homology. That is nonsensical.

We reject the counter-argument that patentee's sequence would enable the public to isolate and use other related sequences and that patentee ought to be given broad protection for providing the public with a tool for isolating related sequences. Proponents of this view argue that providing the public with the sequence of a gene or EST (i.e. expressed sequence tag) effectively provides the only, or at least the most efficient, means for isolating other homologous sequences.

This argument has minimal merit today, and will have even less merit in the foreseeable future. Sequencing information is being generated at an ever-increasing rate, and soon the genomes of many organisms, including human beings, will be available. At the same time, computer-based tools for analyzing sequence information are becoming more sophisticated. Indeed, today actual hybridization experiments are no longer needed to identify related gene sequences. Instead, *in silico* methods based on bioinformatics tools are providing the means for extracting information from genomic sequence data. Thus, hybridization experiments are not the only means, nor even the best means, for identifying important sequence information. Indeed, the rapid advancement of bioinformatics is such that important structural and functional information will soon be discoverable *de novo*, without the need even for *in silico* comparisons between sequences. In the near future sophisticated algorithms will be used to analyze the biological properties of nucleic acids and proteins. In view of these likely developments, granting

broad generic protection based on description by hybridization is manifestly unfair to the public and overly generous to the patentee.

Conclusion:

The written description requirement sets a high standard that ensures that the would-be patentee *declare what the invention is*, thereby demonstrating possession of the invention. Procedural descriptions based on hybridization do not declare accurately *what the genus is*, i.e. what structures comprise it. Instead, the would-be patentee merely discloses a procedural test for inclusion within a poorly-defined genus. Hybridization relates to methods for identification, not to a declarative description, which *Lilly* requires.

The guidelines state that “what constitutes a ‘representative number’ is an inverse function of the predictability of the art.” While the level of skill in the art and the predictability of the technology are considerations in deciding sufficiency of disclosure issues, courts are most likely to give those considerations the most weight when dealing with questions of enablement or obviousness. A separate written description requirement exists in part because of the policy consideration of preventing overreaching by the patentee. Thus, the predictability of the art should not profoundly impact the written description requirement because one skilled in the art cannot know any more about the structure of a particular DNA even if cloning that DNA would be considered routine based on the disclosure of sequences of species homologs.

The proposed guidelines do not and cannot adequately provide direction as to what may be required to describe a particular genus. The inquiry is highly fact-sensitive and must be considered in the context of obviousness. Vague comments regarding what might constitute a “representative number” of species do not provide any guidance to examiners or practitioners as to what might be sufficient to describe a genus. In the biotechnology art, the Federal Circuit has clearly attempted to limit claims that are too broad to justify patent protection through a stringent application of the written description requirement. “A patent is not a reward for the search, but compensation for its successful conclusion.” *In re Ziegler*, 992 F.2d 1197, 1203 (Fed. Cir. 1993). The guidelines as

currently proposed are not consistent with court decisions promoting the policy of disclosing inventions, not research plans.