

**Comments on the Revised Interim Guidelines for Compliance with the
Written Description Requirement of 35 USC 112, first paragraph**

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In recent years, the PTO, especially the biotechnology examining corps, has made great advances in improving examination, which has resulted in better relations with inventors. Moreover, there are numerous procedural improvements that greatly facilitate the patent process. Indeed, at least this commentator recognizes that in developing these Guidelines, the PTO is further attempting to improve examination. However, in my view these efforts are misguided and ineffective at best.

These comments are not intended to be exhaustive, but rather address my concerns about perceived defects in the Revised Interim Guidelines for Compliance with the "Written Description" Requirement (hereinafter "Guidelines") and the accompanying training materials as they apply to biotechnology. These defects include a fundamental disagreement with the impetus for developing these Guidelines, specific concern with the Guidelines for examining genus claims, inconsistencies in the technical examples in the training materials which seem to result from an outcome driven approach, and an apparent effort in the overall process to define general principles that achieve certain preordained outcomes based on case-law that is too highly fact specific to permit extrapolation to the specific issues considered in the Examples. In my view, the highly technical nature of the guidelines and training materials reflect the problem of trying to extrapolate general principles from the fact specific (and scientifically suspect) outcome of *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) ("Lilly"). The whole effort falls short of achieving its goal of improved examination; the Guidelines and especially the training materials ought to be scrapped.

Implementation of the Guidelines elevates form over substance, creating artificial barriers to patentability and impediments to the prompt issuance of patents. This is clear from the training materials. Moreover, experience dictates that the focus on "Written Description" (or enablement, or utility) results in numerous quibbling rejections, rarely supported by adequate specific evidence. Promulgation of Guidelines leads examiners, not surprisingly, to find that each patent application lacks an adequate written description. This result contradicts the "strong presumption that an adequate written description of the claimed invention is present when the application is filed" as set forth in the Guidelines. (Would that examiners implement this element of the Guidelines with the same enthusiasm as provisions that support rejections.) In effect, the Guidelines achieve "fad" examination rather than uniformity and consistency. (I have personally seen this in the metamorphosis of rejections from lack of utility to lack of enablement to, you guessed it, lack of written description; the factual predicate for the rejection remains unchanged.)

Issues of written description, like enablement and utility, ought not supplant novelty and unobviousness as the essential criteria for patentability. Unlike novelty and unobviousness, these issues turn more heavily on subjective determinations by the examiner. If an examiner likes a

particular phrasing, then perhaps the specification satisfies the written description requirement. More frequently (and with highly educated individuals trained as scientists to review critically this is not surprising), the subjective views of the examiner vary from the drafter's choice of terms and language. Applications translated into English face even greater trouble in this respect. Implementation of the Guidelines encourages hair-splitting over choice of language and disputes over efficacy of description in the specification. In my view, written description rejections ought to be brought to bear against clearly deficient specifications to deny patents where description of the invention is lacking, not simply different from the examiner's expectation.

Public policy ought to encourage limiting these quibbling rejections. To deny a patent, or commercially meaningful claims in a patent, by alleging substantive defects on semantic grounds undermines the patent system. It cannot help but lead to greater secrecy and delay public dissemination of information as applicant's uncertainties about getting fair protection outweigh the need to publicize important discoveries, such as new genes or biological pathways identified in non-human systems.

1. Lilly and the Guidelines

One marvels when considering the guidelines for examination of genus claims, at the statement that "[i]n an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" because of its reliance on Lilly. When considering the Lilly case, it seems that the structure of the claimed genus was wholly predictable so as to permit one of ordinary skill in the art to conclude that the inventor had possession of the genus. The rat cDNA actually disclosed in the University of California patent had a predictable relationship to mammalian, and particularly human, cDNA. Predictability was further enhanced by the disclosure of the amino acid sequence of human insulin. Lilly, 43 USPQ2d at 1405. Any set of DNAs have a rather limited structural variety, consisting as it does of C/G and A/T pairs all linked via the same type of phosphate bond; the need to encode a highly conserved, well characterized protein like insulin constrains the arrangement of these pairs. The court's conclusion that the inventors lacked possession of such a highly predictable genus, mammalian insulin cDNA, when they clearly had possession of a species and the art clearly understood the structural relationship between that species and the genus, confounds understanding. One might therefore assume that the outcome in this case was a highly fact specific application of the written description caselaw.

Moreover, the Guidelines give inadequate voice to the corollary proposition: in a predictable art, adequate description of a genus which embraces narrow species variants can be achieved by disclosure of only one species. The Guidelines handle this concept in a footnote, number 51. It ought to embody the theme not the exception for these Guidelines.

2. The Training Materials: Inconsistent and Outcome Driven

In the four cases discussed below, the training materials demonstrate inadequacy of the Guidelines. The identification of four examples here ought not to be construed as a belief that this list is exhaustive by any means.

a. An allele by another name might have even less structural similarity to a species of nucleic acid

Example 11 of the training materials suggests that a claim to an allele of a defined sequence lacks written description. However, the hypothetical specification points out that alleles include single nucleotide polymorphisms. Furthermore, the materials themselves ascribe a definition of alleles that supplies all of the structural relationships one could want: an alternate form of a gene occupying the same locus in a particular chromosome or linkage structure and differing from other alleles of the locus at one or more mutational sites (indeed, were these features included in a hypothetical claim, it is highly likely that the claim would be allowed). If an allele is an alternate form of a given gene, one presumes a high degree of structural similarity since they are, after all, the same gene. Finding alleles in the same locus further enhances the expectation and appreciation of structural relatedness.

The degree of variation of alleles is much less than other "acceptable" forms of generic claiming. For example, postulate a hypothetical small gene, of say 300 nucleotides. If the allelic variant contains a SNP, it has 299 out of 300 nucleotides in common with the first allelic variant, i.e., greater than 99% identity. Yet in practice the PTO indicates that claiming 95% homology is sufficient. As shown in Example 9, the mere ability to hybridize under highly stringent conditions is sufficient. Both 95% homology and high stringency hybridization encompass allelic variant. But they cover more: these terms are likely to encompass homologous genes from the same species and orthologous genes from other species, or species resulting from modifications that are yet to be made. That different terms with greater breadth are acceptable seems to elevate form over substance and demonstrates inconsistency.

It is unclear to me at least how a discovery of any gene made in the past twenty years would not constitute possession of the genus of allelic variants. Note that these variants may or may not function, and may or may not correlate with disease predisposition or responsiveness to therapy – the inventor or others are free to make these discoveries and claim their inventions when they are made.

b. Alleles are not well described, but antibodies are? What is the difference?

In Example 16, the training materials permit claiming an antibody to a novel antigen when there is no actual exemplification of any antibody, much less the entire genus of antibodies specific for that antigen, including antibodies that are more specific for other antigens but that cross react with the novel one. Moreover, such a conclusion comports with Federal Circuit decisions such as the Hybritech cases. Indeed, if the training materials applied the same considerations of predictability to protein variants or alleles, I would support them heartily. The failure to do so

evidences a lack of consistency, and an overriding concern for reaching a desired result at the expense of scientific credibility.

The basis for this argument is that antibodies represent a broad class of polymorphic proteins of highly unpredictable structure within and between species of animals. Antibodies generally share similar structural features: a set of variable and constant domains. Within the variable domains are hyperpolymorphic segments, the complementarity determining regions (CDRs). The CDRs incorporate nearly infinite sequence variability to permit specific binding to the nearly infinite variety of antigens. However, even against one antigen, antibodies demonstrate significant polymorphic variability, for example, by recognizing different epitopes on the antigen. Monoclonal antibodies contain the same CDRs, but these can be engineered to contain different constant regions. Mammals and birds all make antibodies; the claim in this example has no particular species limitation. In short, the sequence variety of proteins within the scope of the term antibody mocks the outcome of Example 11 (allelic variants): very few alleles demonstrate the same degree of polymorphism as antibodies, and none demonstrate the degree of variability found between antibodies of different species. Yet allelic variants (which by definition come from a single species) lack written description support, which antibodies have? How can this be?

Take this one step further: "correct" application of Lilly seemingly ought to result in a determination of insufficient written description of the antibody claims. Certainly the whole genus (and, indeed, with no examples even one species) of the claimed antibody lacks the requisite "precise definition, such as by structure, formula, [or] chemical name" required for such claim breadth. It is a rare occasion indeed that someone actually determines the sequence of an antibody. In the example, the antibody only exists constructively. The analysis of Example 16 cannot be right unless Lilly is, applied as broadly as the PTO attempts in drafting these guidelines, wrong. In my view, Example 16 is fine.

c. Function dominates structure?

Example 7 relates to ESTs. Example 8 relates to a full open reading frame (ORF). Both examples concern claims to nucleic acids comprising the defined sequence.

Chemically speaking, these sequences are practically indistinguishable. Apart from the actual arrangement of nucleotides, which functionally makes all the difference, they have the same composition, physical chemical behavior, and appearance. Either can be readily inserted, like a cassette, in another nucleic acid, such as a cloning or expression (yes, expression) vector. Either can provide PCR primers or hybridization probes. That each has much different utility based on function ought not to weigh into consideration of whether or not the sequence, and a claim to a nucleic acid comprising this sequence, meets the written description requirement. If ESTs may lack patentable utility, it is hard to see where written description comes into play.

The training materials conclude that a claim to a nucleic acid comprising an EST does not comply with the written description requirement, but that the ORF does. The logic behind this determination is baffling. Both claimed nucleic acids are unique in containing a novel, non-obvious sequence. Either unique sequence can be readily embedded in known expression or cloning vectors. Both cover materials and processes yet to be made or discovered. So why the

different outcome in each case? These two examples seem to embody a bias predicated on policies to limit EST claims, rather than adequacy of descriptive support.

d. The more unpredictable, the better the chance for claim breadth?

Example 12 relates to a bioinformatics claim based on a specification that lacks any specific examples. Bioinformatics is a new technology and remains somewhat unproven (unlike, for example, genetics and molecular biology of DNA, which were established decades ago). There are a series of conclusory determinations with respect to the level of skill in the art, e.g., the ability to obtain expression level data (for completely structurally undefined compounds), and accurately representing these data in a computer algorithm. The outcome in this example shows great deference to very new technology, in contrast to the scepticism to well established relationships of DNA (a simple molecule, not a highly complex mixture of biological molecules) demonstrated in Examples 7 and 11.

3. Conclusion

These Guidelines and the accompanying training materials stand in stark contrast to the great strides the PTO has made to develop greater consistency in examination, to educate examiner's to apply the law, and to implement procedural changes that benefit customers and examiners alike.