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Christopher M. Holman

University of Missouri - Kansas City, School of Law

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Is the Chemical Genus Claim Really “Dead” at the Federal Circuit?: Part II

Christopher M. Holman*

ABSTRACT

*A 2020 law review article entitled *The Death of the Genus Claim* (“Death”) purports to document a dramatic shift in the Federal Circuit’s interpretation of 35 U.S.C. 112(a)’s enablement and written description requirements, particularly as applied to chemical genus claims. According to the authors of *Death*, it has become nearly impossible to obtain a chemical genus claim that will be upheld as valid in the face of a challenge for overbreadth under Section 112(a). *Death* was cited extensively in Amgen’s successful petition for certiorari in *Amgen v. Sanofi*, a case asking the Supreme Court to overturn the Federal Circuit’s decision finding Amgen’s claims reciting *genuses of monoclonal antibodies* to be invalid for lack of enablement. *Death* raises important issues for pharmaceutical innovation, a number of which I address in this second installment (“Part II”) of a two-part article. I begin by explaining why it is that I disagree with a particular assertion made in *Death*, i.e., the suggestion that patentees could circumvent the Federal Circuit’s purported heightened application of 112(a) to chemical genus claims by drafting broader claims that define chemical *genuses* solely in structural terms, without the inclusion of any functional limitations. The article then reviews a substantial number of judicial decisions involving chemical genus claims, and basically show that there is little evidence of a pronounced change in the application of 112(a) to chemical genus claims over the time span which *Death* identifies as corresponding to a purported dramatic shift in the law.*

* Christopher M. Holman, Professor of Law, University of Missouri-Kansas City School of Law; Senior Scholar, Center for Intellectual Property x Innovation Policy (CIP-2), George Mason University, Antonin Scalia Law School; and Executive Editor, *Biotechnology Law Report*.

Three preeminent intellectual property scholars recently published a law review article entitled *The Death of the Genus Claim* (“*Death*”), which purports to document a dramatic shift in the Federal Circuit’s interpretation of 35 U.S.C. 112(a)’s enablement and written description requirements, particularly as applied to chemical genus claims.¹ The gist of the article is that chemical genus claims, i.e., patent claims that recite a genus of structurally and/or functionally related chemical species, have long been considered of critical importance for innovators in the chemical arts, particularly with respect to pharmaceuticals, but that the law of the Court of Appeals of the Federal Circuit (“Federal Circuit”) has dramatically shifted in recent years, as a consequence of which it has become nearly impossible to obtain a chemical genus claim that will be upheld as valid in the face of a challenge for overbreadth under Section 112(a).²

The present article is the second installment of my two-part response to *Death*. *Part I* of this response, which appeared in the last issue of *Biotechnology Law Report*, reanalyzed the judicial decisions upon which *Death* bases its claim, and explains why, in my view, they do not actually substantiate a marked shift in the Federal Circuit’s interpretation and application of 112(a).³ *Part I* also explored the ambiguity of the term “chemical genus claim,” an important term that is subject to different interpretations, and provided some excerpts from Judge Lourie’s concurrence in the Federal Circuit’s recent denial of en banc rehearing in *Amgen v. Sanofi*, which explains why, in Lourie’s view, those “bemoaning the so-called death of generic claims are . . . off-base.”⁴

In this second installment of my response, I will begin by explaining why it is that I disagree with a particular assertion made in *Death*, i.e., the suggestion that patentees could circumvent the Federal Circuit’s purported heightened application of 112(a) to chemical genus claims by drafting broader claims that define chemical genres solely in structural terms, without the inclusion of any functional limitations. The article will then review a substantial number of judicial decisions involving chemical genus claims, and basically show that there is little evidence of a pronounced change in the application of 112(a) to chemical genus claims over the time span which *Death* identifies as corresponding to a purported dramatic shift in the law.

¹ Karshtedt, Dmitry and Lemley, Mark A. and Seymore, Sean B., *The Death of the Genus Claim* 35 *Harvard Journal of Law & Technology* 1(2021)(hereinafter, “*Death*”).

² In this article I will often refer generically to 35 U.S.C. 112(a)’s enablement and written description requirements simply as “Section 112(a),” or some permutation of that, which I think is appropriate given that in the context of chemical genus claims the two requirements are largely redundant and often used as alternative doctrines for achieving the same end.

³ Christopher M. Holman, *Is the Chemical Genus Claim Really “Dead” at the Federal Circuit?: Part I*, 41 *Biotechnology L. Rep.* 4 (2022)(hereinafter “*Part I*”).

⁴ *Amgen Inc. v. Sanofi*, Aventisub LLC, 850 F. App’x 794, 795 (Fed. Cir. 2021).

The elimination of functional limitations does not skirt the 112(a) issue

At one point, *Death* suggests that patentees could circumvent the Federal Circuit's purported heightened application of 112(a) to genus claims by employing structural genus claims⁵ rather than functional genus claims,⁶ stating:

Counterintuitively, it may now be better to draft **broader** claims (e.g., pure composition claims) if possible so as to forestall arguments about how numerous “variables would or would not impact the functionality” of the claimed invention.⁷

In context, it is clear that *Death* is using the term “pure compositions claims” to refer to structural genus claims, and that the authors are suggesting that an inventor can transform an invalid chemical genus claim into a valid claim by omitting any functional limitations defining a claimed chemical genus, which would broaden the scope of the claim. As a general matter, any claim drafting strategy that purports to salvage the validity of a patent claim by broadening it should be greeted with some skepticism. As famously stated by Judge Rich, “the stronger a patent claim is, the weaker it is, while the weaker a patent claim is, the stronger it is.” There is generally an inverse correlation between claim scope and claim validity, and to suggest otherwise would appear, on its face, to be nonsensical. For example, if the enablement standard requires the patentee to enable the “full scope” of the claim, then how can broadening the scope of the claim, without removing any embodiments encompassed by the original claim, render the claim enabled?

Surprisingly, it is in fact the case that sometimes courts and the PTO will find a relatively broad claim not invalid, while a narrower claim directed towards a subset of the subject matter encompassed by the broader claim is found to be invalid for lack of enablement. This can occur when the narrower claim specifies a specific method for achieving a result that is claimed in the broader claim, albeit without specifying how the result will be achieved. For example, in *In re Cortright*, the patent claims at issue were directed towards methods of treating baldness with a specific chemical compound.⁸ The Federal Circuit held that a claim broadly reciting a method of “treating scalp baldness” was enabled, but that a claim that specifically recited a mechanism by which the baldness would be treated, i.e., a method of “offsetting the effects of lower levels of a male hormone being supplied by arteries to the papilla of scalp hair follicles” was not enabled, because the patent specification did not substantiate its claim that the chemical compound would act by this particular mechanism.

Still, in most cases broadening a patent claim should not in and of itself overcome an enablement rejection applicable to the original, narrower claim.

⁵ *Part I* defines a “structural genus claim” as a product claim that recites a genus of molecules defined in solely structural terms, with no explicit or implicit functional limitations. The same definition applies in the present article (*Part II*).

⁶ *Part I* defines a “functional genus claim” as a patent claim that defines a genus of chemical compounds, in whole or in part, in functional terms. Functional genus claims often recite both structural and functional limitations. The same definition applies in the present article (*Part II*).

⁷ *Death* at 35 (emphasis added).

⁸ *In re Cortright*, 165 F.3d 1353 (Fed. Cir. 1999).

In proposing its counterintuitive drafting strategy, I think that *Death* fails to adequately account for the utility requirement aspect of the enablement requirement, particularly as it is applied to structural genus claims. This failure to take into account for the utility requirement appears, for example, in this paragraph excerpted from *Death*:

A patentee can claim a structural group of chemicals with an invariant backbone and varied groups attached to that core. As numerous prosecution handbooks confirm, this is the typical kind of chemical genus claim that patent attorneys are taught to draft. Some of those variants will work; others won't. But the inventor of a genus can claim that genus as long as there is enough information that the PHOSITA can figure out *some species* within the genus that will work and how to make those species without too much effort. The prevalence of advice for such claiming reflects a widespread understanding that they are valid.⁹

The only evidence that *Death* provides in support of its assertion that inoperative embodiments will not render a structural genus claim invalid, so long as “the PHOSITA can figure out *some species* within the genus that will work,” is *Death*'s statement that “numerous prosecution handbooks” teach attorneys to draft structural genus claims reciting “an invariant backbone and variance of the groups attached to that core,” and a purported “widespread understanding that they are valid.”

In *Brenner v. Manson*, the most recent Supreme Court decision to directly address patent law's utility requirement, the Court upheld the PTO's determination that a structurally-defined genus of chemical compounds (more particularly, steroids) lacked patentable utility because the patent applicant had failed to disclose “a sufficient likelihood that the steroid yielded by his process would have similar tumor-inhibiting characteristics” to an adjacent homologue purportedly having that utility.¹⁰ In arriving at this conclusion, the PTO Board expressed its “view that the statutory requirement of usefulness of a product cannot be presumed merely because it happens to be closely related to another compound which is known to be useful,” and this view that was adopted by the Supreme Court in *Brenner*.

The structural genus of steroids specifically addressed by the PTO in *Brenner* did not encompass any species that had been specifically shown to be useful. But the logic of *Brenner* dictates that the claim would not have somehow been transformed into a valid claim by broadening it to encompass a single molecule of demonstrated practical utility. The PTO would be justified in rejecting the broadened claim because utility would still not have been established for the vast majority of the molecules encompassed by the claim, particularly given the unpredictability (at that time) of the relationship between steroid structure and function and the limited nature of the disclosure. It seems clear that the Supreme Court would have upheld that decision, for essentially the same reasons as it upheld the Board's decision with respect to the actual claims at issue.

⁹ *Death* at 17(emphasis added).

¹⁰ *Brenner v. Manson*, 383 U.S. 519 (1966).

In fact, the PTO has long applied the utility requirement to structural genus claims in this manner, and continues to do so to this day. In my view, this is entirely consistent with the utility requirement as set forth in *Brenner* and the case law that has emanated from *Brenner*.

An example of this application of the utility requirement can be seen in the prosecution history of a patent that issued in 2021, U.S. Patent 10,941,109, which was mentioned in *Part I*. As originally filed, the broadest claim in the patent application (claim 1) recited a chemical compound defined in terms of a common core structure, with appended R1, R2, R3, and T groups.¹¹ Each of these variant groups encompassed a large number of chemical moieties.

The T group could be

-C(=O)- or -C(=NH)-.

RI and R2 could each be independently selected from the group consisting of:

C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C14 cycloalkyl, aryl, heteroaryl, aryl(C1-C6 alkyl), -CN, amino, (C1-C6)alkylamino, dialkyl(C1-C6)amino, haloalkyl(C1-C6), (C1-C6)alkoxy, (C1-C6)haloalkoxy, heteroaryl(C1-C6 alkyl), (C4-C1s)heterocyclic, (C4-C1s)heterocyclic(C1-C6 alkyl), C3-C7 cycloalkoxy, C6-C10-aryloxy, and the moieties (a-1), (a-2), and (a-3), wherein said alkyl, aryl, cycloalkyl, heterocyclic, heteroaryl, alkoxy, cycloalkoxy, haloalkyl, or haloalkoxy is further optionally substituted with one or more substituents selected from the group consisting of -C1-C6 alkyl, halo, CN, Cf 3, -COOH, -OH, -C1-C6 alkoxy, -NH2, -(C1-C6 alkyl)NH2, -(C1-C6 alkyl)NH(C1-C6 alkyl), -(C1-C6 alkyl)N(C1-C6 alkyl)2, -NH(C1-C6 alkyl), -N(C1-C6 alkyl)2, -CONH2, -NH(CO)(C1-C6 alkyl), -N(C1-C6 alkyl)CO(C1-C6 alkyl), -SO2-(C1-C6 alkyl), and -(SO)NH2,

R3 could be selected from the group consisting of:

hydrogen, deuterium, C1-C6 alkyl, C2-C6 alkenyl, C2- C6 alkynyl, C3-C14 cycloalkyl, aryl, heteroaryl, aryl(C1-C6 alkyl), -CN, amino, (C1-C6)alkylamino, dialkyl(C1-C6)amino, haloalkyl(C1-C6), (C1-C6)alkoxy, (C1-C6)haloalkoxy, heteroaryl(C1-C6 alkyl), (C4-C1s)heterocyclic, (C4-C1s)heterocyclic(C1-C6 alkyl), C3-C7 cycloalkoxy, C6-C10-aryloxy, and the moieties (a-1), (a-2), and (a-3), wherein said alkyl, aryl, cycloalkyl, heterocyclic, heteroaryl, alkoxy, cycloalkoxy, haloalkyl, or haloalkoxy is further optionally substituted with one or more substituents selected from the group consisting of C1-C6 alkyl, halo, CN, CF3, -COOH, -OH, C1-C6 alkoxy, -NH2, -(C1-C6 alkyl)NH2, -(C1-C6 alkyl)NH(C1-C6 alkyl), -(C1-C6 alkyl)N(C1-C6 alkyl)2, -NH(C1-C6 alkyl), -N(C1-C6 alkyl)2, -CONH2, -NH(CO)(C1-C6 alkyl), -N(C1-C6 alkyl)CO(C1-C6 alkyl), -SO2-(C1-C6 alkyl), and -(SO)NH2,

The moieties (a-1), (a-2), and (a-3) were themselves large genres of chemical constituents defined using a variety of R groups.

¹¹ See the prosecution history of U.S. Patent 10,941,109, available on Public Pair.

The examiner rejected the originally filed structural genus claim under 112(a), essentially based on an inadequate disclosure of patentable utility, in a manner entirely consistent with the rationale set forth in *Brenner*. Notably, the application discloses, to use the words of *Death*, “some species within the genus that will work and how to make those species.” In particular, the patent specification specifically discloses 15 compounds falling within the genus that had actually been made, but the examiner found that these compounds were not representative of the scope of the claim given that the compounds are structurally “closer to each other than to the remaining scope.”

While the examiner explicitly acknowledged that the applicant had enabled some of the species falling within the genus, he nonetheless found the genus as a whole nonenabled because the application did not provide an enabling disclosure “for every possible compound encompassed within the formulas disclosed in the instant claims.” The examiner went on to explain:

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. There is no reasonable basis for assuming that the myriad of compounds embraced by all the generic claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. [The claim] encompass molecules that widely vary in the physical and chemical properties such as size, molecular weight, acidity, basicity, and properties that are known in the art to greatly influence pharmacokinetic and pharmacodynamics parameters, not to mention the ability to productively bind to claimed biological target molecules. The claims cover compounds easily in the millions given the number of possible rings, ring systems covered by the claims' scope along with varying choices for remaining variables.

The examiner also invoked 112(a)'s requirement that the patent enable the PHOSITA to “make” the claimed invention, finding that the “synthesis of all possible variations of the compounds [encompassed by the genus] would require much experimentation.” The examiner further found it to be well-established that pharmaceuticals, and the physiological activity of chemical compounds, are generally considered unpredictable, and that as compounds with asserted pharmaceutical utility generally need to be “individually assessed for viability.”

The examiner pointed to Manual of Patent Examining Procedure (MPEP) § 2164.08(b), which states that claims that read on a “significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.”

The examiner emphasized that “chemistry is an inherently experimental science,” and backed up this assertion by quoting from a recently published treatise:

Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most

scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)

The examiner went on to note that “[c]learly, the art of chemical synthesis is not a simple matter of visualizing a desired compound, mixing starting materials together, and obtaining the desired compound.”

The patent applicant responded by filing a series of narrowing amendments that progressively limited the scope of the claimed genus. The examiner repeatedly rejected the amended claims until the claims had been substantially narrowed, such that they only encompassed molecules sharing a relatively high degree of structural similarity with the 15 chemical compounds that were actually disclosed in the application as having been made and tested.

For example, on October 9, 2018, the applicant filed an amendment limiting R1 and R2 to aryl and heteroaryl groups. In a June 3, 2019 office action, the examiner maintained the 112(a) rejection, finding that even after this amendment, which effectively jettisoned most of the chemical moieties originally recited as encompassed by R1 and R2, the claimed genus was still too broad. The examiner explained:

The formula contains R groups which include aryl or heteroaryl groups, each substituted or optionally substituted. The instant specification defines "aryl" as all-carbon monocyclic or fused-ring polycyclic aromatic groups having a conjugated pi-electron system and "heteroaryl" as monocyclic or fused-ring polycyclic aromatic heterocyclic groups with one or more heteroatom ring members (ring-forming atoms) each independently selected from O, S and N in at least one ring.

These compounds encompass molecules that widely vary in the physical and chemical properties such as size, molecular weight, acidity, basicity, and properties that are known in the art to greatly influence pharmacokinetic and pharmacodynamics parameters, not to mention the ability to productively bind to claimed biological target molecules. The claims cover compounds easily in the millions given the number of possible rings, ring systems covered by the claims' scope along with varying choices for remaining variables.

On November 4, 2019, the applicant responded to this rejection by narrowing the scope of R1 and R2 even further, removing heteroaryl groups, as well as some aryl groups having more than one substitution. On June 30, 2020, the applicant narrowed the genus even further, limiting R1 and R2 to phenyl groups, including certain specified substituted phenyl groups (note that a phenyl group is a type of aryl group). At this point, the claim was finally allowed. The issued claim appears in *Part I*.

Of course, this is not to suggest that the PTO is applying, or has ever applied, what *Death* refers to as the “full-scope possession” theory, pursuant to which a genus claim is invalid “unless the patentee can show exactly which species within the genus will work as intended.”¹² The independent claim ultimately allowed in the prosecution history set forth above (U.S. Patent No. 10,941,109) recites a structural genus extending well beyond the 15 working examples disclosed in the patent application, encompassing species that have not been demonstrated to share the utility of the 15 examples, and that might not share that utility, given the unpredictability of structure-function relationships in chemistry.

Atlas Powder Co., discussed in *Death* and *Part I*, is often cited for the proposition that a certain number of inoperative embodiments, i.e., species that failed to satisfy the “use” aspect of the enablement requirement, will not render a genus claim invalid.¹³ And this is indeed the law. However, when the number of inoperative species exceeds a certain threshold, or where the degree of uncertainty exceeds some threshold, a genus claim will be found invalid. As stated in MPEP 2164.08(b), “claims reading on significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.”

Such determinations are necessarily highly fact-specific, and will depend upon the nature of the particular genus at issue, the disclosure in the application, the state of the art, etc. There will always be cases at the margin that could go either way. Judge Lourie is, I believe, referring to this when he asserts in his *Amgen v. Sanofi* denial of en banc rehearing concurrence (discussed in *Part I*) that the standard for compliance with the 112(a) has not changed, but rather that it is changes with respect to how genres are claimed and disclosed that accounts for the recent invalidations of genus claims in *Amgen* and the other cases discussed in *Death*.

Although I feel certain that the PTOs interpretation of 112(a) as applied to structural genus claims is correct and supported by judicial precedent, I am unable to point to an example of this from a reported judicial decision since the inception of the Federal Circuit in the 1980s. There just does not seem to be much case law regarding the validity of structural genus claims under 112(a). In *Part I* I pointed out that *Death* does not identify a single reported decision involving a structural genus claim, or even, for that matter, a patent including such a claim.

One pre-Federal Circuit example of which I am aware is *In re Rainer*, decided in 1967, wherein the CCPA affirmed the PTO’s determination that certain structural genus claims were invalid

¹² *Death* at 4.

¹³ *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

under 112(a) based on the inoperability of some members of the chemical genus. The genus encompassed a host of polymers, defined in structural terms. Here is a representative claim:

9. A bottle made of irradiated polyethylene, the irradiation being to an extent of at least 2×10^6 REP, having grafted thereto a polymer formed by polymerizing a member of the group consisting of a polymerizable ethylenically unsaturated hydrocarbon monomer other than ethylene, halogenated styrene, alkyl acrylates, alkyl methacrylates, N,N-methylene-bis-acrylamide, dialkenyl oxalates, diallyl phthalate, triallyl cyanurate, diallyl maleate, diallyl fumarate, triallyl melamine, dialkyl maleates and dialkyl fumarates on said polyethylene.

There is also the very recent jury verdict in *Plexxikon v. Novartis* that found structural genus claims infringed and not invalid under 112(a), as discussed later in this article.

Returning to *Death's* suggestion that patentees could circumvent the Federal Circuit's purported heightened application of 112(a) to genus claims by employing structural genus claims rather than functional genus claims, I would argue that the authors of *Death* have got it backwards. It has long been understood by patent practitioners in the chemical arts that a structural genus claim will run afoul of 112(a) if the disclosure of the patent does not establish with a certain degree of certainty that at least a significant number of the members of the genus will share the functionality that satisfies the utility requirement, and patent applicants have responded by introducing functional limitations to structurally defined genus claims in order to, at least literally, address this concern.

For example, for many years inventors have secured patents on biomolecules, e.g. proteins and DNA molecules, based on the discovery of a practical utility for the molecule, such as use as a therapeutic, or diagnostic, or perhaps in an agriculturally useful genetically modified plant. To obtain some breadth of coverage, inventors have applied for patent claims covering large genres of related biomolecules. It has been common to claim a genus defined by a specific DNA sequence (identified by SEQ ID NO), and encompassing all DNA molecules sharing a certain degree of similarity, e.g., all DNA sequences at least 90% identical to the specifically recited sequence. Claims of this type have often faced rejection at the PTO under 112(a), based on the examiner's assertion that the applicant had not demonstrated with sufficient predictability that all of the molecule sharing 90% structural identity would share the recited molecules functional attributes. Patent practitioners responded to this concern by including a functional limitation. For example, if the practical utility of the DNA sequence is X, the claim would recite:

A polynucleotide comprising SEQ ID NO:1, or any DNA sequence that is at least 90% identical to SEQ ID NO:1, wherein said DNA sequence possesses the functionality X.

Claim 5 of U.S. Patent No. 7,045,325 provides a real example of such a claim:

5. An isolated polypeptide comprising the amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:5, wherein said polypeptide has dehydrogenase activity.

Note that the functional limitation literally addresses the examiner's concern, by expressly excluding DNA sequences lacking functionality X. However, the courts and the PTO will nonetheless find the claim to be invalid under 112(a) if the patent fails to disclose a sufficiently predictable relationship between function and structure for the PHOSITA to distinguish between molecules sharing 90% identity and having functionality X and those molecules that meet the structural criterion but lack the required functionality. But removing the functional limitation clearly would not address the underlying 112(a) problem, contrary to *Death's* suggestion.

Pushing back on *Death's* assertion that a “shift” has occurred

The authors of *Death*, and others, allege that a dramatic shift in the standard for compliance with Section 112(a), as it is applied to chemical genus claims, has occurred at the Federal Circuit. This section of the article examines this claim, and shows that it is probably overstated.

When did the “shift” occur?

Death does not exactly pinpoint when the purported shift in the law occurred. At one point the article identifies *Wyeth & Cordis v. Abbott*, a case decided by the Federal Circuit in 2013, as the “first opinion in this latest line of cases.”¹⁴ *Death* goes on to state that this shift was “cemented” in 2019 in *Idenix v. Gilead*.¹⁵ These statements would suggest that the purported shift in the law is relatively recent, beginning around 2013.

At another point in the article, however, *Death* states that at least one aspect of the “shift” arguably began in a 1999 Federal Circuit biotech enablement opinion, *Enzo Biochem v. Calgene, Inc.*¹⁶ Elsewhere, *Death* suggests that the shift had begun by the early 1990s, at one point referring to “doctrinal shifts over 30 years.” Indeed, *Death* “conclude[s] that chemical genus claims do not do well against § 112(a) challenges at the Federal Circuit, and have not for almost thirty years.” *Death* states:

Especially in the 1980s, one is hard pressed to find appellate cases invalidating claims under § 112(a) based on notions of claim overbreadth. By contrast, in the past thirty years, there are virtually no significant examples of genus claims in the life science fields upheld on appeal as compliant with § 112(a) outside the unique context of so-called “interference” proceedings.”¹⁷

With regard to the assertion that “one is hard pressed to find appellate cases invalidating claims under 112(a) based on notions of claim overbreadth [in the 1980s],” it bears noting that *Death* only identifies a single judicial decision from the 1980s, *Atlas Powder v. E.I. du Pont De Nemours & Co.*, in which a genus claim was upheld in the face of a 112(a) challenge for overbreadth.¹⁸ *Atlas Powder* is discussed at length in *Part I*, which explains that it is a bit of a stretch to even characterize the claims at issue as a “chemical genus claims,” and that the claimed subject matter certainly does not relate to the life sciences. So while it may be true that

¹⁴ *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013).

¹⁵ *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149 (Fed. Cir. 2019).

¹⁶ *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362 (Fed. Cir. 1999).

¹⁷ *Death* at 23.

¹⁸ *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

it is hard to find appellate decisions striking down genus claims for failure to comply with 112(a), the authors of *Death* were apparently only able to identify a single case in which claims were upheld.

In any event, based on my reading of *Death* it seems to me that the authors are arguing that the purported doctrinal shift had at least begun by the early 1990s, and that the shift was in full swing by 2013. In the remainder of this section of my article, I will provide a number of examples of decisions predating and/or coinciding with the purported shift, wherein functional genus claims comparable to those at issue in *Wyeth*, *Enzo*, *Idenix*, and *Amgen* were found to be invalid under 112(a) for overbreadth, calling into question *Death*'s assertion that there was a substantially more permissive standard in place prior to the purported shift. I then provide examples post-shift cases in which relatively broad chemical genus claims have been upheld in the face of 112(a) overbreadth challenges, including an interesting district court decision from 2021, *Plexxikon v. Novartis*, which bears watching, particularly if the 112(a) issue winds up before the Federal Circuit.

Examples of genus claims invalidated prior to 1990

First off, let us take a look at some reported decisions from prior to 1990, clearly pre-dating *Death*'s purported shift. These decisions provide examples of chemical genus claims being found invalid for overbreadth, with the court applying what I believe to be essentially the same standard as is being used today in the cases *Death* points to as illustrative of a recently heightened 112(a) standard.

Death points to only one Supreme Court decision that directly addresses the validity of a chemical genus claim, *Corona Cord Tire Co. v. Dovan Chem. Corp.*, decided in 1928.¹⁹ In *Corona Cord Tire*, the Court found a claim to be invalid for reciting a genus of 50 to 100 disubstituted guanidines without disclosing “any general quality common to disubstituted guanidines which made them all effective as accelerators.”²⁰ To my knowledge this is the only Supreme Court decision that directly addresses the permitted scope of a chemical genus claim. In other words, Supreme Court precedent would seem to provide little direct support for the existence of a relatively permissive standard governing the breadth of chemical genus claims, from which the Federal Circuit has departed.

A decade after *Corona Cord Tire*, in *In re Soll*, the Court Of Claims and Patent Appeals (CCPA) affirmed the Patent Office's decision to reject claims reciting a “hydrogen halide” limitation.²¹ The term “hydrogen halide” constitutes a structurally defined genus comprising four members: hydrogen fluoride, hydrogen chloride, hydrogen bromide, and hydrogen iodide. The examiner rejected the claims for overbreadth, because the application only disclosed that the invention worked with one of constituents of the genus, hydrogen fluoride. Given the unpredictability of hydrogen halide chemistry, the court agreed with the Patent Office's determination that the scope of the claim exceeded the scope of disclosure.

¹⁹ *Corona Cord Tire Co. v. Dovan Chem. Corp.*, 276 U.S. 358 (1928).

²⁰ *Id.*

²¹ *In re Soll*, 97 F.2d 623 (C.C.P.A. 1938).

At this point it also bears mention that the CCPA's 1976 decision in *Application of Angstadt*, decided by the CCPA in 1976, and one of the two specific cases that *Death* points to as exemplifying the allegedly more permissive standard of an earlier day (the other being *Atlas Powder*), was not a unanimous decision.²² The dissenting judge in *Angstadt* argued that under the 112(a) standard applicable at the time, the claim was invalid for overbreadth. In particular, the dissenting judge argued that the majority's "approach violate[d] the logic of [earlier CCPA] cases [which found] that there must be guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction, whether the claimed product will be obtained." The judge went on to argue that:

Although appellants' specification shows some 38 examples (embodiments) within the broad scope of the claims, this number is minute in comparison with the immense number of combinations of organometallic catalysts and alkylaromatic hydrocarbons within that scope. The specification fails to provide guidance for determining which of the combinations are proper and which are not. . . . There is simply no teaching of how to choose those secondary and tertiary alkylaromatic hydrocarbons and organometallic catalysts which will form hydroperoxides. The need for guidance to enable the invention, with its claims to a myriad of combinations of organometallic catalysts and alkylaromatic hydrocarbons, to be practiced without undue experimentation is evident.²³

The dissenting judge's insistence that the specification must provide guidance as to which species falling within the genus will exhibit the claimed functionality before "performing the reaction" seems consistent with the standard being applied by the modern Federal Circuit in cases such as *Wyeth* and *Idenix*.²⁴

Examples of genus claims invalidated between 1990 and 2013

This section of the article reviews a number of significant decisions in which chemical genus claims were found invalid under 112(a) for overbreadth between 1990 and 2013, the period of time that *Death* identifies as marking the transition between an earlier permissive standard to the today's purportedly heightened standard for compliance with 112(a). These decisions illustrate that chemical genus claims of the type being invalidated today were also being invalidated well before 2013.

Amgen v. Chugai, a seminal biotechnology decision of the Federal Circuit, provides a good example of this from 1991.²⁵ The relevant claim recited:

7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding a polypeptide having an amino acid sequence *sufficiently duplicative* of that of erythropoietin to allow possession of the biological property of causing

²² *Application of Angstadt*, 537 F.2d 498 (C.C.P.A. 1976).

²³ *Id.* at 507–08.

²⁴ See the discussion of these cases in *Part I*.

²⁵ *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991).

bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake.²⁶

This is a functional genus claim (as that term is defined in *Part I*), having a structural limitation (“amino acid sequence sufficiently duplicative of that of erythropoietin”) and functional limitation (“possession of the biological property...”). It is comparable to the claims invalidated in some of the more recent Federal Circuit decisions that *Death* points to as illustrative of the shift. In *Wyeth*, for example, the structural limitation was that the recited molecule was required to be a “rapamycin.”²⁷ Although the “sufficiently duplicative” language of Amgen’s claim does not precisely delineate structure in the way a more canonical structural genus claim does, i.e., through the recitation of a core generic structure and appended R groups, the same can be said for the term “rapamycin,” which the patentee in *Wyeth* argued encompassed a genus of molecules sharing some degree of structural similarity with the form of rapamycin specifically disclosed in the application, i.e., sirolimus. The functional limitation of the *Wyeth* genus was the “anti-restenosis” functionality of the molecule.

Amgen’s claim is also comparable to the claims at issue in *Idenix* and *Amgen v. Sanofi*. In *Idenix*, the claim defined the nucleoside in broad structural terms, along with a functional limitation, i.e., the ability to treat hepatitis C infection. In *Amgen*, the chemical genus’s structural limitation was also expressed in imprecise terms, i.e., the molecule must be a “monoclonal antibody.” The functional limitation of the claimed genus was the ability to bind PCSK9 at a certain location defined by amino acid residues to block the binding of PCSK9 to LDLR.

Conversely, the claim invalidated in *Amgen v. Chugai* bears relatively little resemblance to the claims at issue in *Atlas Powder* and *Angstadt*, the only two decisions which *Death* points to as exemplifying the purportedly more forgiving pre-shift enablement standard. In particular, Amgen’s claim to DNA molecules encoding erythropoietin analogs would appear to encompass as-yet unidentified analogs having substantially superior pharmacological properties relative to the handful of analogs disclosed in Amgen’s patent. As discussed in *Part I*, this is one of the ways in which the claims at issue in cases like *Wyeth*, *Idenix*, and *Amgen v. Sanofi* are fundamentally distinguishable over the claims at issue in *Atlas Powder* and *Angstadt*.

In *Amgen v. Chugai*, Judge Lourie explained:

Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with attendant ***uncertainty as to what utility will be possessed by these analogs***, we consider that more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and ***structural requirements for producing compounds with EPO-like activity***.²⁸

²⁶ U.S. Patent 4,703,008 (emphasis added).

²⁷ *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013).

²⁸ 927 F.2d at 1214 (Fed. Cir. 1991).

In another landmark biotechnology decision, 1997's *Regents of the Univ. of California v. Eli Lilly & Co.*, the Federal Circuit again affirmed a district court's decision finding a genus claim invalid under 112(a).²⁹ The twist in this case was that the Federal Circuit's novel (at the time) application of the written description requirement, rather than the enablement requirement, in finding chemical genus claims invalid for overbreadth.³⁰

A representative claim at issue in the case recited:

1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.³¹

The claim is essentially directed to the genus comprising vertebrate insulin "genes," or more accurately, insulin-encoding cDNA molecules. The Federal Circuit characterized the recited genus as being defined purely in functional terms, although I would argue that the requirement that the cDNA encodes "insulin" imposes inherent structural constraints along the lines discussed above with respect to claim limitations like "rapamycin" or "sufficiently duplicative" of erythropoietin. The patent disclosed (and presumably enabled) a working example falling within the genus, i.e., the rat insulin cDNA. The Federal Circuit agreed with the district court that disclosure of the species did not provide adequate support under 112(a) for the recited genus encompassing all vertebrate cDNAs.³²

UC Regents illustrates the problem with allowing the inventor of a species to leverage the disclosure of that species to obtain a broad genus claim encompassing related species having significantly different and/or superior functionality. This problem is discussed in *Part I*. In *UC Regents*, the species is the rat insulin cDNA, which could be used to produce recombinant rat insulin. The rat cDNA presumably would satisfy the utility requirement, since it could, at least in principle, probably serve as a pharmacological agent for treatment of diabetic patients. Prior to recombinant technology, for example, human insulin was not available in quantities necessary to be used as a drug, and diabetic patients were given insulin from other mammals, such as pigs.

At the same time, the claimed genus of vertebrate insulin genes would also encompass the human gene, which is a clinically superior pharmacological agent for treating humans with diabetes. As discussed in *Part I*, the authors of *Death* seem to suggest that once a species having the desired function has been disclosed, that disclosure should be sufficient to satisfy 112(a) with respect to a broad genus claim encompassing that species. To the contrary, I would argue, based on policy considerations, that the disclosure of the rat gene should only constitute sufficient 112(a) support for a genus claim that encompasses the human gene if the disclosure of the rat gene would enable the PHOSITA to identify and make the pharmacologically superior human gene. In fact, the identification and sequencing of the rat insulin gene was an important milestone in the quest to obtain to isolate the human gene, and arguably would have enabled the

²⁹ *Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997).

³⁰ Christopher M. Holman, *Is Lilly Written Description a Paper Tiger?: A Comprehensive Assessment of the Impact of Eli Lilly and Its Progeny in the Courts and PTO*, 17 ALB. L.J. SCI. & TECH. 1 (2007).

³¹ U.S. Patent 4,652,525.

³² A relatively narrower claim limited to the genus of "mammalian" cDNAs was also found to be invalid.

PHOSITA to obtain the human gene without engaging in undue experimentation, calling into question the wisdom of the Federal Circuit's decision finding the claim invalid for lack of adequate written description.³³ The courts did not address the question of enablement, which would have been the better approach in assessing the scope of the genus claims for compliance with 112(a).

In explaining the court's decision, Judge Lourie noted that:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, *except by function*. It does not specifically define any of the genes that fall within its definition. *It does not define any structural features commonly possessed by members of the genus that distinguish them from others*. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.³⁴

In *Chiron v. Genentech*, decided in 2004, the Federal Circuit held that a claim to a functionally defined monoclonal antibody, comparable to the claim at issue in *Amgen v. Sanofi*, was not enabled under 112(a) by the disclosure of 13 murine antibodies falling within the scope of the defined genus.³⁵ The claim at issue recited a "monoclonal antibody that binds to human [HER2] antigen."³⁶ The application disclosed 13 species falling within the scope of the claim, and that these antibodies likely bind to at least three different epitopes on the antigen, HER2.

Chiron is another good example of a case where the genus recited in the invalidated claim would encompass species with significantly different and/or improved function relative to the explicitly disclosed working examples. In particular, all of the disclosed species were murine antibodies produced using traditional hybridoma technology. The patent explicitly defined the term "monoclonal antibody" as "an antibody composition having a homogeneous antibody population. It is not intended to be limited as regards the source of the antibody or the manner in which it is made." Consistent with this definition, the court interpreted the claim as encompassing homogeneous antibody populations produced by subsequently developed (i.e., post-filing date) technologies, and particularly chimeric antibodies and humanized antibodies. As such, the claim would encompass antibodies much better suited for use as human therapeutics than the disclosed hybridoma-derived murine antibodies.

³³ There is much that could be said about this issue, but it would be a long tangent from the thrust of the present article.

³⁴ 119 F.3d at 1568.

³⁵ *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004).

³⁶ The claim literally recited "c-erbB-2," which later became widely known as HER2, the target of the cancer drug Herceptin.

As explained by the Federal Circuit:

While Chiron's applications certainly enable murine antibodies, they do not enable chimeric antibodies. Although an aspect of the claimed invention included the binding of an antibody to a breast cancer antigen, Chiron's disclosure fell short of providing a “specific and useful teaching[“] of all antibodies within the scope of the claim.³⁷

In *Carnegie Mellon v. Hoffmann-La Roche*, decided in 2008, a representative claims recited:

1. A recombinant plasmid containing a cloned complete structural gene coding region isolated from a bacterial source for the expression of DNA polymerase I, under operable control of a conditionally controllable foreign promoter functionally linked to said structural gene coding region, said foreign promoter being functional to express said DNA polymerase I in a suitable bacterial or yeast host system.³⁸

The relevant genus would encompass bacterial DNA polymerase I genes. The patent only disclosed one species of this genus, the DNA polymerase I gene from *E. coli*. The claims were found to be invalid under the written description prong of 112(a).

Significantly, the product accused of infringing Carnegie Mellon’s patent was a *Thermus aquaticus* (*Taq*) DNA polymerase. *Thermus aquaticus* is a thermophilic bacteria, and *Taq* has the substantial advantage over *E. coli* polymerase of thermal stability, i.e., *Taq* polymerase can be heated to a temperature that results in the denaturation of double-stranded DNA, which is an extremely important attribute in the context of polymerase chain reaction (PCR). The *E. coli* polymerase would be denatured and inactivated at this temperature, and thus could not be used in a process like PCR that involves multiple cycles of heating and cooling in order to denature and then re-hybridize double-stranded DNA.

One could point to other examples of genus claims that were deemed overbroad and thus invalid under 112(a) between 1990 and 2013, some of which are cited in the footnote accompanying this sentence (most of these cases were at least mentioned in *Death*).³⁹

Examples of broad genus claims upheld between 1990 and 2013

Although *Death* argues that the shift began at least 30 years ago, the article does discuss a number of post-2000 Federal Circuit decisions in which relatively broad functional genus claims withstood 112(a) validity challenges. *Death* largely dismisses the significance of these decisions, pointing out, for example, that some of them occurred in the context of a patent interference, and suggesting that a different standard might apply with respect to patent interferences as opposed to infringement litigation. *Death* acknowledges at least two infringement litigations in which broad functional genus claims were upheld, *Invitrogen v.*

³⁷ 363 F.3d at 1256.

³⁸ *Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc.*, 541 F.3d 1115 (Fed. Cir. 2008)

³⁹ *See, e.g.*, *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993). *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362 (Fed. Cir. 1999); *Noelle v. Lederman*, 355 F.3d 1343 (Fed. Cir. 2004); *Univ. Of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004); *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1340 (Fed. Cir. 2010).

*Clontech*⁴⁰ and *Amgen v. Hoechst Marion Roussel*,⁴¹ but again downplays their significance by concluding that “[b]oth decisions were made for reasons that are not easy to classify precisely, but that we believe are unusual.”

I would argue that these decisions are not so much outliers as they are examples that undercut *Death*'s assertion that there has been a dramatic shift in the law.

For example, a representative claim at issue in *Invitrogen v. Clontech* recites:

1. A polypeptide having DNA polymerase activity and substantially no RNase H activity wherein said polypeptide may be used for the preparation of full length cDNA without significant degradation of the mRNA template during first strand synthesis wherein said polypeptide is encoded by a nucleotide sequence derived from an organism selected from the group consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents.

The Federal Circuit acknowledged that the claimed genus of proteins was defined in terms of biological functions, i.e., DNA polymerase activity and lack of RNase H activity. The patent disclosed how to use deletion mutagenesis to eliminate RNase H activity from a DNA polymerase. The accused infringer argued that the claim failed the written description requirement because it did not disclose how to eliminate RNase activity by means of point mutagenesis, even though the claim was not limited to deletion mutagenesis and would encompass a DNA polymerase lacking RNase H activity made using point mutagenesis. The Federal Circuit rejected this argument, upholding the validity of the claims. *Death* found the court's decision “unusual,” but could not offer a rationale for it, finding it was “made for reasons that are not easy to classify precisely.”

I can offer at least one public policy justification for the apparent discrepancy between this decision and other cases striking down genus claims. In *Invitrogen*, there would not seem to be any reason that point mutagenesis would result in a polymerase having improved functional characteristics compared to a polymerase made using deletion mutagenesis, so the public policy concerns attendant to a decision to allow a patent claim to encompass different or superior products, discussed in *Part I*, does not seem to be present in this case.

In *Amgen v. Hoechst Marion Roussel*,⁴² the patents at issue include product claims that recite broad genres of DNA molecules encoding erythropoietin, a pharmaceutically useful protein. A divided panel of the Federal Circuit found these claims not invalid under 112(a)'s enablement and written description requirements.

One of the patent claims at issue recited:

1. Vertebrate cells which can be propagated in vitro and which are capable upon growth in culture of producing erythropoietin in the medium of their growth in excess of 100 U of

⁴⁰ *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052 (Fed. Cir. 2005)

⁴¹ *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003).

⁴² *Id.*

erythropoietin per 10⁶ cells in 48 hours as determined by radioimmunoassay, said cells comprising *non-human DNA sequences that control transcription of DNA encoding human erythropoietin*.⁴³

The claim was interpreted such that the genus of “non-human DNA sequences that control transcription of DNA” encompassed not only not only exogenous transcription-control sequences, but also activation technology employing endogenous transcription-control sequences. The allegedly infringing cells employed endogenous transcription-control sequences. But the technology for achieving endogenous transcription-control had not even been developed as of the filing date of the patent claim. On its face, the decision seems inconsistent with *Chiron v. Genentech*, where the claim was found invalid because it encompassed post-filing date antibody technology.

But again, I think the apparent discrepancy can be rationalized in terms of public policy. In *Chiron*, the patent did not disclose an antibody that would be useful to human therapeutic, which required significant post-filing date advances in antibody technology. On the other hand, Amgen had figured out a way to manufacture pharmaceutical-grade human erythropoietin at scale, and the accused infringer was essentially trying to manufacture the same product (or at least a very similar product) using after-developed technology that Amgen could not have been expected to literally disclose when it filed its patent application.

Another claim upheld by the Federal Circuit recited:

2. An isolated erythropoietin glycoprotein having the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells, wherein said erythropoietin glycoprotein comprises the mature erythropoietin amino acid sequence of FIG. 6 and is *not isolated from human urine*.⁴⁴

Note that the recited genus of erythropoietin glycoproteins would encompass any glycoprotein having the recited amino acid sequence, regardless of the nature of the glycosylation, so long as the glycoprotein is “not isolated from human urine.” In terms of chemical structure, this is quite a broad genus, given all the possible glycosylation patterns of a large protein like erythropoietin. Note that some people might mistakenly interpret a genus limited to a particular amino acid sequence as a species claim, rather than a genus claim, by failing to take into account that courts have generally interpreted these claim to encompass glycosylated versions of the protein, and that glycosylation of eukaryotic proteins can be quite structurally diverse, even though the amino acid sequence of two proteins is identical.

Another claim upheld in the case recited:

1. A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or

⁴³ U.S. Patent 5,756,349 (emphasis added).

⁴⁴ U.S. Patent 6,621,080

carrier, wherein said erythropoietin is *purified from mammalian cells grown in culture*.⁴⁵

Again, note the broad, functional definition of the recited genus of proteins, purporting to encompass any erythropoietin purified from cultured mammalian cells.

Judge Clevenger filed a dissenting opinion in the case, arguing that the court's application of the written description requirement was not "faithful" to the Federal Circuit's articulation of the doctrine in *Regents of the University of California v. Eli Lilly*.⁴⁶ I think that Judge Clevenger was exactly right, but the majority's decision in *Amgen* was justified based on the pioneering nature of their invention, and the fact that they did disclose how to make an actual pharmaceutical product. I would argue that the real problem was the *UC Regents* decision itself.

Beyond *Capon* and *Amgen*, there are quite a few other decisions of the Federal Circuit over the last couple of decades that have upheld claims in the face of 112(a) challenges based on the breadth of a recited chemical genus.

For example, in *Singh v. Brake* (2003), the Federal Circuit found the following claim to be in compliance with the written description and enablement requirements:⁴⁷

1. A DNA construct comprising a sequence of the following formula:

5'-L-S-Gene*-3',

where:

L encodes a *Saccharomyces* alpha-factor leader sequence recognized by a yeast host for secretion;

S encodes a spacer sequence providing processing signals resulting in the enzymatic processing by said yeast host of a precursor polypeptide encoded by L-S-Gene* into the polypeptide encoded by Gene*, S containing the sequence 5'-R1-R2-3' immediately adjacent to the sequence Gene*, R1 being a codon for lysine or arginine, R2 being codon for arginine, with the proviso that S not contain the sequence 5'-R3-R4-X-3', where R3=R1, R4=R2, and X encodes a processing signal for dipeptidylaminopeptidase A; and Gene* encodes a polypeptide foreign to *Saccharomyces*.

Note the broad functional definition of the "L," "S," and "Gene*" genres of DNA molecules.

In *Falko-Gunter Falkner v. Inglis*, decided in 2006, the Federal Circuit upheld a Board decision finding, in the context of a patent interference, that the following claim satisfied the enablement and written description requirements.⁴⁸

⁴⁵ U.S. Patent 5,925,422.

⁴⁶ 314 F.3d at 1360-61.

⁴⁷ *Singh v. Brake*, 317 F.3d 1334 (Fed. Cir. 2003).

⁴⁸ *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357 (Fed. Cir. 2006).

A vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of a mutant virus, wherein said mutant virus is a ***mutant poxvirus and has a genome which has an inactivating mutation in a viral gene***, said viral gene being essential for the production of infectious new virus particles, wherein said mutant virus is able to cause production of infectious new virus particles in a complementing host cell gene expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than a complementing host cell; for prophylactic or therapeutic use in generating an immune response in a subject.

Note that the poxvirus genome is essentially a DNA molecule, and the claimed genus of DNA molecules broadly encompasses poxvirus genomes that have been modified by deletion of any “essential” gene, the function of which can be replaced by a host cell expressing the gene.

In *Monsanto Co. v. Scruggs*, decided in 2006, a representative claim recited a “chimeric gene which is expressed in plant cells comprising . . . a CaMV (35S) promoter isolated from CaMV protein-encoding DNA sequences . . . and a structural sequence which is heterologous with respect to the promoter.”⁴⁹ The infringer argued that the claims were invalid for lack of enablement because, while the claims recite a genus of DNA molecules (CaMV 35S promoter sequence), the patent only disclosed a few species falling within the genus. In particular, the accused products (genetically modified soybeans) used a CaMV 35S promoter sequence that was different, both in terms of sequence and length, than anything disclosed in the patent. Nonetheless, the Federal Circuit found the claims not invalid for lack of enablement, and infringed by the accused products.⁵⁰

In 2008, in *In re Biogen '755 Pat. Litig.*, a jury had found the following claim not invalid for lack of enablement or lack of adequate written description.⁵¹

1. A method for immunomodulation or treating a viral condition[], a viral disease, cancers or tumors comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of a composition comprising:

a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:

(a) DNA sequences which are capable of hybridizing to any of the DNA inserts of G-pBR322(Pst)/HFIF1, G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and GpBR322(Pst)/HFIF7 (DSM 1793) under hybridizing conditions of 0.75 M NaCl at 68° C. and washing conditions of 0.3 M NaCl at 68° C., and which code for a polypeptide displaying antiviral activity, and

⁴⁹ U.S. Patent 5,352,605

⁵⁰ *Martek Biocis. Corp. v. Nutrinova, Inc.*, 579 F.3d 1363 (Fed. Cir. 2009).

⁵¹ *In re Biogen '755 Pat. Litig.*, 335 F. Supp. 3d 688 (D.N.J. 2018).

(b) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a);

said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule.

The district court denied the accused infringer's motion for judgment as a matter of law (JMOL) that the claim was invalid under 112(a), finding that substantial evidence supported the jury's verdict. The district court explained that:

Defendants' motion appears to focus on the scope of the non-human hosts and recombinant polypeptides. [It] is not the genus of non-human hosts or recombinant polypeptides that must be enabled and described, it is the method of treatment that must be enabled and described. Even if Defendants' proposed framework were correct, however, there is ample evidence in the record for a reasonable jury to conclude that the claims are not invalid for either lack of enablement or lack of adequate written description.

On appeal, the Federal Circuit found the claim to be anticipated and reversed the district court's decision upholding the validity of the claims.⁵² This rendered the issue of validity under 112(a) moot, so we cannot know how the Federal Circuit would have ruled in that regard. This is unfortunate, since this is a very good example of a genus of DNA molecules broadly defined in terms of both structure and function, a type of claim for which there is little direct Federal Circuit case law directly addressing the question of claim scope and 112(a).

In *Martek Biocis. Corp. v. Nutrinova, Inc.*, decided in 2009, the Federal Circuit affirmed a district court's denial of a motion asserting the invalidity of the following claim:

A food product, comprising:

a) lipids extracted from a fermentation process for growing microorganisms selected from the group consisting of microorganisms of the genus *Thraustochytrium*, microorganisms of the genus *Schizochytrium* and mixtures thereof, wherein said microorganisms are capable of effectively producing lipids containing mixtures of omega-3 and omega-6 highly unsaturated fatty acids under conditions comprising:

i) salinity levels less salinity levels found in seawater;

ii) a temperature of at least about 15° C.; and

b) food material.⁵³

Note that the claim recites a genus of lipids (a type of chemical compound) defined in terms of the source microorganism, and the microorganism could be a member of either of two recited genera. Although this patent claim does not relate to pharmaceuticals, it seems to me it is as much a chemical genus claim as the claims in *Atlas Powder* and *Angstadt*, the two primary

⁵² *Biogen MA Inc. v. EMD Serono, Inc.*, 976 F.3d 1326 (Fed. Cir. 2020).

⁵³ *Martek Biocis. Corp. v. Nutrinova, Inc.*, 579 F.3d 1363 (Fed. Cir. 2009).

examples of “genus claims” cases identified in *Death*. Notably, the motion for invalidation in *Martek* was based on anticipation, not 112(a), which the accused infringer apparently did not even see as an issue with respect to this claim.

In *Streck, Inc. v. Rsch. & Diagnostic Sys., Inc.*, decided by the Federal Circuit in 2012, a representative claim recites:

A hematology control composition comprising:

- a) a stabilized *reticulocyte* component; and
- b) a fixed and stabilized white blood cell component capable of exhibiting
a five-part differential.⁵⁴

Reticulocytes are “anucleate immature red blood cells containing some ribonucleic acid.” The claim was interpreted such that the “reticulocyte” limitation encompasses both naturally-occurring “true reticulocytes” and synthetic reticulocyte analogs. The Federal Circuit affirmed the lower court’s determination that the claims satisfied both the enablement and written description requirements, in spite of the fact that the patent only disclosed the use of analog reticulocytes, not true reticulocytes.

Post-2013 decisions upholding the validity of chemical genus claims

The Federal Circuit has continued to uphold the validity of chemical genus claims after 2013, the year which some statements in *Death* state that the shift in the law had occurred. There are numerous post-2013 examples of claims comparable to the claims at issue in *Atlas Powder* and *Angstadt* claims that have withstood judicial challenge and been successfully enforced.

In *Alcon v. Barr Lab'ys.*, for example, the Federal Circuit reversed a district court’s decision to invalidate the following chemical genus claim for lack of enablement:

A method of enhancing the chemical stability of an aqueous composition comprising a therapeutically-effective amount of *a prostaglandin*, wherein the method comprises adding *a chemically-stabilizing amount of a polyethoxylated castor oil [(“PECO”)]* to the composition.⁵⁵

One could make the case that the *Alcon* claim is comparable to the claim upheld in *Angstadt*. In both cases, the claim is directed towards a method that employs a chemical genus. In *Angstadt*, it was a genus of hexaalkylphosphoramides, while in *Alcon* it is a genus of polyethoxylated castor oils. In both cases, a lower tribunal had found the claims invalid for lack of enablement, based on a determination that the patent did not provide enough teaching as to how to identify which specific member of the structurally defined genus, i.e., which specific hexaalkylphosphoramides, or polyethoxylated castor oils, would possess the necessary functional attribute of catalyzing a reaction, or stabilizing a formulation, respectively. In both cases, on appeal the Federal Circuit reversed.

⁵⁴ *Streck, Inc. v. Rsch. & Diagnostic Sys., Inc.*, 665 F.3d 1269 (Fed. Cir. 2012).

⁵⁵ *Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180 (Fed. Cir. 2014).

Another example from 2014 is *GlaxoSmithKline LLC v. Banner Pharmacaps*, wherein the claim at issue recited “[dutasteride] or a pharmaceutically acceptable solvate thereof.”⁵⁶ The district court characterized the term “solvate” as defining a “genus” defined by two properties.

First, a solvate is a complex of dutasteride molecules and solvent molecules, with dutasteride being . . . “the key structural component.” Second, the structure is one that is created by an identified process—specifically, by dissolving dutasteride (the solute) in a solvent.

The court further construed the term “solute” as broadly encompassing any complex formed by reaction, precipitation, or crystallization of dutasteride with a solvent, with no limitation on the solvent used, the process used, or whether the resulting “solute” is crystallized or non-crystallized. The defendant argued that under this broad interpretation of “solvate” the claim was invalid for lack of adequate written description, but the district court rejected this argument, a decision that was affirmed by the Federal Circuit on appeal.

In 2017, in the case of *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, a jury found the following claim infringed and not invalid for lack of enablement or inadequate written description, and the Federal Circuit affirmed without issuing an opinion under Rule 36.⁵⁷

A method for prophylaxis or treatment of benign prostatic hyperplasia comprising administering to a person in need thereof an effective amount of ***an inhibitor of phosphodiesterase (PDE) V excluding*** a compound selected from the group consisting of

dipyridamole,

2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylenedioxy)benzyl)amino)quinazoline,

2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate.

4((3,4-(methylenedioxy)benzyl)amino)-6,7,8-trimethoxy-quinazoline,

1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,

2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,

1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,

7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chronan-4-one,

and pharmacologically compatible salts thereof.

⁵⁶ *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725 (Fed. Cir. 2014).

⁵⁷ *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629 (E.D. Tex. 2017), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018).

This is a functional genus claim that defines the chemical genus in terms of the ability to inhibit phosphodiesterase V (PDE5) and treat benign prostatic hyperplasia. There is also a structural limitation, in that the claim explicitly excludes from the genus eight structurally defined compounds.⁵⁸ The claimed chemical genus encompasses many compounds; according to the district court, it was “generally undisputed that the claimed genus is... very large.” The district court nonetheless rejected enablement and written description challenges raised by the defendant Eli Lilly, even though experts testified that “at least tens of thousands” PDE5 inhibitors had been developed.

In 2019, the Federal Circuit upheld the validity a functional genus claim in *Ajinomoto v. ITC*.⁵⁹ The claim at issue essentially⁶⁰ covered:

A method for producing an aromatic L-amino acid, which comprises cultivating a recombinant *Escherichia coli* bacterium, which has the ability to accumulate aromatic L-amino acid in a medium, wherein the aromatic L-amino acid production by said bacterium is enhanced by enhancing activity of a protein in a cell of said bacterium beyond the levels observed in a wild-type of said bacterium,

[1] and in which said protein consists of the amino acid sequence of SEQ ID NO: 2

[2] and said protein has the activity to make the bacterium resistant to L-phenylalanine, fluoro-phenylalanine or 5[-]fluoro-DL-tryptophan,

[3] wherein the activity of the protein is enhanced by [replacing the native promoter which precedes the DNA on the chromosome of the bacterium with a *more potent promoter*].

At the ITC, an administrative law judge (ALJ) found the claim invalid for lack of an adequate written description of the “more potent promoter” limitation. The full Commission reviewed the ALJ’s decision and reversed, concluding that “lack of an adequate written description for the genus of ‘more potent promoter[s]’ recited in” the claim had not been proven.

In affirming the Commission’s decision upholding the validity of the claim, the Federal Circuit found it significant that the patent:

makes clear that its invention was ‘identifying the yddG gene encoding a membrane protein’ and discovering that the gene ‘conferred on a microorganism resistance to phenylalanine and several amino acid analogues’ when the gene was amplified or its expression enhanced, not the well-known techniques for performing the amplification or expression enhancement. . . . Here, the genus of more potent promoters was already well explored in the relevant art by the time of the ’655 patent’s invention. In these circumstances, the Commission permissibly

⁵⁸ According to the district court decision, these compounds were excluded to avoid a double patenting rejection, since they were apparently claimed in an earlier patent.

⁵⁹ *Ajinomoto Co. v. Int'l Trade Comm'n*, 932 F.3d 1342 (Fed. Cir. 2019).

⁶⁰ The actual structure of the claims is more complex, but for ease of presentation and explanation the substance of the claim is presented in this article.

found in the specification, read in light of the background knowledge in the art, a representative number of species for the genus of more potent promoters.”

This appears to be a clear example of a case in which the court takes into account the invention’s “point of novelty,” i.e., the heart of the invention. The invention’s point of novelty (which the court refers to simply as the “invention”) had to do with the identification of a novel gene and a practical use for that gene. It was not the discovery of a new, more potent promoter. If the point of novelty had been the discovery of a more potent promoter, I think it is likely the claim would have been found invalid for overbreadth, based on the broad recitation of a genus of “more potent promoters.” Such a decision would be consistent with the outcome in cases like *Amgen*, *Idenix*, and *Wyeth*, where the point of novelty resided exactly at the claimed chemical genus. In *Ajinomoto*, the court recognized that the genus of “potent promoters” did not lie at the heart of the invention, and found that the patent’s disclosure of four examples of “potent promoters,” along with a citation to a scientific article that disclosed “examples of potent promoters” and “methods for the evaluation of the strength of promoters” sufficient for the purposes of 112(a).

The *Ajinomoto* court explained that the accused infringer’s argument:

assumes too strict a legal standard Adequate written description does not require a perfect correspondence between the members of the genus and the asserted common structural feature; for a functionally defined genus like the one at issue here, we have spoken more modestly of a “correlation between structure and function.” *Ariad*, 598 F.3d at 1350.

The [cited cases] in which we have held genus claims to lack an adequate written description are inapposite. In *Boston Scientific*, the specification contained “no examples of macrocyclic lactone analogs of rapamycin” (the claimed genus) and essentially “no guidance on how to properly determine whether a compound is a macrocyclic lactone analog of rapamycin.” 647 F.3d at 1364. In *AbbVie*, there was “no evidence to show any described antibody to be structurally similar to, and thus representative of,” an antibody accused of coming within the claim, nor was there “evidence to show whether one of skill in the art could make predictable changes to the described antibodies to arrive at other types of antibodies such as” the accused antibody. 759 F.3d at 1301. And in *Regents of the University of California v. Eli Lilly & Co.*, the specification described “a process for obtaining human insulin-encoding cDNA” (such cDNA required by the claim at issue) but not any “sequence information indicating which nucleotides constitute human cDNA” or “further information in the patent pertaining to that cDNA’s relevant structural or physical characteristics.” 119 F.3d 1559, 1567 (Fed. Cir. 1997). Here, by contrast, the ’655 patent expressly provides four examples of “more potent promoters,” and the Commission supportably found that a skilled artisan could make relatively predictable changes to the native promoter to arrive at a more potent promoter.

In a 2020 decision, *Par Pharm. v. Hospira*, the Federal Circuit affirmed a district court decision finding the following claim not invalid and infringed by the defendant’s abbreviated new drug application (ANDA):⁶¹

A composition comprising:

- in the range of about 0.5 to 1.5 mg/mL of epinephrine and/or salts thereof,
 - in the range of about 6 to 8 mg/mL of a tonicity regulating agent,
 - in the range of about 2.8 to 3.8 mg/mL of a pH raising agent,
 - in the range of about 0.1 to 1.1 mg/mL of an antioxidant,
 - in the range of about 0.001 to 0.010 mL/mL of a pH lowering agent, and
 - in the range of about 0.01 to 0.4 mg/mL of a transition metal complexing agent,
- wherein the antioxidant comprises sodium bisulfite and/or sodium metabisulfite.

This claim is similar to the claims it issue in *Atlas Powder*, and if anything, it is more convincingly characterized as a chemical genus claim than the *Atlas Powder* claims. The *Par Pharm.* claim recites multiple chemical genres defined in broad, functional terms, e.g, a “tonicity regulating agent,” a “pH raising agent,” and a “pH lowering agent,” comparable to the “fuel” and “emulsifier” genres recited in the *Atlas Powder* claim. Significantly, there is no indication, in the either the district court or Federal Circuit decision, that the issue of compliance with 112(a) was even raised.

Similarly, in *Bracco Diagnostics v. Maia Pharm.*, another case decided by the Federal Circuit in 2020, the following claim was successfully enforced in a patent infringement action brought under the Hatch-Waxman Act.:⁶²

1. A stabilized, physiologically acceptable formulation of sincalide comprising:

- (a) an effective amount of sincalide,
- (b) at least one stabilizer,
- (c) a surfactant/solubilizer
- (d) a chelator,
- (e) a bulking agent/tonicity adjuster, and
- (f) a buffer.

Again, we see multiple functionally-defined chemical genres, e.g., a “stabilizer”, a “surfactant/solubilizer,” a “chelator,” a “bulking agent/tonicity adjuster,” and a “buffer.” And as

⁶¹ *Par Pharm., Inc. v. Hospira, Inc.*, No. 2020-1273, 2020 WL 6846347(Fed. Cir. 2020).

⁶² *Bracco Diagnostics Inc. v. Maia Pharm., Inc.*, No. 2020-1387, 2020 WL 7393233 (Fed. Cir. 2020).

was the case in *Par Pharma*,, neither the Federal Circuit decision nor the district court even mention 112(a).

In another unpublished 2020 decision, *Vectura Ltd. v. Glaxosmithkline*, the following claim was successfully enforced.⁶³

1. Composite active particles for use in a pharmaceutical composition for pulmonary administration, each composite active particle comprising a particle of active material and particulate additive material on the surface of that particle of active material, wherein the composite active particles have a mass median aerodynamic diameter of not more than 10 μm , and wherein the additive material promotes the dispersion of the composite active particles upon actuation of a delivery device.

Bayer v Baxalta, decided by the Federal Circuit in March of 2021, provides another good example.⁶⁴ The claim at issue recites:

An isolated polypeptide conjugate comprising a functional factor VIII polypeptide and one or more biocompatible polymers, wherein the functional factor VIII polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or an allelic variant thereof and has a B-domain, and further wherein the biocompatible polymer comprises polyalkylene oxide and is covalently attached to the functional factor VIII polypeptide at the B-domain.

The district court construed the claim term “at the B-domain” in claim 1 to mean “attachment at the B-domain such that the resulting conjugate retains *functional* factor VIII activity.” The claim recites a number of variables in the definition of the genus of claimed “polypeptide conjugates.” For one thing, the genus of polypeptides is relatively broad, since it contains any amino acid sequence that comprises a specifically recited sequence, or an allelic variant thereof, so long as it has a B-domain. Because of the “comprises” language, the claim encompasses polypeptides that include additional amino acid sequence added to either end of the recited sequence (or allelic variant thereof). The biocompatible polymer element of the polypeptide conjugate is also defined in broad terms, encompassing any polyalkylene oxide, so long as it is “biocompatible,” i.e., another functional limitation. The site of covalent attachment of the biocompatible polymer to the polypeptide can be anywhere in the B-domain of the protein, which comprises multiple amino acid locations at which conjugation could occur (including a cysteine and multiple lysines). This is a quite broad chemical genus claim, and the Federal Circuit explicitly held the claim not invalid for lack of enablement.

One could easily argue that the *Bayer* claim is actually broader claim than the *Atlas Powder* and *Angstadt* claims. It encompasses a huge number of functionally defined variants, and one can assume that it encompasses a number of species having different and/or superior functional

⁶³ *Vectura Ltd. v. Glaxosmithkline LLC*, 981 F.3d 1030 (Fed. Cir. 2020).

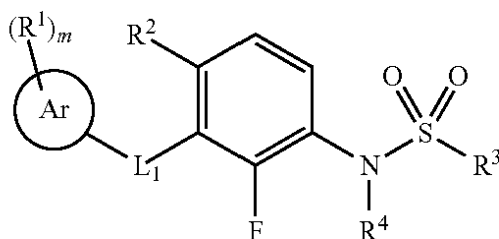
⁶⁴ *Bayer Healthcare LLC v. Baxalta Inc.*, 989 F.3d 964 (Fed. Cir. 2021).

characteristics compared to the disclosed species, albeit with no specific guidance as to how to identify those variants.

The patent owner, Baxalta (a subsidiary of Takeda) markets rurioctocog alfa pegol (Adynovate), a recombinant PEGylated factor VIII product which is the basis for the patent. The accused infringer, Bayer, markets its own PEGylated factor VIII product, Damoctocog alfa pegol (Jivi). Chemically, the two products are substantially different, including with regards to where on the protein's B domain it is pegylated. The precise location and nature of the pegylation will no doubt impact the pharmacological properties of a pegylated factor VIII. Indeed, a study published in 2020 concluded that "damoctocog alfa pegol [Jivi] had a superior [pharmacokinetic] PK profile versus rurioctocog alfa pegol (Adynovate). In other words, it appears that a patent Baxalta obtained based on Jivi could be used to impede market entry by a superior product for patients suffering from hemophilia.⁶⁵

In July of 2021, in the case of *Plexxikon v. Novartis Pharmaceuticals*, a jury found the following patent claims infringed and not invalid for failure to satisfy the enablement and written description requirements.⁶⁶

1. A compound of formula (Ia):



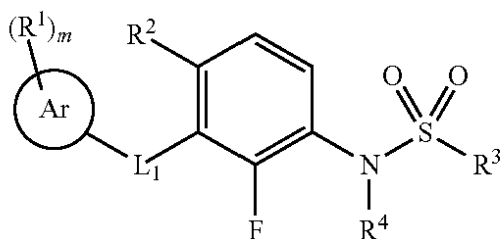
or a pharmaceutically acceptable salt thereof, wherein: L₁ is a bond or --N(H)C(O)--; each R₁ is optionally substituted lower alkyl or optionally substituted heteroaryl; R₂ is hydrogen or halogen; R₄ is hydrogen; R₃ is optionally substituted lower alkyl or optionally substituted aryl; m is 0, 1, 2, 3, 4, or 5; and Ar is a monocyclic heteroaryl containing 5 to 6 atoms wherein at least one atom is nitrogen.⁶⁷

1. A compound of formula (Ia):

⁶⁵ Solms, A., Shah, A., Berntorp, E. et al. *Direct comparison of two extended half-life PEGylated recombinant FVIII products: a randomized, crossover pharmacokinetic study in patients with severe hemophilia A*. *Ann Hematol* 99, 2689–2698 (2020), available at <https://link.springer.com/article/10.1007/s00277-020-04280-3>.

⁶⁶ Verdict form, *Plexxikon Inc. v. Novartis Pharmaceuticals Corp.*, Case No. 17-cv-04405-HSG, Document 565, July 22, 2021 (N.D. CA). See also Dorothy Atkins, *Jury Hits Novartis With \$178M Verdict In Drug Patent Fight*, *Law360* (July 22, 2021), available at https://www.law360.com/ip/articles/1405818/jury-hits-novartis-with-178m-verdict-in-drug-patent-fight-?nl_pk=25c34423-88c2-4609-9c2e-0e64d15ee6ea&utm_source=newsletter&utm_medium=email&utm_campaign=ip&read_more=1

⁶⁷ U.S. Patent 9,469,640 (claims 1 and 9 were found infringed and not invalid).



or a pharmaceutically acceptable salt thereof, wherein: L_1 is a bond or $--N(H)C(O)--$; each R_1 is optionally substituted lower alkyl or optionally substituted heteroaryl; R_2 is hydrogen or halogen; R_4 is hydrogen; R_3 is optionally substituted lower alkyl or optionally substituted aryl; m is 0, 1, 2, or 3; and Ar is a monocyclic heteroaryl containing 5 to 6 atoms wherein at least one atom is nitrogen.⁶⁸

This is a very interesting decision, since it provides a rare example of a structural chemical genus claim, i.e., a claim that defines a chemical genus in purely structural terms, being found infringed and not invalid after being challenged for an alleged failure to comply with the enablement and written description requirements. At the time I am writing this, the case is still pending before the district court, where Novartis is resisting Plexxikon's bid for enhanced damages based on the jury's finding of willful infringement. If the case reaches the Federal Circuit, it will be interesting to see how the claims fare on appeal, given *Death's* assertion that genus claims are "dead" in the Federal Circuit. If that were in fact the case, it is hard to see how these claims could be upheld, but perhaps time will tell.

One of the interesting aspects of this case is that is not the typical pharmaceutical patent infringement case, in that Novartis is not seeking to market a generic version of Plexxikon's drug, but rather a structurally different chemical compound that falls within the scope of Plexxikon's genus claims, which apparently encompass both products.⁶⁹ The product developed by Plexxikon (which is now a subsidiary of Daiichi-Sankyo) is vemurafenib, marketed under the tradename Zelboraf. Vemurafenib, which is an inhibitor of the B-Raf enzyme, was developed for the treatment of late-stage melanoma by Plexxikon in collaboration with Genentech. The accused product, dabrafenib, which is marketed by Novartis under the brand name Tafenlar, is an inhibitor of the same target and also used for the treatment of cancer

Finally, not only does the Federal Circuit continue to uphold chemical genus claims, the PTO continues to issue them. Example of recently issued broad genus claims can be found, for example in U.S. Patent Nos. 9,382,323; 9,365,655; and 8,999,324.

⁶⁸ U.S. Patent 9,844,539 (claims 1, 5 and 7 were found infringed and not invalid).

⁶⁹ For another recent example of such a case, see Nayanah Siva, *Gilead and ViiV Healthcare reach settlement over HIV drug*, 399 *The Lancet* 618 (Feb. 12, 2022), DOI:[https://doi.org/10.1016/S0140-6736\(22\)00269-0](https://doi.org/10.1016/S0140-6736(22)00269-0).

Concluding thoughts

This is not to say that all is well with the Federal Circuit's current approach to policing the scope of chemical genus claims. The genesis of *Death's* thesis that genus claims are "dead" no doubt lies in the understandable frustration of pharmaceutical innovators with the recent string of decisions striking down issued patent claims relating to important biopharmaceutical products, in some cases overturning jury verdicts awarding over \$1 billion in damages. But in my view, chemical genus claims are not dead, in this article I have provided numerous examples of relatively broad chemical genus claims that have recently withstood judicial scrutiny. I have also explained why, in my view, *Death* fails to substantiate its claim that there has been a dramatic shift in the court's application of 112(a) to chemical genus claims.

But I would agree that the Federal Circuit's use of 112(a) to police the scope of chemical genus claims leaves much to be desired. It is relatively easy to identify the problems. I think it is much more difficult to identify realistic solutions, and I think that the solutions would likely require a pretty significant rethinking of 112(a), and perhaps other fundamental aspects of U.S. patent law, such as claim interpretation, the doctrine of equivalents, the reverse doctrine of equivalents, and/or remedies, to name a few. These ideas will likely be the subject of future Holman Reports.