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# Is the Chemical Genus Claim Really "Dead" at the Federal Circuit?: Part I

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# Is the Chemical Genus Claim Really "Dead" at the Federal Circuit?: Part I

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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 Amgens'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 *raise important issues for pharmaceutical innovation, a number of which I address in this first installment ("Part I") of a two-part article. I begin by providing some excerpts from Judge Lourie's concurrence in the Federal Circuit's denial of en banc rehearing of* Amgen v. Sanofi*, in which he refutes the key arguments raised in* Death *and by Amgen. I then take a deep dive, exploring what in particular we mean when we refer to a patent claim as a "chemical genus claim," an important term that is subject to different interpretations. Those who use the term, including the authors of* Death*, often do so without explicitly defining it, which can result in some lack of clarity. In the remainder of this Part I, I reanalyze the judicial decisions upon which* Death *bases its claim, and explain why, in my view, the article does not actually substantiate its claim of a marked shift in the Federal Circuit's interpretation and application of 112(a).*

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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]

*Death* is cited extensively in a petition for certiorari recently filed with the Supreme Court, in which Amgen asks the Court to overturn the Federal Circuit's decision in *Amgen v. Sanofi*, wherein Amgen's claims reciting genuses of monoclonal antibodies were found invalid for lack of enablement.[3] Amgen has alleged that the claims are infringed by Sanofi's biologic therapeutic alirocumab (Praluent), a biosimilar version of Amgen's (Repatha). In its petition, Amgen largely echoes *Death*, arguing that the Federal Circuit has "rewritten the substantive enablement standard" to such an extent that it has become "impossible to satisfy for any invention of sufficiently broad application that it encompasses a nontrivial number of embodiments."[4] The Federal Circuit rejected this argument in the proceedings below, denying Amgen's petition for rehearing.[5] In a concurring opinion, Judge Lourie (the court's leading voice in the realm of pharmaceuticals and biotechnology) emphatically denies Amgen's assertion that the Federal Circuit has created a new test for enablement, and explains why those "bemoaning the so-called death of generic claims are …. off-base."[6]

I have a great deal of respect for the authors of *Death*, and think their article does raise important concerns. There have been a number of high-profile Federal Circuit decisions in recent years striking down patent claims directed towards functionally-defined chemical genuses for failure to comply with 35 U.S.C. 112(a)'s enablement and/or written description requirements. A good example of this can be seen in the recent *Juno v. Kite* decision, as reported on in the last installment of the Holman Report.[7] These cases are indeed troubling because they involve

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[1] Karshtedt, Dmitry and Lemley, Mark A. and Seymore, Sean B., The Death of the Genus Claim (August 5, 2020)("*Death")*. Harvard Journal of Law & Technology, Forthcoming, GWU Legal Studies Research Paper No. 2021-06, GWU Law School Public Law Research Paper No. 2021-06, Available at SSRN: https://ssrn.com/abstract=3668014 or http://dx.doi.org/10.2139/ssrn.3668014D.

[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] Petition for a Writ of Certiorari, Amgen Inc. v. Sanofi-Aventis LLC, Docket No. No. 21-757, November 18, 2021, 2021 WL 5506421 (U.S.).

[4] *Id.* (Citing *Death* at 4).

[5] Amgen Inc. v. Sanofi, Aventisub LLC, 850 F. App'x 794 (Fed. Cir. 2021).

[6] *Id.* at 795.

[7] Christopher M. Holman, *In* Juno v. Kite *the Federal Circuit Strikes Down Patent Directed Towards Pioneering Innovation in CAR T-Cell Therapy*, 40 BIOTECHNOLOGY LAW REPORT 372 (2021).

issued patents claiming important pharmaceutical products, and which presumably formed the basis for substantial investments in innovation. The repeated invalidation of these issued patents calls into question the value of some important pharmaceutical patents, and could cause investors to discount their worth in making investment decisions relating to the next generation of pharmaceutical breakthroughs.

On the other hand, I think that *Death* overstates the problem in a number of respects. For one thing, it is not literally the case that chemical genus claims are "dead," there are plenty of examples of recent decisions by the Federal Circuit and district courts upholding the validity of broad chemical genus claims in the face of Section 112(a) challenges. I also disagree with their assertion that Federal Circuit case law represents a dramatic shift in the law. Instead, I would argue that the purported change in the law can be better explained as simply reflecting the different nature of the claimed inventions at issue in the cases cited by *Death* in support of its thesis. My interpretation of the case law is more consistent with Judge Lourie's position, i.e., that "[w]hat is new today is not the law, but generic claims to biological materials that are not fully enabled."

*Death* raise important issues for pharmaceutical innovation, a number of which I will address in a two-part installment of the Holman Report.

In this first installment, Part I, I will begin by providing some excerpts from Judge Lourie's concurrence in the Federal Circuit's denial of en banc rehearing, which seeks to refute the key arguments raised in *Death*, and by Amgen's petition for certiorari. I will then take a deep dive, exploring what in particular we mean when we refer to a patent claim as a "chemical genus claim," an important term that is subject to different interpretations. Those who use the term, including the authors of *Death*, often do so without explicitly defining it, which can result in some lack of clarity. In the remainder of Part I of the article, I reanalyze the judicial decisions upon which *Death* bases its claim, and explain why, in my view, they do not actually substantiate a marked shift in the Federal Circuit's interpretation and application of 112(a).

## Judge Lourie's Concurrence in *Amgen v. Sanofi*

On June 21, 2021, a unanimous Federal Circuit denied Amgen's petition for en banc rehearing of *Amgen v. Sanofi*, a panel decision that found patent claims directed towards an isolated, functionally defined monoclonal antibody to be invalid for failure to comply with patent law's enablement requirement.[8] In their petition, Amgen argued that the panel's decision had "announced a new and heightened [enablement] standard for genus claims with functional limitations," conflicting with Supreme Court precedent and previous decisions of the Federal Circuit and its predecessor, the Court of Claims and Patent Appeals (CCPA). The company aargued that this purported "new" enablement standard "threatens to invalidate an entire category of [genus] claims," by rendering "it is nearly impossible to have a valid genus claim. According to Amgen, "[p]atents with functional limitations now lack enablement, no matter how routine it is to make any embodiment, simply because the genus is large."

[8] Amgen Inc. v. Sanofi, Aventisub LLC, 987 F.3d 1080 (Fed. Cir. 2021).

The Federal Circuit's *per curiam* denial of en banc rehearing was accompanied by a separate opinion, authored by the court's preeminent voice in the realm of pharmaceuticals and biotechnology, Judge Lourie, with whom Judges Prost and Hughes joined. Lourie emphatically denies Amgen's assertion that the Federal Circuit has created a new test for enablement, and explains why, in his opinion, those "bemoaning the so-called death of generic claims are …. off-base."[9]

Lourie posits that traditional, pre-biotechnology chemical genus claims were, as a general matter, enabled by actual or constructive (i.e., prophetic) examples, and that "[g]enus claims, to any type of invention, when properly supported, are alive and well. . . . What is new today is not the law, but generic claims to biological materials that are not fully enabled."

He goes on to explain that:

> in order to have invented a genus, one needs to have invented species that constitute the genus. Drawing a broad fence around subject matter, without filling in the holes, is not inventing the genus. It in fact discourages invention by others. If one has disclosed or enabled only a small number of invented species, then one has not invented a broad genus. Invention of a genus means to conceive and reduce to practice a reasonable number and distribution of species constituting the genus. Mere statement of a genus does not demonstrate that one has invented a generic concept, without the enablement of constituent species.
>
> …
>
> It seems to [Amgen and its amici] that the sky is falling. But enablement is part of our law, and for good reason. One should not gain exclusivity over claimed subject matter without disclosing how to make and use it. And if one considers that one has invented a group of compositions defined by a genus but does not know enough to fully enable that genus, one would suppress innovation if one were able to claim such a broad genus, not enhance it. Amgen, by asserting such broad, unsupported claims is doing just that, by trying to control what it has not invented. And, contrary to assertions by amici that broad, unenabled claims are necessary to protect investment, claims to materials properly supported by inventive work and disclosure can be protected. Amgen in fact has separate patent protection on the PCSK9 antibody that it has invented and additionally purports to cover by the generic claim we have invalidated. See U.S. Patent 8,030,457. Thus, the failure to obtain unsupported, unenabled claims has not deprived it of patent protection on the fruits of its investment.
>
> …
>
> Claims defining a composition of matter by function raise special problems because one may not know whether a species is within the scope of a generic claim until one has made it and one can ascertain whether it possesses the claimed function, hence that it has been enabled. In such cases, it is circular; enablement comes only with success, which depends upon enablement. It is not the law that

[9] Amgen Inc. v. Sanofi, Aventisub LLC, 850 F. App'x 794, 795 (Fed. Cir. 2021).

> one can put forth an idea, or a result or function, and claim all methods of achieving it; one cannot claim everything that works.

## What do we mean by chemical genus claim?

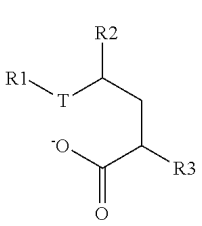
In order to meaningfully discuss patentability of chemical "genus claims," it is important to define what is meant by that term. *Death* does not provide a single, explicit definition, but at various points offers multiple (perhaps not entirely consistent) implicit definitions. The article's Abstract begins by referring to a genus claim in the "chemical, biotechnology, and pharmaceutical industries" as "a patent that covers not just one specific chemical but a group of related chemicals." Later, *Death* explains that:

> Genus claims . . . use functional language or generic formulas to cover embodiments of the invention (species) that share a common attribute or property. For example, consider a claim to a plastic-coated steel screw. Given that there are many different plastics (e.g., nylon, polystyrene, polypropylene, polyvinyl chloride), the genus claim encompasses many species.

*Death*'s conclusion that recitation of a term like "plastic" renders a patent claim a "genus claim" suggests that the authors have adopted an expansive definition of the term. But surely they cannot be suggesting that patent claims employing generic terms such as "plastic" have literally been rendered "dead" under the Federal Circuit's purported "new and heightened" law of enablement.

Indeed, other sections of *Death* suggest a narrower definition for the term, more consistent with what I think most patent practitioners would consider a chemical genus claim. For example, at one point the article describes a claim reciting "a structural group of chemicals with an invariant backbone and variance of the groups attached to that core" as "the typical kind of chemical genus claim that patent attorneys are taught to draft." *Death* goes on to observe that "[a] common claiming technique is to draw a core generic chemical structure with an array of variables appended to it—which can each represent numerous chemical moieties."

This narrower definition is what I think of when I encounter the term "chemical genus claim," and this is the sort of chemical genus claim described in books on claim drafting, as noted in *Death*. A good example of this sort of claim appears in recently issued U.S. Patent No. 10,941,109 (Claim 1):

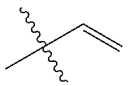
> A compound of Formula (1):
>
> 
> 
> (1)
>
> or an N-oxide thereof, or a pharmaceutically acceptable salt of the compound or N-oxide, wherein:

T is selected from the group consisting of —C(═O)— or —C(═NH)—,

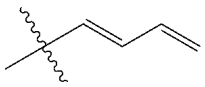
R1 and R2 are independently selected from the group consisting of $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_{14}$ cycloalkyl, aryl, heteroaryl, aryl($C_1$-$C_6$ alkyl), —CN, amino, ($C_1$-$C_6$)alkylamino, dialkyl($C_1$-$C_6$)amino, haloalkyl($C_1$-$C_6$), ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)haloalkoxy, heteroaryl($C_1$-$C_6$ alkyl), ($C_4$-$C_{15}$)heterocyclic, ($C_4$-$C_{15}$)heterocyclic($C_1$-$C_6$ alkyl), $C_3$-$C_7$ cycloalkoxy, $C_6$-$C_{10}$-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 —$C_1$-$C_6$ alkyl, halo, CN, $CF_3$, —COOH, —OH, —$C_1$-$C_6$ alkoxy, —$NH_2$, —($C_1$-$C_6$ alkyl)$NH_2$, —($C_1$-$C_6$ alkyl)NH($C_1$-$C_6$ alkyl), —($C_1$-$C_6$ alkyl)N($C_1$-$C_6$ alkyl)$_2$, —NH($C_1$-$C_6$ alkyl), —N($C_1$-$C_6$ alkyl)$_2$, —$CONH_2$,—NH(CO)($C_1$-$C_6$ alkyl), —N($C_1$-$C_6$ alkyl)CO($C_1$-$C_6$ alkyl), —$SO_2$—($C_1$-$C_6$ alkyl), and —(SO)$NH_2$,

R3 is selected from the group consisting of hydrogen, deuterium, $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_{14}$ cycloalkyl, aryl, heteroaryl, aryl($C_1$-$C_6$ alkyl), —CN, amino, ($C_1$-$C_6$)alkylamino, dialkyl($C_1$-$C_6$)amino, haloalkyl($C_1$-$C_6$), (C-$C_6$)alkoxy, ($C_1$-$C_6$)haloalkoxy, heteroaryl($C_1$-$C_6$ alkyl), ($C_4$-$C_{15}$)heterocyclic, ($C_4$-$C_{15}$)heterocyclic($C_1$-$C_6$ alkyl), $C_3$-$C_7$ cycloalkoxy, $C_6$-$C_{10}$-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 $C_1$-$C_6$ alkyl, halo, CN, $CF_3$, —COOH, —OH, $C_1$-$C_6$ alkoxy, —$NH_2$, —($C_1$-$C_6$ alkyl)$NH_2$, —($C_1$-$C_6$ alkyl)NH($C_1$-$C_6$ alkyl), —($C_1$-$C_6$ alkyl)N($C_1$-$C_6$ alkyl)$_2$, —NH($C_1$-$C_6$ alkyl), —N($C_1$-$C_6$ alkyl)$_2$, —$CONH_2$,—NH(CO)($C_1$-$C_6$ alkyl), —N($C_1$-$C_6$ alkyl)CO($C_1$-$C_6$ alkyl), —$SO_2$-($C_1$-$C_6$ alkyl), and —(SO)$NH_2$,

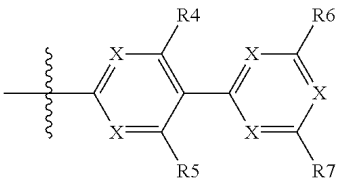
(a-1)



(a-2)



(a-3)




X is either N or CR8, and

R4, R5, R6, R7, and R8 are independently selected from the group consisting of hydrogen, deuterium, $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_{14}$ cycloalkyl,

> aryl, heteroaryl, aryl($C_1$-$C_6$ alkyl), —CN, amino, ($C_1$-$C_6$)alkylamino, dialkyl($C_1$-$C_6$)amino, haloalkyl($C_1$-$C_6$), ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)haloalkoxy, heteroaryl($C_1$-$C_6$ alkyl), ($C_4$-$C_{15}$)heterocyclic, ($C_4$-$C_{15}$)heterocyclic($C_1$-$C_6$ alkyl), $C_3$-$C_7$ cycloalkoxy, $C_6$-$C_{10}$-aryloxy, 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 $C_1$-$C_6$ alkyl, halo, CN, $CF_3$, —COOH, —OH, $C_1$-$C_6$ alkoxy, —$NH_2$, —($C_1$-$C_6$ alkyl)$NH_2$, —($C_1$-$C_6$ alkyl)NH($C_1$-$C_6$ alkyl), —($C_1$-$C_6$ alkyl)N($C_1$-$C_6$ alkyl)$_2$, —NH($C_1$-$C_6$ alkyl), —N($C_1$-$C_6$ alkyl)$_2$, —$CONH_2$,—NH(CO)($C_1$-$C_6$ alkyl), —N($C_1$-$C_6$ alkyl)CO($C_1$-$C_6$ alkyl), —$SO_2$-($C_1$-$C_6$ alkyl), and —(SO)$NH_2$.

I think it bears noting that none of the cases discussed in *Death* as illustrative of the purported shift in the law actually uses this canonical format, and so clearly the authors of the article are using the term genus claim in broader sense.

For the sake of clarity, in this section of my article I identify and define two distinct categories of chemical genus claims, which I refer to as "structural genus claims" and "functional genus claims." These author-defined terms are used throughout the present article (Parts I and II). The authors of *Death* at times appear to refer to "structural genus claims" as "traditional genus claims." But first, let us be reminded that virtually all patent claims are genus claims if that term is broadly defined to include any patent claim encompassing multiple "species."

## Virtually all patent claims encompass multiple species

One might be tempted to define the term "genus claim" to include any patent claim reciting multiple embodiments, i.e., multiple species. The problem with this definition is that it encompasses virtually every patent claim, because, by their nature, patent claims generally cover not only multiple embodiments, but an infinite number of distinct embodiments. This conclusion, which flows inherently from the nature of patent claims, was explained in a 2008 law review article by Professor Jeffrey Lestin.[10] *Death* explicitly cites Lefstin's article, noting that "Lefstin argues that most claims are genus claims." In fact, Lefstin goes further than that, pointing out that:

> ***All patent claims are of infinite scope***.. . . It is an essential characteristic of all patent claims that they cover a set of entities rather than a single entity. Otherwise claims could not be infringed, save perhaps by the use of the one physical entity that the inventor constructed. Yet, the set of entities covered by a claim, despite being bounded by the language of the claim and the various doctrines of patent law, ***must be infinite in scope***. This conclusion follows not from legal doctrine, but from the ontological nature of patent claims themselves. . . . In reality, then ***there is no such thing as a "species" claim***, for claims are never restricted to a

[10] Jeffrey A. Lefstin, The Formal Structure of Patent Law and the Limits of Enablement, 23 BERKELEY TECH. L.J. 1141 (2008).

> single physical entity. Insofar as both genus and species are abstractions, the difference between the two is ***less in kind and more in degree***.[11]

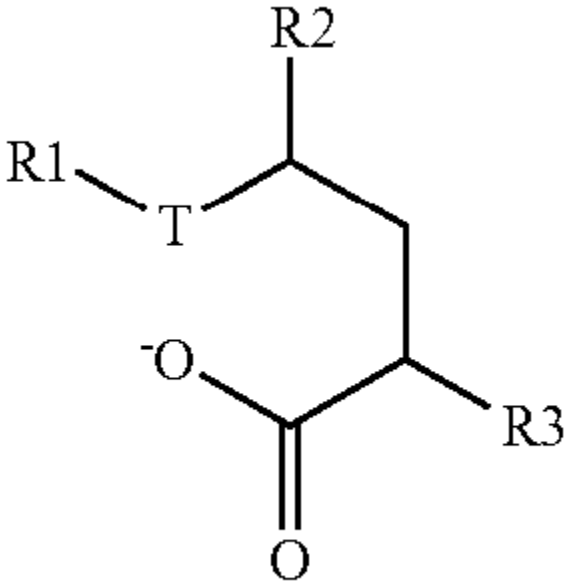
In the chemical arts, even claims that on their face might appear to be limited to a single chemical compound have been found to encompass multiple distinct chemical entities. For example, in *Pfizer Inc. v. Ranbaxy Lab'ys Ltd.*, the claim at issue recited a specific chemical compound defined in terms of structure.[12] The compound was an enantiomer, and the court interpreted the claim as encompassing the various stereoisomers, as well as a racemic mixture of the stereoisomers. Stereoisomers are clearly different chemical compounds, and in some cases can have vastly different pharmacological properties.[13] Similarly, it is generally assumed that a patent claim reciting a protein defined by a specific amino acid sequence encompasses proteins in which some of those amino acids have been post-translationally modified, for example, by glyosylation.[14]

## Structural genus claims

For the purposes of this article, I will use the term "structural genus claim" to refer to a ***product*** claim that recites a genus of molecules defined in ***solely*** structural terms, with no explicit or implicit functional limitations. Here is an example of such a claim, taken from a patent that issued in 2021.

> 1. A compound of Formula (1):

[11] *Id.* (emphasis added).
[12] Pfizer Inc. v. Ranbaxy Lab'ys Ltd., 405 F. Supp. 2d 495 (D. Del. 2005), aff'd in relevant part, rev'd in part and remanded, 457 F.3d 1284 (Fed. Cir. 2006).
[13] Christopher M. Holman, *In Defense of Secondary Pharmaceutical Patents: A Response to the UN's Guidelines for Pharmaceutical Patent Examination*, 50 Indiana Law Review 759 (2017).
[14] For an example of this, see Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1334 (Fed. Cir. 2003).




or a pharmaceutically acceptable salt of the compound, wherein:

T is --C(=O)--;

R1 is a phenyl group substituted with one substituent selected from the group consisting of halo, CN, --COOH, --$NH_2$, --$NH(CH_3)$, --$N(CH_3)_2$, and --$CONH_2$, and optionally further substituted with one or more substituents selected from the group consisting of –$C_1$-$C_6$ alkyl, halo, --OH, alkoxy, --$NH_2$, --COOH, --$NH(CH_3)$, --$N(CH_3)_2$, and --$CONH_2$;

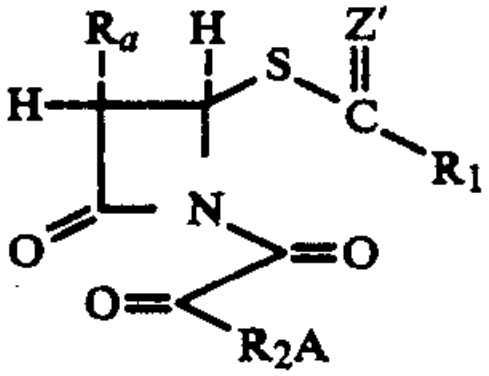
R2 is a phenyl, optionally substituted with one or more substituents selected from the group consisting of –$C_1$-$C_2$ alkyl, halo, CN, --COOH, --OH, alkoxy, --$NH_2$, --COOH, --$NH(CH_3)$, --$N(CH_3)_2$, and --$CONH_2$; and

R3 is hydrogen.[15]

Claims of this sort have been part of chemical patent practice for a long time, here's another example appearing in a patent issued in 1990:

1. A compound of the formula

[15] U.S. Patent 10,941,109, Claim 1.




wherein Ra is (1R)-1-hydroxyethyl;

R2 A together with the carbonyl to which it is attached is a protected carboxyl group;

R1 is -R, in which R is C1-7 alkyl, phenyl, phenylalkyl having 7-13 carbon atoms, or heterocyclyl or heterocyclylalkyl having up to 10 carbon atoms and up to 4 ring hetero atoms selected from nitrogen, oxygen, and sulphur, with the proviso that two oxygen atoms or two sulfur atoms or one oxygen atom and one sulfur atom are not adjacent to each other, each R being unsubstituted or substituted by amino, mono C1-7 alkylamino, di-C1-7 alkylamino, hydroxy, C1-7 alkoxy, mercapto, C1-7 alkylthio, chloro, bromo, fluoro, or by carboxyl; and

Z' is oxygen, sulfur, methoxycarbonylmethylidene or 1-menthyloxycarbonylmethylidene; and

the functional groups in the radicals designated Ra and R1 are either in protected or unprotected form.[16]

Claims of this canonical format figure prominently in some books purporting to teach the art of claim drafting, and it is these books that *Death* points to as the primary evidence that such claims are very important in the pharmaceutical arts. Indeed, the U.S. Patent and Trademark Office (PTO) has issued many claims of this type over the years, as exemplified by the two claims presented above.

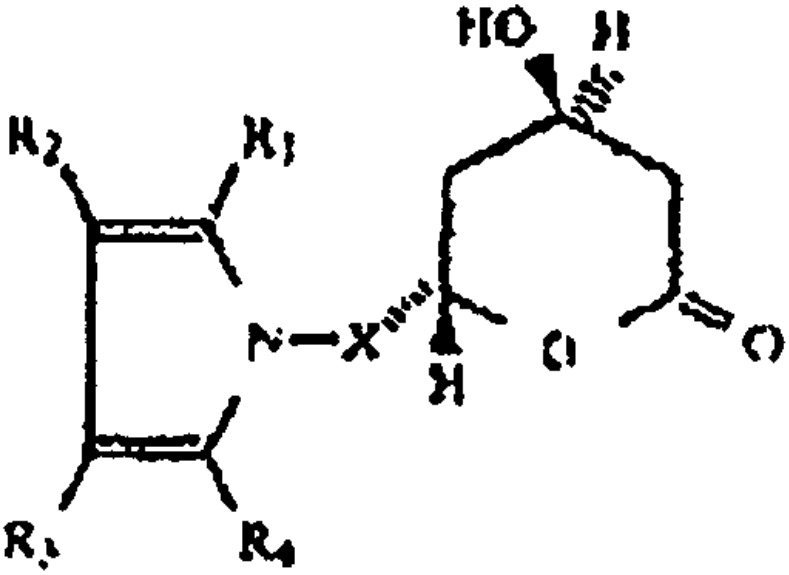
Although *Death* points to this canonical claiming format as an important and traditional way of claiming inventions in the chemical arts, it is perhaps notable that *Death*, as far as I can tell, does not identify a single case involving such a patent claim, or even, for that matter, a patent that includes such a structural genus claim.[17]

[16] U.S. Patent 4,952,690, Claim 1.

[17] At one point *Death* seems to suggest that such a claim was at issue in *Idenix v. Gilead Sciences*, a case which is addressed later in this article. As explained below, the claim is actually functional genus claim. The core generic structure that the authors of *Death* reproduce in their article actually appears in the *Idenix* patent's written description, not the claims themselves.

I am myself not aware of many cases in which a structural genus claim has been the subject of a reported judicial decision. One example that I know of is *Pfizer v. Ranbaxy*, wherein a district court found claim 1 of U.S. Patent No. 4,681,893 to be infringed and not invalid, and this aspect of the court's decision was upheld by the Federal Circuit on appeal.[18]

1. A compound of structural formula I

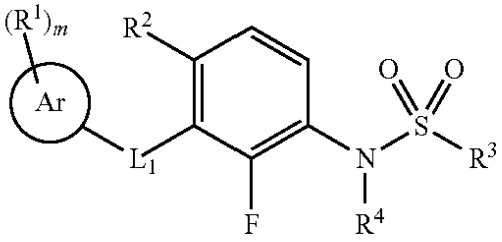


wherein X is —CH2—, —CH2CH2 —, —CH2CH2CH2—, or —CH2CH(CH3)—; R1 is 1-naphthyl; 2-naphthyl; cyclohexyl; norbornenyl; phenyl; phenyl substituted with fluorine, chlorine, bromine, hydroxyl, trifluoromethyl, alkyl of from one to four carbon atoms, alkoxy of from one to four carbon atoms, or alkanoyloxy of from two to eight carbon atoms; either of R2 or R3 is —CONR5R6 where R5 and R6 are independently hydrogen; alkyl of from one to six carbon atoms; phenyl; phenyl substituted with fluorine, chlorine, bromine, cyano, trifluoromethyl, or carboalkoxy of from three to eight carbon atoms; and the other of R2 or R3 is hydrogen; alkyl of from one to six carbon atoms; cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; phenyl; or phenyl substituted with fluorine, chlorine, bromine, hydroxyl, trifluoromethyl, alkyl of from one to four carbon atoms, alkoxy of from one to four carbon atoms, or alkanoyloxy of from two to eight carbon atoms; R4 is alkyl of from one to six carbon atoms; cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; or trifluoromethyl; or a hydroxy acid or pharmaceutically acceptable salts thereof, corresponding to the opened lactone ring of the compounds of structural formula I above./

[18] Pfizer Inc. v. Ranbaxy Lab'ys Ltd., 405 F. Supp. 2d 495, 510 (D. Del. 2005), aff'd in part, rev'd in part and remanded, 457 F.3d 1284 (Fed. Cir. 2006).

In July of 2021, in the case of *Plexxikon v. Novartis*, a jury in in the Northern District of California found multiple structural chemical genus patent claims of the canonical type infringed and not invalid under Section 112(a).[19] It remains to be seen whether that decision will hold up on appeal. Here is a representative example of one of these claims:

1. A compound of formula (Ia):




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, 3, 4, or 5; and Ar is a monocyclic heteroaryl containing 5 to 6 atoms wherein at least one atom is nitrogen.[20]

The PTO has also issued patents with claims reciting structural genuses of biomolecules. With biomolecule genuses, the core structure is typically defined in terms of amino acid or nucleic acid sequence, set forth by means of SEQ ID NO. For example, here are three claims reciting structural genuses of isolated polypeptides, isolated monoclonal antibodies, and isolated nucleic acids, respectively.

1. An isolated polypeptide comprising an amino acid sequence which is at least 55% identical to the amino acid sequence of SEQ ID NO:2 with or without the signal peptide or an amino acid sequence encoded by the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number 98546.[21]

1. An isolated monoclonal antibody (mAb) or immunoreactive fragment thereof wherein:

[19] 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

[20] U.S. Patents No. 9,469,640 (claims 1 and 9 were found infringed and not invalid). Claims 1, 5 and 7 of U.S. Patents No. 9,844,539 were also found to be infringed and not invalid.

[21] U.S. Patent 6,410,232, Claim 1.

(a) the heavy chain comprises the CDR1, CDR2 and CDR3 regions of the variable region of MAB4A2 (SEQ ID NO:2); or

(b) comprises the CDR1, CDR2 and CDR3 regions of the heavy chain variable region of MAB19B10 (SEQ ID NO:6); or

(c) comprises the CDR1, CDR2 and CDR3 regions of the heavy chain variable region of MAB313 (SEQ ID NO:13); or

(d) comprises the CDR1, CDR2 and CDR3 regions of the heavy chain variable region of MAB338 (SEQ ID NO:20); or

(e) comprises the CDR1, CDR2 and CDR3 regions of the heavy chain variable region of MAB345 (SEQ ID NO:22).[22]

1. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:

(a) a polynucleotide that encodes a polypeptide of SEQ ID NO: 2;

(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO: 1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NOS: 1; and

(d) a polynucleotide complementary to a polynucleotide of (a) through (c).[23]

## Functional genus claims

For the purposes of this article, a "functional genus claim" is a patent claim that defines a genus of chemical compounds, in whole or in part, in functional terms. Notably, all of the functional genus claims discussed in this article (as well as *Death*) include a structural limitation, at least implicitly. For example, the patent claim at issue in *Amgen v. Sanofi* recites an "isolated monoclonal antibody," which implicitly limits the claimed genus to molecules having a chemical structure that can be characterized as an "antibody," which would exclude the vast majority of chemical structures.

Recall that the term "structural genus claim," as I have defined it for purposes of this article, explicitly excludes method claims, i.e., it is limited to product claims. The reason for this is that, as a general matter, courts faced with a method claim will limit the scope of a structurally defined genus of chemical compounds to molecules that are operable with respect to the claimed method. Indeed, this is the case with all of the method claims discussed in this article, including the method claims discussed in *Death*.

[22] U.S. Patent 9,017,668, Claim 1.
[23] U.S. Patent 6,777,590, Claim 1.

For example, *Idenix v. Gilead* is one of the cases that *Death* particularly focuses on.[24] The claim at issue recites:

> 1. A method for the treatment of a hepatitis C virus infection, comprising administering an effective amount of a purine or pyrimidine β-D-2'-methyl-ribofuranosyl nucleoside or a phosphate thereof, or a pharmaceutically acceptable salt or ester thereof.

Even though the claim recites a nucleoside, i.e., purine or pyrimidine, in structural terms, the court construed the preamble, "[a] method for the treatment of a hepatitis C virus infection," as a narrowing functional limitation, and held that the claim "encompasses any β-D nucleoside meeting both the structural limitations (including a methyl group at 2'-up) and the functional limitations (efficacy in treating HCV)."

## Genus and species as relative terms

Although it often makes little sense to categorize a patent claim in isolation as a "genus" or "species" claim, the terms can be useful when used in a relative sense, in the same way one might characterize a patent claim as "broad" relative to a more "narrow" claim. Professor Lefstin made this point in his article, observing that the difference between genus and species claims is "less in kind and more in degree."[25]

The PTO uses the terms in a similar, relative sense. For example, regulations promulgated by the PTO relating to restriction practice provide:

> In the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will be restricted if no claim to the genus is found to be allowable. . . . .[26]

In many cases, the "species" referred to in the PTO regulation will itself encompass a genus of related chemical compounds. Such use of genus and species as relative terms makes sense, and I will at times do so myself in this article.

## *Death* does not substantiate its claim that the law has changed dramatically

*Death*'s core conclusion is that "the law has changed dramatically in the last thirty years, to the point where it is nearly impossible to have a valid genus claim." In my view, however, the authors fail to substantiate any substantial change in the law, let alone a dramatic one. I would also disagree with their assertion that today it is "nearly impossible to have a valid genus claim." In Part II of this article, I willprovide many examples of relatively broad chemical genus claims that have been upheld in recent years, all the way up through 2021. In this section of the article,

[24] Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149 (Fed. Cir. 2019).
[25] Supra, Lefstin article.
[26] 37 C.F.R. 1.146 Election of species.

I examine the evidence that *Death* relies on to support its assertion that the law has changed dramatically, and find that the article actually provides little if any support for it. My interpretation of the caselaw is more consistent with Judge Lourie's concurring opinion in the *Amgen* denial of en banc rehearing.

I do not mean to suggest that the authors of *Death* have not identified an important issue, which is that in recent years seen a string of functional genus claims relating to high-value pharmaceuticals struck down under Section 112(a) for overbreadth, particularly in cases like *Idenix*, *Amgen*, and *Juno*. All of these cases involved issued patents, suggesting a disconnect between the standard for compliance with 112(a) being applied at the PTO and at the Federal Circuit. One can readily imagine that a patent prosecutor who has been successfully securing allowance of claims of this sort from the PTO will perceive this as a shift in the law. The same can be said for companies and investors who have been obtaining relatively broad patent claims in recent years, and attributed substantial value to them, only to have them invalidated when they try to enforce them.

The apparent disparity between the way 112(a) is being applied by the PTO is probably, to large extent, a temporal anomaly. The pharmaceutical functional genus claims being struck down by the Federal Circuit were typically issued years prior to their ultimate invalidation. In an article-in-progress, my co-author Sean Tu and I present data showing that the PTO appears to have substantially tightened the 112(a) standard for monoclonal antibody claims.

In the past, the PTO tended to issue relatively broad, functionally defined genus claims, of the type invalidated in *Amgen* and *AbbVie*. Over the years they have increasingly pushed back against broad claims of that type, such that in recent years the office will generally only allow much narrower, structurally limited monoclonal antibody claims. So the invalidation of the previously issud claims by the Federal Circuit does not necessarily mean that the PTO and Federal Circuit are applying a different standard today. It could well be that today the PTO would not allow claims of the sort invalidated in *Amgen* and *AbbVie*. Note that in his concurrence, Judge Lourie points out that Amgen has another patent (U.S. Patent 8,030,457) covering its body, and finds that the company's "failure to obtain unsupported, unenabled claims has not deprived it of patent protection on the fruits of its investment."

Claim 1 of the '457 patent recites:

> 1. An isolated neutralizing antigen binding protein that binds to a PCSK9 protein comprising the amino acid sequence of SEQ ID NO: 1, wherein the neutralizing antigen binding protein comprises: a heavy chain polypeptide comprising the following complementarity determining regions (CDRs): a heavy chain CDR1 that is a CDR1 in SEQ ID NO: 49; a heavy chain CDR2 that is a CDR2 in SEQ ID NO: 49; a heavy chain CDR3 that is a CDR3 in SEQ ID NO: 49 and a light chain polypeptide comprising the following CDRs: a light chain CDR1 that is a CDR1 in SEQ ID NO: 23; a light chain CDR2 that a CDR2 in SEQ ID NO: 23; and a light chain CDR3 that is a CDR3 in SEQ ID NO: 23.

This patent claim, limited to antibodies having define CDR sequences, is more typical of the sorts of patent claims the PTO will allow in recent years. The patents invalidated in *Amgen*, U.S. Patents 8,829,165 and 8,859,741 were issued in 2014.

The purported shift in the law with respect to genus claims is reminiscent of what happened with so-called gene patents, with the PTO issuing thousands of them over the course of many years, companies making investment decisions based on them, and then the Supreme Court wiping out those patents with the *Myriad* decision. But there is a crucial difference between what has been happening with respect to broad, functionally defined chemical genus claims in recent years and what happened to gene patents. In the case of gene patents, we have a Supreme Court decision (*Myriad*) that clearly did dramatically change the law, and one can point to specific evidence of that change, in the Supreme Court's decision itself, and in the clear change in how the patent eligibility requirement was applied at the PTO and in the lower courts post-*Myriad*.

This was just part of a more sweeping change to the law of patent eligibility brought about by the Supreme Court's other patent eligibility decisions that came out around the time of *Myriad*, *Mayo* and *Myriad*. This was a literal, and dramatic change in the law, documented not only by the language of the Supreme Court decisions, but by a clear and unambiguous change in the way in which the patent eligibility requirement was applied to many inventions, including in the area of biotechnology. This change in the law can be documented by pointing to judicial decisions upholding patents issued prior to the change in the law of patent eligibility, and then comparing those decisions to a host of judicial decisions issued after the change in the law, wherein patents were struck down that are comparable to patents that were upheld in the prior decisions.

This stands in marked contrast to what I see when I look at the cases that *Death* points to as evidence of the purported dramatic shift in the law. In this section the article, I look carefully at the cases *Death* relies on for evidence of the shift, and explain why, in my view, the decisions are reconcilable and are consistent with Judge Lourie's insistence that it is not the law that has changed, but rather the nature of the patent claims that are being brought before the court.

I think that one explanation for my divergence of opinion with the authors of *Death* is that, in my view, they attempted to document a shift in the law by selectively focusing on some of the language used by the court in a number of judicial decisions that they looked at. In contrast, I focus more on the detail of what is going on, i.e., what exactly does the claimed genus encompass, and what is the context of the patent claims, both in terms of the prior art, the disclosure of the patent, and the likely impact of the claim on future innovation. One might say that I am more interested in what the courts actually do, as opposed to the language they use in explaining their actions.

If there had been a substantial shift in this area of the law, there should be judicial decisions, and particularly Federal Circuit decisions, exemplifying that shift. While *Death* does provide a number of examples of functional chemical genus claims that the court has found invalid under 112(a) for overbreadth, it provides little if any in the way of examples of decisions that upheld the validity of comparable claims prior to the purported change in the law. In this section of the article, I go through the evidence for the shift provided in *Death*, and explain why I do not think

it actually substantiates the assertion. The standards for compliance with the written description and enablement requirements, particularly in the context of chemical genus claims, is flexible, and allows the courts a great deal of discretion. As observed by Judge Lourie, 112(a) determinations are highly fact specific and made on a case-by-case basis, so of course it is impossible to entirely reconcile all of the cases that have been decided in recent decades. But overall, I tend to agree with Judge Lourie that the standard, which has always been broadly stated and open to interpretation, has not demonstrably changed in recent years.

### Supreme Court precedent

*Death* discusses two relatively old Supreme Court decisions involving genus claims, the *Incandescent Lamp Patent* case[27] and *Corona Cord Tire*,[28] and acknowledges that in both cases the Court found that genus claims at issue to be invalid for overbreadth. *Incandescent Lamp* is discussed in more detail in Part II of this article.

The relevant claims in *Corona Cord* recite a process of treating rubber by combining the rubber with '"a disubstituted guanidine." The court found that the genus of "disubstituted guanidine" encompasses not only the specific disubstituted guanidine disclosed in the patent, which functions as an "accelerator," but also between 50 and 100 other genus members, of which "quite a number … are not accelerators at all." Citing to *Incandescent Lamp*, the Court held:

> [the inventor] could certainly not claim the entire group of such compounds. He makes no showing that there is any general quality common to disubstituted guanidines which made them ***all effective as accelerators***. Claims for their exclusive use cannot therefore be sustained.[29]

Nothing in *Corona Cord* or *Incandescent Lamp* appears inconsistent with the Federal Circuit's recent decisions in cases like *Wyeth*, *Idenix* and *Amgen*, of which *Death* complains. Notably, *Death* does not identify a single instance in which the Supreme Court has upheld the validity of a chemical genus claim.

### Pre-Shift Federal Circuit precedent

As far as I can tell, *Death* only points to a single Federal Circuit decision as illustrative of the purportedly more permissive 112(a) standard that prevailed prior to the alleged doctrinal shift. That decision is *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, a case decided in 1984, shortly after the establishment of the Federal Circuit in 1982.[30] The case involved the following independent claim, directed towards a blasting agent, i.e., an explosive:

> 1. An emulsion blasting agent consisting essentially of:
>
> an aqueous solution of ammonium nitrate forming a discontinuous emulsion phase;
>
> a carbonaceous fuel forming a continuous emulsion phase;

[27] Consol. Elec. Light Co v. McKeesport Light Co, 159 U.S. 465 (1895).
[28] Corona Cord Tire Co. v. Dovan Chem. Corp., 276 U.S. 358 (1928).
[29] *Id.* (emphasis added)
[30] Atlas Powder Co. v. E.I. du Pont De Nemours & Co., 750 F.2d 1569 (Fed. Cir. 1984).

> an occluded gas dispersed within said emulsion and comprising at least 4% by volume, thereof at 70°F. and atmospheric pressure; and
>
> a water-in-oil type emulsifying agent;
>
> said carbonaceous fuel having a consistency such that said occluded gas is held in said emulsion at a temperature of 70°F.[31]

In my experience, this is not the sort of claim most people would think of as an example of a "chemical genus claim." The *Atlas Powder* court never refers to this as a genus claim. *Atlas Powder* is, of course, widely cited for the proposition that the existence of inoperative species within the scope of the claim does not necessarily render the claim invalid. But prior to reading *Death*, I do not recall ever seeing this claim referred to as an example of a chemical genus claim. It is clearly not a structural genus claim (what *Death* refers to as a "traditional" chemical genus claim), but under the broad definition I am using for purposes of this article, it can be characterized as a functional genus claim. Somewhat along the lines of the hypothetical claim reciting the term "plastic" that *Death* pointed to as an example of a genus claim. Assuming that *Atlas Powder* is a chemical genus claim, the two relevant chemical genuses would have to be the functionally defined recitations of "a carbonaceous fuel" and "a water-in-oil type emulsifying agent."

Both of these chemical genuses were, of course, well known in the prior art. They were also tangential to the inventive aspect of the claimed blasting agents, i.e., the claimed invention's point of novelty, which resided in the use of "occluded gas," i.e., entrapped air, as the sensitizer, rather than the high explosives or chemicals used as sensitizers in prior art explosives. In particular, prior to the invention the patentee manufactured a gelled slurry blasting agent that used nitric acid as a "sensitizer." But there were problems with this product. For one thing, nitric acid is highly caustic to skin and clothing and tended to separate out of the product, even in the presence of a gelling agent, thereby reducing the product's stability and shelf life. The product is also "hypergolic", i.e., it ignited wood, coal and various chemicals upon contact, which was suspected of causing the blasting agent to detonate prematurely.

The patented invention addresses the problems with the original product by providing a product that is sensitized with occluded, i.e., entrapped, air rather than high explosives or chemicals. Significantly, the inventions point of novelty lies in the use of entrapped air as the sensitizer, which is tangential to the nature of the carbonaceous fuel and the emulsifying agent.

In *Atlas Powder*, the alleged infringer argued that the patent listed "numerous salts, fuels, and emulsifiers that could form thousands of emulsions but there is no commensurate teaching as to which combination would work." This argument does not go to the invention's point of novelty, i.e., the occluded gas, but rather focuses on the recited salt (ammonium nitrate), fuel, and emulsifying agent, and more particularly on an emulsion containing these three constituents. A variety of emulsions made from ammonium nitrate, carbonaceous fuel, and an emulsifying agent were well known in the prior art, and, as the court pointed out, one of skill in the art knew that

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[31] *Id.* at 1572.

"Bancroft's Rule," a "basic principle of emulsion chemistry," could be used to determine the proper emulsifier for any given combination of salt and fuel

In affirming the district court's decision rejecting DuPont's effort to invalidate the claim under 112(a), the Federal Circuit found:

> [although] Du Pont asserts that Atlas was able to produce suitable emulsions with only two emulsifiers, Du Pont did not prove that the other disclosed emulsifiers were inoperable. The district court credited testimony by Atlas' expert, Dr. Fowkes, to the effect that he had successfully formed a number of detonable emulsions using a variety of emulsifiers specified in the '978 patent. Further, the district court found that one skilled in the art would know which emulsifiers would work in a given system. Indeed, the district court found that Du Pont's own researchers had little difficulty in making satisfactory emulsions with the emulsifying agents, salts, and fuels listed in the '978 patent. Those findings have not been shown to be clearly erroneous.

If *Atlas Powder* is to serve as evidence of a doctrinal shift, the outcome must be inconsistent with post-shift Federal Circuit decisions finding chemical genus claims invalid. I do not think it is, based on a number of factors that were at play in *Atlas Powder* that distinguish it from these later cases. These include the fact that neither the chemical genuses nor the claimed invention relate to a pharmaceutical, that the chemical genuses are only tangential to the invention's point of novelty, that the patent provides numerous working examples, that the court found that the structure of and functional relationship of the chemical genuses was relatively predictable, and the fact that there was no evidence that the chemical genuses encompassed undisclosed species that were likely to have a substantially different or superior functionality than the specifically disclosed examples, at least in the context of the invention.

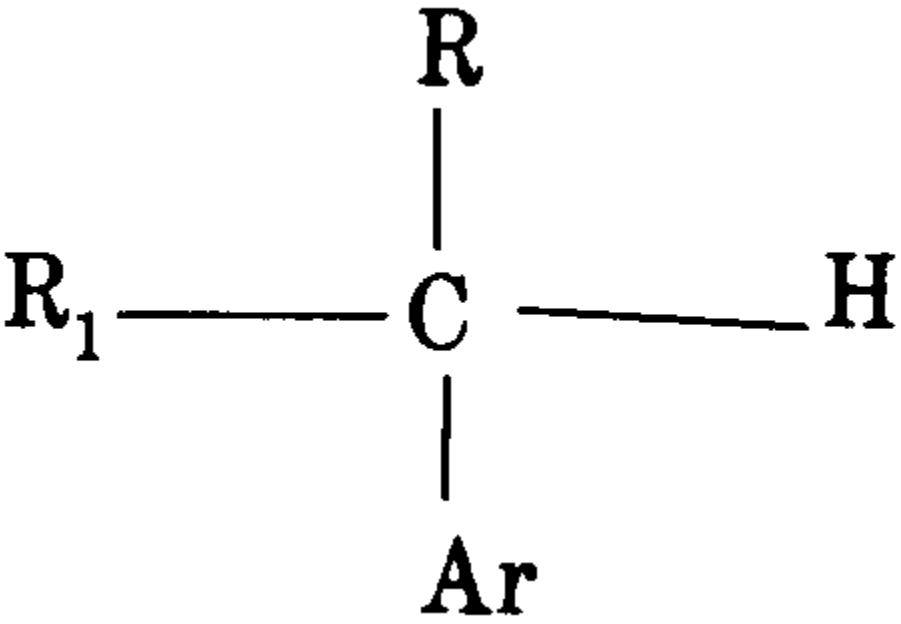
### Other Pre-Shift Precedent

Based on my reading of the article, *Death* only identifies one other example, beyond *Atlas Powder*, of a judicial decision purportedly exemplifying the more permissive, pre-shift 112(a) standard. This was the case of *Application of Angstadt*, decided by the Federal Circuit's predecessor, the Court of Court of Claims and Patent Appeals (CCPA) in 1976.[32]

The relevant claim at issue in *Angstadt* recited:

> In the process for the catalytic oxidation of secondary or tertiary alkylaromatic hydrocarbons of the formula

[32] Application of Angstadt, 537 F.2d 498 (C.C.P.A. 1976).




> wherein R is lower alkyl; R 1 is lower alkyl or hydrogen; and Ar is an aromatic nucleus selected from the group consisting of phenyl and naphthyl, in the presence of air or oxygen at a temperature of from about 80 to 150° C to form a reaction mixture comprising the corresponding hydroperoxides, the improvement wherein the catalyst is of the formula
>
> MX n(HAPA) m
>
> wherein HAPA is a hexaalkylphosphoramide, the alkyl moiety of which has from one to thirty carbon atoms; MX is metal salt wherein M is a transition metal cation of Group IB, IIB, IIIB, IVB, VB, VIB, VIIB, VIIIB or IIA of the Periodic Table and X is an inorganic anion of said metal salt; m is an integer of from 1 to 8; and n is an integer of from 1 to 4, wherein the ratio of said catalyst to said alkylaromatic hydrocarbon is from about 0.1 to 5.0 parts by weight of catalyst per 100 parts by weight of alkylaromatic hydrocarbon.

Again, this is not a traditional chemical genus claim, it is a process claim that falls under my definition of a functional genus claim. While the claim recites a structurally defined genus of chemical catalysts, it is also implicitly limited to those catalysts that are able to perform the recited function of catalyzing the oxidation of an alkylaromatic hydrocarbon falling within another structurally defined chemical genus. Indeed, the *Angstadt* court explicitly characterized this as a functional genus claim, noting that "the claim limitation 'to form . . . hydroperoxides'

must be given effect," and that "th[is] ***functional limitation*** was inserted in the claims at the specific insistence of the examiner."[33]

The PTO rejected the claim for lack of enablement, but in a split decision the CCPA reversed the board, noting:

> [although] appellants are not required to disclose every species encompassed by their claims even in an unpredictable art such as the present record presents, each case must be determined on its own facts. In the instant case, appellants' invention is the use of a complex catalyst comprising a hexaalkylphosphoramide and a transition metal salt to catalyze the oxidation of secondary or tertiary alkylaromatic hydrocarbons to form hydroperoxides. Appellants have, in effect, provided those skilled in this art with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants have actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramides. If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

As was the case with *Atlas Powder*, I think this decision provides little support for *Death*'s asserted doctrinal shift. For one thing, the *Angstadt* decision is over 45 years old, predating the Federal Circuit, which undercuts its evidentiary value with respect to a shift in the law that has occurred at the Federal Circuit. Furthermore, it does not involve a pharmaceutical, there is no indication that the claimed genus encompasses undisclosed but functionally different/superior species, the structure-function relationship of the claimed genus seems relatively predictable, and the patent provides numerous working examples.

### Death's post-shift Federal Circuit decisions

Now let us compare the decisions in *Atlas Powder* and *Angstadt* with the decision specifically identified in Death as representative of the "new," more restrictive interpretation of 112 that has supposedly killed the genus claim.

As a preliminary matter, I will note that *Death* is not entirely clear as to exactly when the purported shift occurred. Clearly the authors feel that it occurred sometime after 1984, the year *Atlas Powder* was decided. At one point *Death* states that the authors are unaware of any decision from the 1980s in which a genus claim was invalidated under 112(a). It bears noting,

[33] *Id.* at 501 (emphasis added).

however, that Death only identifies a single case from the 1980s in which a genus claim was found to be not invalid, i.e., *Atlas Powder*. In any event, the authors of *Death* must believe that the shift occurred sometime after the 1980s. At some points, the article talks about the shift beginning almost 30 years ago, i.e., in the early 1990s. But it seems to me that *Death* focuses in particular on some high-profile decisions that have occurred since 2013, and so I will focus on those particular decisions, which are *Wyeth* (2013), *Enzo Life Sciences* (2019), and *Idenix* (2019). Consistent with this focus, *Death* includes a section entitled "the new law of genus claim enablement," and the first case discussed in this section is *Wyeth*, which the authors refer to as "the first opinion in this latest line of cases." I will also consider *Amgen v. Sanofi*, a decision that apparently came out after *Death* was written. Even though *Amgen* is not explicitly discussed in *Death*, the authors of *Death* did file an amicus brief in *Amgen* arguing that the decision is yet another example of their "death of the genus claim" thesis.[34]

### *Wyeth*

The patent claims at issue in *Wyeth & Cordis v. Abbott* were directed towards methods of preventing restenosis through the administration of an effective amount of "rapamycin." Restenosis refers to when a section of blocked artery that was opened up by means of angioplasty or a stent has become narrowed again.[35] A representative claim at issue in *Wyeth* recites:

> A method to of preventing restenosis in a mammal resulting from said mammal undergoing a vascular catheterization, vascular scraping, vascular surgery, or laser treatment procedure which comprises administering an antirestenosis ***effective amount of rapamycin*** to said mammal orally, parenterally, intravascularly, intranasally, transdermally, rectally, or via a vascular stent impregnated with rapamycin.[36]

The patent specification describes a "rapamycin" as "a macrocyclic triene antibiotic produced by *Streptomyces hygroscopicus*." However, during the infringement litigation Wyeth successfully argued for a more expansive interpretation of the term. As a result, the district court construed "rapamycin" as "a compound containing a macrocyclic triene ring structure produced by *Streptomyces hygroscopicus*, having immunosuppressive and anti-restenotic effects." This construction was important for Wyeth, because the specific compound disclosed in Wyeth's patents was actually "sirolimus," a compound that is often referred to simply as "rapamycin." Sirolimus is also the active ingredient Wyeth uses in its commercial embodiment of the invention. The patent never used the term "sirolimus," but instead always refer to the compound simply as "rapamycin."

The products accused of infringement, on the other hand, used different active ingredients, everolimus and zotarolimus, two drugs that have the same macrocyclic ring as sirolimus but different substituents at the C–42 position. Had the court construed "rapamycin" to be limited to "sirolimus," there would have been no literal infringement. By convincing the court to construe

[34] Amgen Inc. v. Sanofi, Aventisub LLC, 987 F.3d 1080 (Fed. Cir. 2021).
[35] Wyeth & Cordis Corp. v. Abbott Labs., 720 F.3d 1380 (Fed. Cir. 2013).
[36] U.S. Patent 5,563,146.

the term more broadly, encompassing a genus of structurally-related molecules, Wyeth hoped to be able to establish infringement by two competing products that employed different active ingredients than Wyeth uses in its product and discloses in its patent.

Based on the court's construction of the term "rapamycin," the claim is clearly a functional genus claim. The court construed rapamycin" as "a compound containing a macrocyclic triene ring structure produced by *Streptomyces hygroscopicus*, having immunosuppressive and anti-restenotic effects." The court found the claim invalid for lack of enablement, pointing in particular to the dearth of disclosure regarding the relationship between molecular structure and the functional attributes defining the genus, i.e., immunosuppressive and anti-restenotic effects. In *Wyeth* the district court explained:

> given that numerous analogs that, structurally speaking, fall within the scope of the claims here, the question becomes how to narrow down that universe based on the relevant ***function***. In *BSC I*, the court recognized that "functional claim language can meet the written description requirement when there is an established correlation between structure and function" 647 F.3d at 1366. However, it was found in *BSC I* that, as of at least 1997 (and even as late as 2001)—five to nine years later than the priority date of the [patents at issue in *Wyeth*], "the alleged correlation between structure and function was not well known."[37]

The Federal Circuit affirmed the district court's decision that the claim is invalid for lack of enablement, precisely because the claimed genus of chemical compound is defined in functional terms, and the patentee did not provide enough disclosure of a predictable relationship between structure and function.

> Under the district court's unchallenged construction of "rapamycin," the invention is a new method of use of a known compound (sirolimus) and any other compounds that meet the construction's ***structural and functional*** requirements.[38]

The Federal Circuit found the finding of lack of enablement supported for two reasons:

> First, there [are] at least tens of thousands of candidates. The specification is silent about how to structurally modify sirolimus, let alone in a way that would ***preserve the recited utility***. Second, there is no genuine dispute that it would be necessary to first synthesize and then screen each candidate compound using the assays disclosed in the specification to determine whether it has immunosuppressive and antirestenotic effects. There is no evidence in the record that any particular substitutions outside of the macrocyclic ring are preferable. Indeed, a Wyeth scientist confirmed the ***unpredictability*** of the art and the ensuing need to assay

[37] Wyeth v. Abbott Lab'ys, No. CIV.A. 08-1021 JAP, 2012 WL 175023, at *16 (D.N.J. Jan. 19, 2012), aff'd sub nom. Wyeth & Cordis Corp. v. Abbott Lab'ys, 720 F.3d 1380 (Fed. Cir. 2013).

[38] Wyeth & Cordis Corp. v. Abbott Lab'ys, 720 F.3d 1380 (Fed. Cir. 2013).
Wyeth also appealed the district court's grant of summary judgment that the claims are invalid for lack of written description based on the "rapamycin" limitation, and invalid for lack of written description and nonenablement based on another limitation. In light of its holding on nonenablement with respect to the "rapamycin" limitation, the Federal Circuit did reach these other issues.

> each candidate by testifying that, "until you test [compounds], you really can't tell whether they work or not [i.e., have antirestenotic effects]."
>
> …
>
> The specification offers no guidance or predictions about particular substitutions that might preserve the immunosuppressive and antirestenotic effects observed in sirolimus. The resulting need to engage in a systematic screening process for each of the many rapamycin candidate compounds is excessive experimentation. We thus hold that there is no genuine dispute that practicing the full scope of the claims, measured at the filing date, required undue experimentation.[39]

*Wyeth* provides a good example of a case in which the chemical genus encompasses species having improved or different function relative to any disclosed species. Although sirolimus, everolimus, and zotarolimus all fall within the genus, these are different chemical entities with different pharmacological properties. For example, a 2021 research article reports that the allegedly infringing everolimus-eluting stents (EES) outperforms Wyeth's sirolimus-eluting stents (SES).[40]

> EES showed obvious advantages over SES for diabetes mellitus (DM) patients, as it induced the lowest rate of target vessel revascularization and target lesion revascularization. In addition, EES induced lower in-segment late luminal loss than [SES]. Moreover, EES effectively reduced all-cause mortality compared to [SES]. Furthermore, EES could reduce the stent thrombosis rate compared with [SES].

Not surprisingly, the article concluded that EES should be recommended over SES for DM patients.

The claims invalidated in *Wyeth* are clearly distinguishable from the claims upheld in *Death*'s two examples of pre-shift case law, *Atlas Powder* and *Angstadt*. The chemical genus at issue is pharmaceutically useful, which raises policy concerns that are not present in non-pharmaceutical cases like *Atlas Powder* and *Angstadt*. As is typically the case with a pharmaceutical, one would predict that the genus includes species having different and/or superior functional characteristics relative to the disclosed chemical compound, and as discussed above this is actually been shown to be the case. The structure-function relationship of the chemical genus is relatively unpredictable, as is generally the case with pharmaceuticals. Furthermore, the claimed chemical genus is coextensive with the claimed invention's point of novelty, i.e., the identification of a chemical compound useful in the prevention of restenosis post-angioplasty.

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[39] *Id.* at 1385–86.

[40] Ouyang, H., Zeng, X., Zhang, C. et al. *A meta-analysis of everolimus-eluting stents versus sirolimus-eluting stents and paclitaxel-eluting stents in diabetic patients*. J Cardiothorac Surg 16, 90 (2021). https://doi.org/10.1186/s13019-021-01452-8, https://cardiothoracicsurgery.biomedcentral.com/articles/10.1186/s13019-021-01452-8.

### *Enzo*

The next case to be considered is *Enzo Life Scis. v. Roche Molecular Sys.*, decided in 2019.[41] The relevant claims relate to the use of non-radioactively labeled polynucleotides in nucleic acid hybridization and detection applications, wherein the label is attached at the phosphate position of a nucleotide. The claimed priority date of the patents at issue was June 1982. At that time, the prevailing method of labeling DNA probes was through the use of radioactive labeling, which generally involved replacing certain atoms in the nucleotide sequence with corresponding radioactive isotopes. As explained in the Federal Circuit's decision,

> Non-radioactive labeling was just developing at the time of the claimed inventions. In 1981, Dr. David Ward and others at Yale University successfully developed a nonradioactive probe by attaching a label to a polynucleotide via a chemical linker at a base position of a nucleotide. Dr. Ward demonstrated that attaching labels at certain positions of the nucleotide ("the Ward positions") would not disrupt the polynucleotide's ability to hybridize and be detected upon hybridization.
>
> In December 1981, Enzo licensed the exclusive rights to the patent portfolio covering Dr. Ward's discovery. Shortly thereafter, in June 1982, Enzo filed a patent application covering non-radioactive labeling at additional positions on a nucleotide. The two patents in this appeal issued from applications filed in 1995 that claim priority from this 1982 application.

Claim 1 of U.S. patent 6,992,180 is representative:

> 1. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide or modified nucleotide analog having the formula
>
> > Sig-PM-SM-BASE
> >
> > wherein PM is a phosphate moiety, SM is a furanosyl moiety and BASE is a base moiety comprising a pyrimidine, a pyrimidine analog, a purine, a purine analog, a deazapurine or a deazapurine analog ***wherein said analog can be attached to or coupled to or incorporated into DNA or RNA wherein said analog does not substantially interfere with double helix formation or nucleic acid hybridization***, said PM being attached to SM, said BASE being attached to SM, and said Sig being covalently attached to PM directly or through a non-nucleotidyl chemical linkage, and wherein said Sig comprises a non-polypeptide, non-nucleotidyl, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, and wherein Sig comprises biotin, imino-biotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent

[41] Enzo Life Scis., Inc. v. Roche Molecular Sys., Inc., 928 F.3d 1340 (Fed. Cir. 2019).

> component, a chemiluminescent component, a chromogenic component, a hapten or a combination of any of the foregoing.[42]

The court noted that "the claims are not directed to any specific polynucleotide, nor do they focus on the chemistry or linker used to attach a label, the number of labels to attach to a polynucleotide, or where within the polynucleotide to attach those labels. Instead, the claims encompass all polynucleotides with labels attached to a phosphate, as long as the polynucleotide remains hybridizable and detectable upon hybridization." Note that the claim encompasses a huge genus defined in terms of both structure and function, i.e., the polynucleotide must remain "hybridizable and detectable upon hybridization" with the label attached.

The claim was found invalid for lack of enablement. Significantly, the court noted that during the patent's prosecution the applicant had notified the PTO that the patent included no working examples. During litigation, there appears to have been some dispute as to whether example V from the patent might have represented a working example. Example V states in full:

> Biotin and polybiotinylated poly-L-lysine were coupled to oligoribonucleotides using a carbodiimide coupling procedure described by Halbran and Parker, J. Immunol., 96 373 (1966). As an example, DNA (1 ug/ml), 1 ml) in tris buffer pH 8.2, sheared with 0.1 N sodium hydroxide was denatured by boiling for 10 minutes and quick cooling in an ice bath. Biotinyl-1,6-diaminohexane amide (2 mg, 6 umol) or polybiotinylated poly-L-lysine (2 mg) and l-ethyl-3-diisopropylaminocarboimide HCl (10 mg, 64 umol) were added, and the pH readjusted to 8.2. After 24 hours at room temperature in the dark, the mixture was dialyzed against 10 mM tris buffered saline. DNA was precipitated ethanol.

The court found that, during prosecution, Enzo had admitted that Example V is a "paper" rather than a "working example." Moreover, regardless of whether Example V constitutes a working example or not, it clearly does not purport to show that the labeled oligonucleotide was "hybridizable," a defining attribute of the defined genus. Additionally, Enzo's expert testified that he was not aware of Enzo having ever tested a phosphate-labeled probe for hybridizability and detectability. During deposition, the expert was asked if there was "any bench experiment disclosed in the '180 patent in which the '180 inventors attempted to determine whether the product of Example V, that is, the Sig moiety attached to an oligo- or polynucleotide could be detected after it had hybridized to a compl[e]mentary nucleic acid of interest?" He answered "... no, they did not do an actual bench experiment to that effect."

In addition, at the time of the invention, this area of technology was highly unpredictable. The court noted that:

> all parties acknowledge that serious doubts existed in the art as to whether the use of non-radioactive probes at non-Ward positions would be useful as probes. For example, an inventor of the '180 patent who is also Enzo's CEO explained that, at the time, it was thought "aggressive chemical modification of nucleic acid would lead to destruction of his [sic] content." Enzo's expert, Dr. Backman, also pointed out the view of the art at the time, stating that "[a]t the time of the inventions of

[42] *Id.* at 1343–44.

> the '180 patent, it was commonly thought that the addition of a nonradioactive label to a nucleic acid sequence at positions other than [the Ward positions at the base] would interfere with or disrupt the hybridization process." Indeed, Enzo's expert explained that for one of skill in the art to be comfortable that a particular polynucleotide would work as a probe, "they would need to actually make the compound and test it in a hybridization experiment, which they would have been dissuaded from doing because of Ward."
>
> Given such ***unpredictability*** in the art, and considering the testimony of Enzo's expert that each labeled polynucleotide would need to be tested to determine whether it is hybridizable and detectable upon hybridization, the breadth of the claims here is particularly concerning in the enablement inquiry.

The court further observed:

> [T]he issue in this appeal is not simply whether the specification enables labeling; the question is whether it enables creation of a labeled probe that is both hybridizable and detectable upon hybridization. [Even] if we assume that the specification teaches one of skill in the art how to create the broad range of labeled polynucleotides covered by the claims, as explained below, the specification still fails to teach one of skill in the art ***which combinations will produce a polynucleotide that is hybridizable and detectable upon hybridization, as required by the claim language***.[43]

In my view, the outcome in *Enzo* can be convincingly reconciled with *Atlas Powder* and *Angstadt*. In those cases, the court found that the particular area of chemistry in question was well-developed and highly predictable, and that the patents had disclosed numerous working examples. In addition, it is clear that Enzo's extremely broad genus claim would encompass species having greatly improved function compared to the specific species disclosed. Example V describes attachment of biotin, a well-established nonradioactive label. But subsequent researchers developed probes having much superior nonradioactive labels.

For example, the list of products accused of infringing the '180 patent in Enzo's complaints include a number of Gen-Probe/Hologic's Aptima kits and reagents.[44] Aptima reagents include probes labelled with acridinium ester (AE) molecules. These The AE labeled probes combine with amplicon to form stable hybrids.[45] A 1990 article reported, for example, that "chemiluminescent hybridization assays using acridinium esters … have been described with sensitivities comparable to those obtained with radioactive labels."[46]

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[43] *Id.* at 1346.
[44] Hologic, Aptima General Purpose Reagents - Product Insert, available at https://www.hologic.com/sites/default/files/package-insert/500106-IFU-PI_001_01.pdf (last visited Jan. 4, 2022).
[45] Hologic, Aptima® SARS-CoV-2 Assay – Instructions for Use, available at https://www.fda.gov/media/138096/download (last visited Jan. 4, 2022).
[46] Norman C. Nelson and Daniel L. Kacian, Chemiluminescent DNA probes: A comparison of the acridinium ester and dioxetane detection systems and their use in clinical diagnostic assays, 194 Clinica Chimica Acta 73 (1990). https://www.sciencedirect.com/science/article/abs/pii/000898190903O4B.

### *Idenix*

*Idenix Pharmaceuticals v. Gilead Sciences*, decided shortly after *Enzo*, is the decision that according to *Death*, "cemented" the purported "shift" in the law.[47] The claim at issue recites:

> A method for the treatment of a hepatitis C virus infection, comprising administering an effective amount of a purine or pyrimidine β-D-2'-methyl-ribofuranosyl nucleoside or a phosphate thereof, or a pharmaceutically acceptable salt or ester thereof.

Significantly, at Idenix's urging, the district court construed the preamble, "[a] method for the treatment of a hepatitis C virus infection," as a narrowing functional limitation, i.e., this is indisputably a functional genus claim. The Federal Circuit found the key enablement question to be "whether a person of ordinary skill in the art would know, without undue experimentation, which 2'-methyl-up nucleosides would be effective for treating HCV." The court concluded that this hypothetical person would not.

In reaching its decision, the court found it undisputed that "billions and billions" of compounds literally meet the structural limitations of the claim, while the patent only disclosed four examples on a single sugar. It was also undisputed that the area of technology was highly unpredictable at the time.

This case provides another example in which a genus claim encompasses variants having improved function relative to the specific molecules disclosed. In particular, Idenix sold its HCV product (Uprifosbuvir )to Merck, and that company has spent years attempting to obtain FDA approval to market the drug, so far without success. Gilead's allegedly infringing product, sofosbuvir (sold under the tradename Sovaldi) has been on the U.S. market since it obtained FDA approval in 2013.

This is also a pharmaceutical case, and the claimed chemical genus correspond to the claimed invention's point of novelty, i.e., the identification of a chemical compound useful in the treatment of HCV, which renders the decision non inconsistent with *Atlas Powder* and *Angstadt*.

### *Amgen*

As mentioned above, authors of *Death* filed an amicus brief in support of Amgen's petition for en banc rehearing of *Amgen v. Sanofi*,[48] arguing that the panel's decision represented yet another example of the doctrinal shift in the Federal Circuit's interpretation of 112(a). A representative claim invalidated in *Amgen* recites:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.

[47] Idenix Pharm. LLC v. Gilead Sci. Inc., 941 F.3d 1149 (Fed. Cir. 2019).
[48] Amgen Inc. v. Sanofi, Aventisub LLC, 987 F.3d 1080 (Fed. Cir. 2021).

Note that, aside from the presumed limitation of the claim to "isolated monoclonal antibodies" (an extremely large genus, although distinct from the vast majority of molecules lacking a sufficiently "antibody-like" structure to fall within the scope of the term), the genus of monoclonal antibodies is defined entirely in functional terms, i.e., by its ability to bind to a specific protein, PCSK9, at a specified region of the protein, as defined by certain amino acids present in PCSK9, and by the ability of the antibody to block binding of PCSK9 to LDLR. The accused product is used as a cholesterol-lowering therapy.

The court in *Amgen* explains:

> What emerges from our case law is that the enablement inquiry for claims that include functional requirements can be particularly focused on the breadth of those requirements, especially where predictability and guidance fall short. In particular, it is important to consider the quantity of experimentation that would be required to make and use, not only the limited number of embodiments that the patent discloses, but also the full scope of the claim.[49]

Amgen argued that "the embodiments in the patent are structurally representative for the purpose of fulfilling the written description requirement, and such evidence is sufficient to indicate a structure/function correlation establishing enablement."[50] The court explained that:

> we are not concerned simply with the number of embodiments but also with their ***functional breadth***. Regardless of the exact number of embodiments, it is clear that the claims are far broader in functional diversity than the disclosed examples. If the genus is analogized to a plot of land, the disclosed species and guidance "only abide in a corner of the genus." AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc., 759 F.3d 1285, 1299–300 (Fed. Cir. 2014)."[51]
>
> We also agree with the district court that this invention is in an ***unpredictable*** field of science with respect to satisfying the full scope of the functional limitations. One of Amgen's expert witnesses admitted that translating an antibody's amino acid "sequence into a known three-dimensional structure is still not possible." Another of Amgen's experts conceded that "substitutions in the amino acid sequence of an antibody can affect the antibody's function, and testing would be required to ensure that a substitution does not alter the binding and blocking functions." And while some need for testing by itself might not indicate a lack of enablement, we note here the conspicuous absence of nonconclusory evidence that the full scope of the broad claims can predictably be generated by the described methods. Instead, we have evidence only that a small subset of examples of antibodies can predictably be generated.[52]

Once again, we have a functional genus of pharmaceutically active ingredients, and as such the claim is likely to encompass presently unknowm species having have different and/or superior therapeutic function, in terms of safety and efficacy, to any species specifically identified in the

[49] *Id*. at 1086.
[50] *Id.* at 1085.
[51] *Id.* at 1087.
[52] *Id.* at 1087–88.

patent. Although, at this point, evidence for this does not seem to be available. A recently published meta-analysis found little, if any, significant difference between Amgen's PCSK9-targeting antibody product is Repatha (alirocumab) and Sanofi's allegedly infringing product Praluent (evolocumab), marketed by Regeneron, in terms of safety and efficacy, aside from a finding that alirocumab was associated with a 27% increased risk of injection site reaction compared to evolocumab.[53]

In *Amgen*, we again see a case where the claimed invention's point of novelty, the discovery of an antibody capable of blocking the binding of PCSK9 to LDLR through an affinity for a specified region of PCSK9, constitutes the relevant chemical genus. As has been the case with the other Federal Circuit decisions *Death* points to as representative of the shift, the invalidation of Amgen's claim can be reconciled with *Atlas Powder* and *Angstadt*, and is not evidence a dramatic change in the law.

## Conclusion

This concludes Part I of this two-part article. In Part II, which will appear in the next installment of the Home Report, I will push back further against *Death*'s assertion that there has been a dramatic shift in Federal Circuit case law over recent years resulting in the death of the chemical genus claim. This will include a number of judicial decisions (mostly Federal Circuit) in which chemical genus claims (comparable to the genus claims *Death* points to as evidence of the shift in the law) were found to be invalid under 112(a) due to overbreadth well before *Death*'s purported shift in the law. Conversely, there are a number of judicial decisions subsequent to the time of the purported shift, some as recent as 2021, in which the court has upheld the validity of quite broad chemical genus claims in the face of a 112(a) challenge. A number of these decisions are summarized in Part II.

Part II of the article will also offer my critique of some other aspects of *Death* with which I respectfully disagree. For example, *Death* fails to acknowledge the significance of the fact that a chemical genus claim typically encompasses embodiments (i.e., species) that have substantially different and/or superior functional characteristics than embodiments that the patent specifically discloses and makes available to the public. *Death* also, in my view, errs in suggesting that the Federal Circuit's purported heightened standard for complying with 112(a) could be circumvented by means of "structural genus claims" rather than "functional genus claims."

Finally, Part II concludes by identifying a number of considerations, often unstated, and not explicitly included within the Federal Circuit's *Wands* and *Ariad* factors, which I believe come into play when the court is assessing a chemical genus claim for compliance with 112(a). These considerations include whether the recited chemical genus resides at the invention's "point of novelty," the extent to which the chemical genus appears to encompass important embodiments with significantly different and/or improved function relevant to embodiments disclosed in the

[53] Paul Guedeney et al., Indirect comparison of the efficacy and safety of alirocumab and evolocumab: a systematic review and network meta-analysis Eur Heart J Cardiovasc Pharmacother. 2021 May 23;7(3):225-235.

patent, and whether the chemical genus encompasses molecules whose primary functional significance is as pharmaceutically active compounds.