USPTO Publishes Enablement Guidelines in view of Amgen v. Sanofi

On January 10, 2024, the USPTO **published** guidelines for assessing enablement in view of *Amgen v. Sanofi* and other recent court cases ("the Guidelines"). The Guidelines state that they are not intended to "announce any major changes to USPTO practice or procedure" but instead "incorporat[e] guidance from the *Amgen* decision and several post-*Amgen* enablement court decisions that are consistent with current USPTO policy."

"The enablement requirement refers to the requirement of 35 U.S.C. § 112(a) that the specification must describe the invention in such terms that one skilled in the art can make and use the claimed invention." The Guidelines emphasize that an enablement assessment during prosecution still requires use of the *Wands* factors, including "(A) the breadth of the claims, (B) the nature of the invention, (C) the state of the prior art, (D) the level of one of ordinary skill, (E) the level of predictability in the art, (F) the amount of direction provided by the inventor, (G) the existence of working examples, and (H) the quantity of experimentation needed to make and use the invention based on the content of the disclosure." Per the Guidelines, use of the *Wands* factors is consistent with *Amgen* and several of the Federal Circuit's post-*Amgen* decisions, including *Baxalta*. The Guidelines state "[t]he *Wands* analysis should provide adequate explanation and reasoning for a lack of enablement finding in order to facilitate the USPTO's clarity of the record goals, as well as the USPTO's goals of providing consistency between examination and post-grant challenges."

Federal Circuit Remands to USPTO to Clarify Analysis of Jepson-Format and Means-Plus-Function Claims in the Field of Biotechnology

On January 23, 2024, the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") issued its **decision** granting the USPTO's request to remand Xencor's appeal of the rejection of U.S. Patent App. No 16/803,690 ("'690 patent application") back to the USPTO. The USPTO requested remand so that the USPTO's Appeals Review Panel can "clarify the USPTO's position on the proper analysis of Jepson-format and means-plus function claims in the field of biotechnology, and particularly in the antibody art," and issue "a revised decision."

The claims at issue in the '690 patent application cover use of anti-C5 antibodies with an Fc domain. The claims were drafted in both the "Jepson" and means-plus-function format (claims 8 and 9, respectively):

8. **In a method** of treating a patient by administering an anti-C5 antibody with an Fc domain, **the improvement** comprising said Fc domain comprising amino acid substitution M428L/N434S as compared to a human Fc polypeptide, wherein numbering is according to the EU index of Kabat, wherein said anti-C5 antibody with said amino acid substitution has increased in vivo half-life as compared to said antibody without said substitutions.
9. A method of treating a patient by administering an anti-C5 antibody comprising: a) **means for** binding human C5 protein; and b) an Fc domain comprising amino acid substitution M428L/N434S as compared to a human Fc polypeptide, wherein numbering is according to the EU index of Kabat, wherein said anti-C5 antibody with said amino acid substitution has increased in vivo half-life as compared to said antibody without said substitutions.

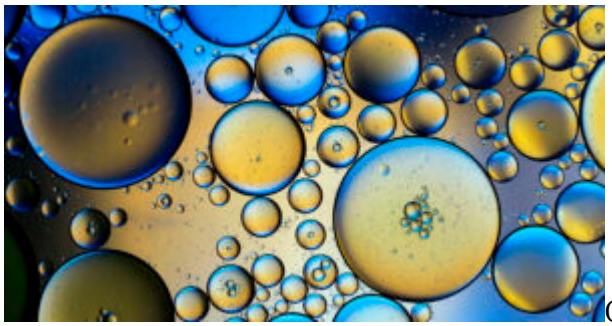
The examiner had rejected the claims as unpatentable (a) for failing to comply with the written description requirement, and (b) under the obviousness-type double patenting doctrine. Xencor appealed the rejection to the Patent Trial and Appeal Board ("PTAB"), after which the examiner withdrew the written description rejection.

In its **decision**, the PTAB reinstated the written description rejection. Xencor **appealed** to the Federal Circuit. Following the filing of Xencor's appeal brief, the Director of the USPTO filed a **motion** for remand back to the USPTO "to permit further consideration and issuance of a revised decision by the Appeals Review Panel." The Director's motion for remand stated that:

> Xencor's pending claims present novel questions involving the application of the Supreme Court's and this Court's precedent for both Jepson-format and means-plus-function claims in the field of biotechnology, and in particular the antibody art. The use of Jepson format and means-plus-function claims in the life sciences is exceedingly rare. Therefore, the USPTO seeks remand in order to issue a revised decision that clearly and thoroughly expresses the Agency's view on application of the case law to this important area of technology.

While Xencor **opposed** the USPTO's request as arising too late, the Federal Circuit ultimately sided with the USPTO. In its decision, the Federal Circuit wrote that the Director raised legitimate concerns and that it was "confident that proceedings will be conducted expeditiously."

K-Fee Provides a Warning to Life Sciences Companies – What You Say in Foreign Prosecution May Affect Your U.S. Claim Scope

 On December 26, 2023, the United States Court of Appeals for the Federal Circuit issued its **decision** in K-Fee System GMBH v. Nespresso USA, Inc. While nominally a case related to coffee makers, its teachings are highly applicable to life science companies as they tend to file large numbers of ex-U.S. patent cases. The lesson: under certain circumstances, a court may consider statements made in patent prosecution proceedings outside of the U.S. when construing the scope of related U.S. claims, and as such those statements should be carefully weighed against implications in your U.S. patent portfolio.

K-fee System GmbH ("K-fee") owns U.S. Patent Nos. 10,858,176, 10,858,177, and 10,870,531. K-fee filed suit against Nespresso USA ("Nespresso") in the Central District of California ("District Court") alleging that Nespresso's coffee system infringed claims in each of the three patents. Nespresso filed a motion for summary judgment of non-infringement, arguing that its products did not infringe the asserted patent claims. The District Court agreed and granted Nespresso's motion for summary judgment. K-fee appealed to the Federal Circuit, which agreed with K-fee that the District Court erred in construing certain terms in the K-fee claims. The Federal Circuit remanded the case back to the District Court for further proceedings.

Previously, Nespresso had filed an opposition against a European patent related to the three U.S. patents K-fee asserted in its U.S. case. K-fee filed a motion asking the EPO to deny the opposition. K-fee argued that its claims were patentable over certain prior art cited by Nespresso based on the plain meaning of the term "barcode." In its motion, K-fee provided what it alleged to be the plain meaning of that term. K-fee provided the opposition filings to the USPTO, including the motion containing this claim construction argument. The District Court and the Federal Circuit would both treat K-fee's motion as intrinsic evidence as it had been made part of the U.S. file history by K-fee.

In deciding the motion for summary judgment in favor of Nespresso, the District Court referred to K-fee's definition of barcode provided in the opposition filings. Accordingly, the District Court accepted Nespresso's argument that its products fell outside of the asserted claims as interpreted according to the K-fee's proffered definition. K-fee appealed to the Federal Circuit, arguing that the District Court's narrowing of the term "barcode" was effectively a holding of disclaimer based on its prior arguments to the EPO, which, K-fee argued, did not meet the standard for disclaimer. In finding in favor of K-fee, the Federal Circuit held that the District Court's conclusion regarding the definition of barcode based on K-fee's EPO statements "was too confining," agreeing with K-fee that its arguments to the EPO did not rise to the level of disclaimer. The case was again remanded to the

District Court for further proceedings.

The Federal Circuit concluded its opinion by writing “we note that K-fee makes the legal argument that a conclusion of disclaimer cannot be premised on statements made when defending a related but distinct patent against a different legal standard—here the European standard for novelty. We do not address that contention because we have concluded that K-fee’s statements were too unclear to constitute disclaimer.”

PTAB Issues Final Written Decision Finding Seagen Antibody-Drug Conjugate Patent Claims to be Unpatentable

On January 16, 2024, the Patent Trial and Appeal Board (PTAB) of the United States Patent and Trademark Office issued a **Final Written Decision** in a post-grant review (PGR) (PGR2021-00030) of claims in US Patent No. 10,808,039 (“the ’039 patent”) owned by Seagen. The PGR, filed by Daiichi Sankyo, Inc. and AstraZeneca Pharmaceuticals, LP, requested review of claims 1-5, 9, and 10 of the ’039 patent, which are directed to antibody-drug conjugates (ADC) capable of intracellular cleavage. The ’039 patent is at issue in a patent infringement lawsuit brought by Seagen against Daiichi Sankyo over Daiichi’s FDA-approved ADC cancer therapy ENHERTU®. Previously, a federal jury has found that ENHERTU infringed the ’039 patent and awarded $41.8 million in royalty revenue to Seagen.

Issues raised in the PGR included whether claims 1-5, 9, and 10 of the ’039 patent were not patentable for lack of written description and enablement under 35 U.S.C. §112(a), indefiniteness under 35 U.S.C. §112(b), and anticipation under 35 U.S.C. §102.

On the issue of written description, Daiichi argued that the claims were not sufficiently supported because (a) the disclosure lacked descriptive support for the claimed gly/phe tetrapeptide component (W_w) of the ADC, and (b) the disclosure did not describe a representative number of species for the genus of “drug moiety” nor did the disclosure demonstrate common structural features for the “drug moiety” component.

On enablement, Daiichi argued that the ’039 patent does not enable the full scope of the claimed ADCs. Specifically, it noted that “[c]omplex chemical interactions among ADC components affect its structure and properties,” and that “[w]hile the claim does limit one aspect of the linker … the structural limitations of the claim still encompass an astronomical number of structurally and functionally disparate compounds.”

In the Final Written Decision, the PTAB held that claims 1-5, 9, and 10 are unpatentable for failing to comply with the written description and enablement requirements under Section 112(a).

Among its findings for written description, the PTAB determined that the specification of the ’039 patent did not have sufficient written descriptive support for claimed gly/phe tetrapeptide component. Noteworthy, with regards to the “drug moiety,” the PTAB opinion distinguished the Seagen patent from the patent at issue in *Juno v. Kite*, stating that the ’039 specification disclosed dozens of different known chemotherapeutic agents in multiple classes. Further, the opinion referred to *Falko-Gunter Falkner v. Inglis* in noting that “the recitation of known structures … ‘would serve no goal of the written description requirement’.” The opinion also stated that “the claims of the ’039 patent are not focused on the particular cancer drugs selected from the large number of known cancer drugs or the antibody used, but rather focus entirely on the linker joining a drug moiety and an antibody or other ligand moiety.”

The PTAB also found that the claims were not enabled. After going through the Wands Factors, the PTAB concluded that undue experimentation would have been required to make and use the claimed invention in view of, for example, the large scope of the ADC claims, the limited working examples and guidance provided by the patent, the unpredictability of the art around ADCs, and the quantity of experimentation needed. The claims were also found to be anticipated under Section 102.

Daiichi’s general counsel issued a statement saying that the company is “pleased” with the PTO’s decision. Seagen issued a statement indicating that it would appeal the decision.

Some Much-Needed (Applicant-Friendly) Clarification on Priority Claims at the European Patent Office

On October 10, 2023, the Enlarged Board of Appeal of the European Patent Office (EPO) issued a **consolidated decision in cases G1/22 and G2/22** clarifying a common issue regarding the validity of a priority claim made at the EPO. **Per the Board of Appeal, there is a rebuttable presumption that an Applicant claiming priority is entitled to claim that priority**.

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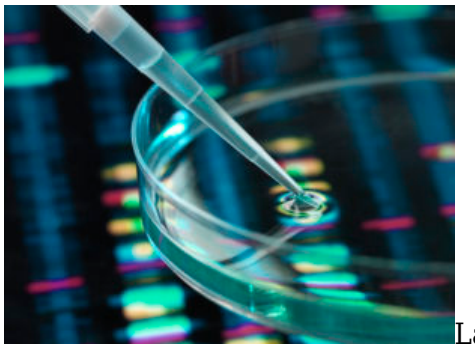
Is it Biosimilar or Interchangeable? It Won’t

Be Easy to Tell Under FDA's Latest Draft Labeling Guidance

 Last week, **FDA released** a draft guidance, "**Labeling for Biosimilar and Interchangeable Biosimilar Products**" that—when finalized—will revise and replace its July 2018 final guidance, "**Labeling for Biosimilar Products**." FDA noted that this 2023 Draft Guidance reflects recommendations based on the "valuable experience about labeling considerations" that FDA has gained through its approval of 42 biosimilar products, including four interchangeable biosimilar products.

Notably, the 2023 Draft Guidance provides further recommendations regarding when to use a biosimilar or interchangeable biosimilar product name, and when to use the reference product name in labeling:

- The biosimilar or interchangeable biosimilar product's proprietary name[1] (or if the product does not have a proprietary name, its proper name[2]) should be used when –
  - Information in the labeling is *specific to the biosimilar (or interchangeable biosimilar) product*, including such references to the product in the INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections, and/or
  - For "directive statements and recommendations for preventing, monitoring, managing, or mitigating risk," including such references to the product in the BOXED WARNING, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and DRUG INTERACTIONS sections.

- When referring to the *drug substance* in the labeling, the biosimilar or interchangeable biosimilar product's proper name should be used.

- When information *specific to the reference product* is described in the biosimilar or interchangeable biosimilar product's labeling (for example, data from clinical trials of the reference product in the ADVERSE REACTIONS and CLINICAL STUDIES sections), the reference product's proper name should be used.

- In sections of the labeling containing *information that applies to both the biosimilar (or interchangeable biosimilar) product and the reference product*—such as BOXED WARNING, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS—the labeling should use the core name of the reference product followed by the word "products."[3]

FDA acknowledges that the application of these recommendations is highly context-dependent and may not always be clear, but recommends that biosimilar and interchangeable biosimilar product sponsors evaluate all statements in product labeling carefully to determine the most appropriate

product identification approach in each instance.

Another noteworthy aspect of the 2023 Draft Guidance is the Agency's recommendation regarding the biosimilarity statement and footnote in the HIGHLIGHTS section of a biosimilar or interchangeable biosimilar product's labeling.[4] Previously, FDA recommended a biosimilarity statement for a biosimilar product and an interchangeability statement for an interchangeable biosimilar product. The 2023 Draft Guidance now recommends a statement and footnote in the HIGHLIGHTS section that the product is biosimilar to the reference product, *regardless of* whether the product is a biosimilar or an interchangeable biosimilar to the reference product. In the **Federal Register notice** announcing the 2023 Draft Guidance, FDA acknowledges that this marks an "evolution in our thinking" and explains that "a labeling statement noting that certain products within a 351(k) [Biologics License Application] have been approved as interchangeable, and explaining the interchangeability standard, is not likely to be useful to prescribers, who can prescribe both biosimilar and interchangeable biosimilar products in place of the reference product with equal confidence that they are as safe and effective as their reference products." FDA further states that "information about interchangeability is more appropriately located in the Purple Book rather than labeling."

Other notable elements of the 2023 Draft Guidance include recommendations regarding how to describe pediatric use data in a range of scenarios and how to incorporate immunogenicity data. With respect to immunogenicity data, the 2023 Draft Guidance suggests that a contextual paragraph[5] generally be included in the relevant CLINICAL PHARMACOLOGY subsection before describing the available immunogenicity data for the reference product and the biosimilar or interchangeable biosimilar product. The 2023 Draft Guidance also outlines the Agency's expectations for patient labeling—such as a Medication Guide, Patient Information, or Instructions for Use—for a biosimilar or interchangeable biosimilar product, if the reference product has such patient labeling.

Information on how to submit comments on the 2023 Draft Guidance can be found at **https://www.regulations.gov/docket/FDA-2016-D-0643.**

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[1] The proprietary name of a biosimilar product is a brand name determined by the sponsor. The fictitious example provided in the 2023 Draft Guidance is "NEXSYMEO."

[2] The proper name of a biosimilar product is the nonproprietary name designated by FDA that consists of a biological product's core name plus a unique four-letter suffix. The fictitious example provided in the 2023 Draft Guidance is "replicamab-cznm."

[3] The fictitious example provided by FDA in the 2023 Draft Guidance is "replicamab products".

[4] The fictitious example provided by FDA in the 2023 Draft Guidance is "NEXSYMEO (replicamab-cznm) is biosimilar* to JUNEXANT (replicamab-hjxf)" and the accompanying footnote is "Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of *[BIOSIMILAR OR INTERCHANGEABLE BIOSIMILAR PRODUCT'S PROPRIETARY NAME]* has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration) described in its Full Prescribing Information."

[5] The Agency's suggested paragraph is, "The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of [*proper name of reference product*] or of other [*core name*] products."

Supreme Court Affirms Amgen Patents' Invalidity in Closely Watched Enablement Case

The U.S. Supreme Court has decided a closely watched case regarding patent law's enablement requirement, *Amgen Inc. v. Sanofi*. The Supreme Court affirmed the Federal Circuit's decision that Amgen's patent claims were invalid, holding that the patents' disclosures "offer[ed] persons skilled in the art little more than advice to engage in 'trial and error.'"

The Court's decision was unanimous. Although Amgen and various amici had urged the Court to adjust the standard for enablement in ways that would favor patent validity, the Court's decision announced no major changes to the doctrine.

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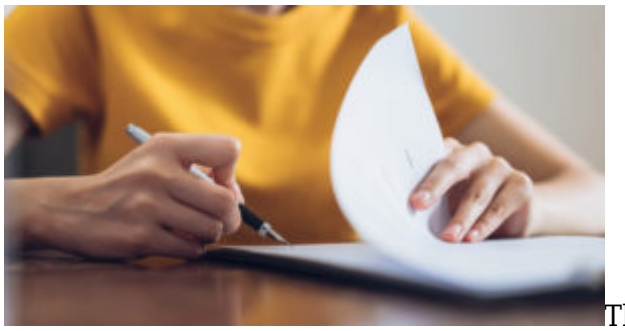
Proposed USPTO Fee Changes Will Make It Much More Expensive to Patent and to Challenge Patents on Therapeutics. You Have an Opportunity to Comment...

 The United States Patent & Trademark Office (USPTO or PTO) recently announced **proposed changes** to certain fees it charges with respect to patent applications, design patents, and America Invents Act (AIA) trials. These changes may significantly increase costs associated with building a robust patent portfolio for New Chemical Entities (NCEs) and Biologics, and to challenge patents at the PTAB. An oral hearing on the proposed changes will be held on **May 18, 2023**, and the USPTO is accepting written comments until **May 25, 2023**.

Read the client alert **here**.

NIH Again Refuses to Exercise March-In Rights to Control Drug Price

In a letter dated March 21, 2023, the National Institutes of Health ("NIH") again refused the request of petitioners to exercise march-in rights under the Bayh-Dole Act to control the price of a drug. Here, as before, the NIH found that the statutory criteria for the use of march-in rights were not satisfied by the petitioners.

March-in rights can permit the government to require a patent owner to grant additional licenses to the invention to avoid situations such as a company licensing the technology but then not commercializing it. The Bayh-Dole Act enumerates the circumstances under which march-in rights and the grant of additional licenses are warranted, for example, to achieve practical application of the invention or to alleviate health and safety needs that are not being reasonably satisfied.

In November 2021, the Secretary of the Department of Health and Human Services ("HHS") received a petition from individuals Robert Sachs and Clare Love requesting the exercise of march-in rights under the Bayh-Dole Act to lower the price of the prostate cancer drug, Xtandi (enzalutamide). The patented drug product was invented at the University of California, Los Angeles, with funding from the NIH and U.S. Army. Xtandi, which is marketed in the United States by Astellas and Pfizer, costs more in the U.S. than it does elsewhere including other high-income countries. Petitioners argued that drug price can forbid access, specifically at prices that are allegedly unreasonable, contrary to the Bayh-Dole Act.

While the NIH's response letter expressed its concern about the high cost of drugs and the burden it places on patients, the letter explained the purpose of the Bayh-Dole Act is to promote the commercialization and public availability of government funded inventions. The overarching proposition of the Act is to permit recipients of federal government funding to retain ownership of patent rights and thereby commercialize the inventions by partnering with the private sector. Prior to the Bayh-Dole Act, most government funded inventions were not licensed or commercialized, including not one drug product.

The letter indicated that the NIH's analysis found that Xtandi is widely available to the public. The NIH stated that consistent with past march-in determinations in response to petitions for controlling drug prices, practical application of the invention is evidenced by practice of the invention and the invention's availability to the public. Astellas, the maker of Xtandi, estimated that more than 200,000 patients since 2012 were treated with the drug. Accordingly, the NIH concluded that the patent owner, the University of California, which licenses the patents to Astellas, meets the requirement for bringing Xtandi to practical application.

In addition, the NIH also stated that given the remaining patent life of the drug and the lengthy

administrative procedure for the exercise of march-in rights, the NIH does not believe that the use of march-in rights would be an effective way at lowering the cost of the drug. Therefore, for these reasons, the NIH determined that march-in rights were not warranted in this situation.

The letter ends stating that the NIH and HHS would pursue a "whole of government approach," informed by public input, to ensure the use of march-in rights is consistent with the Bayh-Dole Act, promotes commercialization of federally funded research, maximizes the potential for federally funded technologies to become products, and is in the interests of the American public. To that end, on the same day as the NIH letter, HHS and the Department of Commerce ("DOC") announced a plan to review march-in authority as found in the Bayh-Dole Act with these same goals.

The NIH decision is in line with the several other petitions that have been filed for other drugs over the last few decades as well as previous petitions involving Xtandi. The exercise of march-in rights by a federal agency likely would have a negative impact on companies developing products invented using federal funding if investors believe that the price of such products could be controlled by the federal government based on public input. We will continue to monitor developments in this area, including for any recommendations from the HHS and DOC inter-agency working group on this important topic.

USPTO Director Issues Precedential Review Decision Regarding Multiple Dependent Claims

Director Katherine Vidal of the U.S. Patent and Trademark Office ("USPTO") issued a precedential review decision with respect to the interpretation of multiple dependent claims, in a case of first impression before the Patent and Trial Appeal Board ("PTAB"). In the review of the PTAB's final written Decision and Order, the Director modified it consistent with her determination of the treatment of multiple dependent claims, which are claims that refer to and incorporate by reference more than one other claim.

More specifically, at issue in the *inter partes* review captioned, Nested Bean, Inc. v. Big Beings Pty Ltd., was the interpretation of 35 U.S.C. § 112, fifth paragraph, which is the controlling statute for multiple dependent claims. The Patent Owner contended that the statute requires the PTAB to consider the patentability of each claim referenced separately. In contrast, the Petitioner argued that if any claim of a multiple dependent claim is unpatentable, then the entire claim is unpatentable. For the reasons that follow, the Director agreed with the Patent Owner.

35 U.S.C. § 112, fifth paragraph, states in relevant part, "[a] multiple dependent claim shall be

construed to incorporate by reference all the limitations of the particular claim in relation to which it is being considered." The related Codified Rule, 37 C.F.R. § 1.75(c) states, in relevant part, "[a] multiple dependent claim shall be construed to incorporate by reference all the limitations of each of the particular claims in relation to which it is being considered." With other statutes and Rules considered, the Director reasoned that the plain language of 35 U.S.C. § 112, fifth paragraph, conveys that a multiple dependent claim is the equivalent of several single dependent claims.

In addition to relying upon the applicable statute and Rules, the Director also considered Federal Circuit case law, legislative history, and USPTO procedure.

More specifically, with respect to precedent, neither party identified a judicial or administrative decision addressing the issue at hand. However, the Director found that Federal Circuit cases identified were supportive of the Patent Owner's position.

The Director found that USPTO guidance and procedures further supported the Patent Owner's interpretation. For example, the Manual for Patent Examining Practice (M.P.E.P.) advises examiners that "a multiple dependent claim must be considered in the same manner as a plurality of single dependent claims." M.P.E.P. § 608.01(n)(I)(B)(4).**[1]** Further, as the Director found, the USPTO claim fee structure is such that applicants must pay separately for each multiple dependent combination, e.g., for a multiple dependent claim that refers to three independent claims, the USPTO charges for three dependent claims.

Thus, after reviewing the PTAB's Decision and the relevant information, Director Vidal acknowledged that it was an issue of first impression before the Board. And based on the plain meaning of the statute, 35 U.S.C. § 112, fifth paragraph, requires that the patentability of a multiple dependent claim be considered separately with respect to each claim to which it refers. Accordingly, the Director's Review Decision modifies the PTAB's final written Decision and Order consistent with her interpretation of determining the patentability of multiple dependent claims, each separately as if multiple single dependent claims.

The Director's Review Decision clarifies the interpretation of U.S. patents containing multiple dependent claims and determining the patentability thereof. In particular, a patentee now knows that each claim of a multiple dependent claim should stand or fall by itself, independent of the invalidity of other dependent claims of the same multiple dependent claim.

[1] Eighth Ed., Rev. 7 (July 2008), which was the version in effect as of the earliest priority date of the relevant patent.