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.

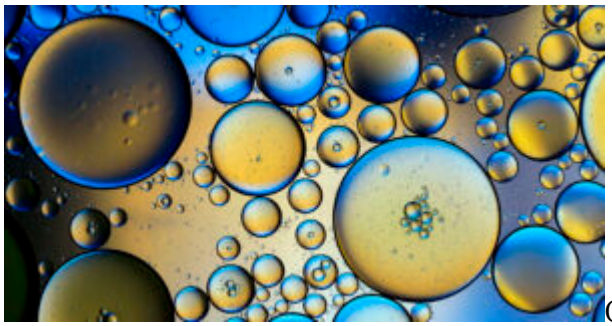
The examiner had rejected the claims as unpatentable (a) for failing to comply with the written description requirement, and (b) under the obviousness-type double patenting doctrine. Xencor appealed the rejection to the Patent Trial and Appeal Board ("PTAB"), after which the examiner withdrew the written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

Master(ing) Protocols for Randomized Umbrella and Platform Trials

The U.S. Food and Drug Administration (FDA) recently issued a draft guidance, "**Master Protocols for Drug and Biological Product Development**", that echoes and builds on principles that the Agency previously set forth in guidance for **COVID-19 master protocols (2019)**, **master protocols in oncology (2022)** and **clinical trials for multiple versions of cellular or gene therapy products (2022)**. The draft guidance offers numerous (and at times *very* detailed) recommendations to facilitate the design, efficient analysis of data, and regulatory review of clinical trials conducted under such master protocols.

As a starting point, this draft guidance defines several key terms, including the types of trials that can be conducted under a master protocol:

Master Protocol	a protocol designed with multiple substudies, which may have different objectives and involve coordinated efforts to evaluate one or more medical products in one or more diseases or conditions within the overall study structure.

Umbrella Trial	evaluates multiple medical products concurrently for a single disease or condition
Platform Trial	evaluates multiple medical products for a disease or condition in an ongoing manner, with medical products entering or leaving the platform
Basket Trial	evaluates a medical product for multiple diseases, conditions, or disease subtypes

Master protocols offer sponsors the ability to streamline drug development through shared control groups, study infrastructure and oversight. However, these protocols also involve increased complexities and design challenges that generally require a higher degree of coordination. Here, we highlight some key design and analysis considerations addressed in the draft guidance:

Randomization

Sponsors should consider allocating more subjects to control arms than for each individual drug arm to increase power and reduce the risk of a poorly or highly performing control arm. For a platform trial, a sponsor should create a plan for changes to the randomization ratios that can occur as products enter and exit a platform trial. In umbrella or platform trials comparing different drugs, the sponsor should ensure that the randomization process prevents subjects from being randomized to drugs they are not eligible to receive given each drug's exclusion criteria.

Informed Consent

Sponsors should cover all treatment arms in their informed consent and obtain consent prior to randomization. In a platform trial where drugs are entering and exiting the study, consent forms should be modified accordingly to reflect the drugs currently under evaluation. FDA also recommends the use of a central IRB to review informed consent forms, the protocol, and other relevant documents for monitoring of a trial conducted under a master protocol.

Blinding

Given the potential for different administration methods for various drugs included in umbrella or platform trials, unique blinding challenges may arise and sponsors should discuss their proposed approach to blinding with FDA early in the planning stage.

Safety Data

Safety data from a master protocol can be considered part of overall safety database but data from other sources may be needed to support approval. The type of master protocol and the drugs being evaluated will impact the approach to safety data collection. FDA also recommends that a data monitoring committee (DMC) or other independent, external entity review accumulating safety and efficacy data to minimize inadvertent dissemination of information that could pose risks to trial integrity.

Regulatory Review Considerations

Each master protocol should be submitted as a new IND, and FDA recommends that the sponsor request a pre-IND meeting to discuss the protocol and other IND submission details. Given the potentially rapid pace of changes in a master protocol, the draft guidance recommends specific

procedures for protocol amendments, including cover letters for each protocol amendment that update on the status of each drug and notifying the RPM at least 48 hours before submitting any protocol amendment that could substantively affect the master protocol. The IND should also include a well-designed communication plan to facilitate timely and effective communication between multiple stakeholders, including rapid communication of serious safety information and protocol amendments to investigators and FDA.

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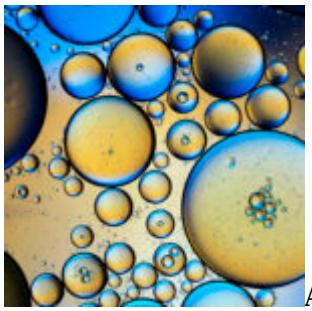
Comments on this draft guidance are due February 22, 2024. Please contact the authors or your Goodwin attorney with any questions or if you would like to submit a comment.

A Look Ahead in Life Sciences: What We Are Tracking in Q1 2024 and Beyond

 As the life sciences, medtech, and diagnostic industries continue to expand and grow increasingly complex, so does the legal, regulatory, and compliance landscape. To help companies and investors navigate the many evolving and emerging laws and regulations across pharmaceuticals, biologics, medical devices, diagnostics, and laboratory testing, our Life Sciences Regulatory & Compliance team has provided an overview of key developments. We update and publish a quarterly tracker detailing these developments. You can read about the Q1 2024 updates **here**.