**Structure and Function in Biomolecular Obviousness**

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During the late 20th Century, American patent doctrine for macromolecules developed around a structural obviousness paradigm drawn from cases concerning small molecules. This body of law was thrown into doubt by the Federal Circuit's 2009 decision in *In re Kubin*, which seems to have adopted a functional paradigm for biotechnology obviousness. But this shift in obviousness standards leaves troublesome gaps in the fabric of biotechnology patenting that remain unresolved a decade later, particularly with regard to the reciprocal requirements of patent disclosure. In this paper I carefully examine the history and substance of macromolecule obviousness to determine whether structural approaches can or should be the dominant paradigm.

**Antitrust and Biosimilars:**
**What's New and What's Not**

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Biologic drugs are the wave of the future. They make up 8 of the 10 top-selling drugs in the world. They offer revolutionary advances like treatments for cancer and incurable diseases. They are predicted to be a nearly $400 billion market by 2020. The importance of biologics is matched by their high price. Biosimilars offer hope. They are forecast to save as much as $250 billion in a 10-year period. But biosimilars cannot fulfill their promise if they cannot enter the market. In the early days of the industry, a range of activity that potentially violates the antitrust laws has blocked biosimilars.

This article discusses six types of conduct. Three have appeared in the small-molecule setting and promise to appear in similar form in the context of biologics: product hopping from one version of a drug to another, "citizen petitions" filed with the FDA, and denials of samples biosimilars need to enter the market. Two others have appeared but present novel issues: "reverse-payment" settlements between brands and generics (particularly in the context of "patent thickets") and a combination of bundling and rebates. And one is completely new: disparagement. As we go forward, we need to consider how old and new conduct in the biologics industry presents critical issues of competition, innovation, and public health.

# The Proposed EU IP Exception for Generics & Biosimilars Exports - A Cure Worse Than the Disease?

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The European Union plans to introduce an SPC waiver for Generics and Biosimilars intended for export to countries without patent protection. The aim is to minimize counterfeit medicines in developing countries and to promote more competition and earlier access to generics and biosimilars in Europe. But many challenges remain, including potential conflict with international treaty obligations, enforcement difficulties, and business decisions that could undermine a fundamental assumption of the new policy. This presentation will describe the proposal and discuss how it relates to US positions.

**Regulating Biosimilars at the FDA:**
**Current Issues and Trends**

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The Patient Protection and Affordable Care Act (ACA) is well known for introducing substantial changes to health care law. Nearly a decade later, the ACA remains politically contested and subject to judicial review. Less known is that the legislation also created a significant new abbreviated approval process for biological products, a process that is now well established by the implementing agency, the U.S. Food and Drug Administration (FDA). The Biologics Price Competition and Innovation Act (BPCIA), Title 7 of the ACA, sets forth a "biosimilar" route to market for biologics based on a product demonstrating that it is highly similar to an innovator biologic. A heightened showing of interchangeability garners interchangeable status, which subjects a product to recently-enacted state biologic substitution laws. The BPCIA also provides a twelve year exclusivity period for biologic innovator products, a one year exclusivity period for interchangeable products, and introduces a complicated disclosure process for industry dealing with patent rights. This presentation will highlight significant attributes of the biosimilar regulatory process and provide an overview of FDA activity to date.

**Patent Thickets in Biological Manufacturing**

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Competition and innovation in biosimilars are hindered by the complex, idiosyncratic manufacturing methods used to produce innovator biologics. One strategy is for biologics manufacturers to limit later competition by keeping their manufacturing methods as trade secrets, eschewing the limited disclosure of the patent system to rely on secrecy. In prior work, we have explored the problems with this approach, and why patents on biologics themselves provide insufficient disclosure to prevent secrecy. But at least some manufacturers have pursued a blended approach, where they complement some manufacturing secrecy with a set of patents on manufacturing methods, rather than just the biologic itself. Humira is a case in point, and is engaged in extensive litigation with respect to these patents. In this project, we examine the mechanics and implications of this strategy. We highlight what seems to be a logical catch-22 of manufacturing patents, especially those patents which are filed more than a year after approval (all of the patents in the case of Humira, in fact). For any patented processes that were used to make the biologic at the time of approval, under *Metallizing Engineering*, those patents should be invalid as in public use, even if the manufacturing processes were kept secret. For any patented processes that were *not* used to make the biologic at the time of approval, it is hard to see how biosimilar competitors are necessarily infringing those patents by making their versions of the approved biologic. In either case, this mixed strategy seems to raise problems both with enabling competition and with promoting post-approval manufacturing innovation.

**Form Follows Function:**
**Proper Antibody Patents After *Amgen v. Sanofi***

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There is an overlooked connection between software patents and patents for antibodies, a group of extraordinarily complex molecules that regulate the immune system. Software patents have long been criticized for being drafted too abstractly to meaningfully disclose concrete solutions to the problems they purport to solve, a practice known as functional claiming. After some academic criticism, especially in 2012, strictures to limit software patents gained substantial traction at a national level; courts and the patent office have begun to rein in functional claiming for software. But this has recently bled over to biologics patents, especially those concerning antibodies. Recently, in *Amgen v. Sanofi* (Fed. Cir. 2017), the Federal Circuit invalidated an otherwise robust antibody patent for a lack of sufficient written description while its analysis echoed that of functional claiming in software. This connection, sub rosa or not, is in error; functional claiming has and can play a positive role in antibody patents in a way it has not traditionally done for software. The promise and success of antibodies in the biotechnology industry stems from how they function: by uniquely binding to particular complex molecules on the surfaces of other cells. But it is often difficult, time consuming, and costly to determine precisely where on a surface molecule an antibody binds to. And, because antibodies are often inordinately large and complex molecules, it is too cumbersome to describe them at an atomic level, as is often done with small molecule drugs. For these reasons, patents on antibodies have long been drafted as functions of the molecules to which the antibodies bind. Explicitly understanding this practice as a species of functional claiming should help assess the propriety and limits of antibody patents. At a higher level, this way of thinking about antibody patents may provide insight into at least one normatively positive application of functional claiming.

**Are Methods of Treatment Patent Eligible?**

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Patent protection can encourage innovation in the biologic and biosimilar space, given the significant costs associated with developing and commercializing these types of inventions. Although innovators will often be able to obtain claims to protect compositions-of-matter and methods of manufacturing, claims related to methods of treatment are likely to be called into question.

Courts and the United States Patent and Trademark Office (USPTO) have struggled to apply the eligibility framework articulated by the Supreme Court. The two-step test set forth in Mayo/Alice instructs a court to determine (1) whether a claim is directed to a concept that is not patent eligible (such as a law of nature), and if so, (2) whether the elements of the claim, both individually and as an ordered combination, show an "inventive concept" that amounts to "significantly more" than the ineligible concept itself.

In recent years, both the USPTO and the courts have attempted to whittle the test into something more manageable. In the hopes of providing a workable approach to determining eligibility for patent examiners, who are typically not attorneys, the USPTO has issued Eligibility Guidance, though it sometimes seems inconsistent with decisions from the Federal Circuit Court of Appeals. And the Federal Circuit, after unsuccessful attempts to persuade the Supreme Court to clarify Mayo and Alice, has focused on the margins of the two-step test: questioning whether methods of treatment are necessarily "directed to" ineligible concepts, and holding claims that append a treatment step can be sufficiently transformative to rise to the level of eligibility. This discussion will describe the current state of patent eligibility for methods of treatment as they relate to biologics and biosimilars.

**The Impact of the Entry of Biosimilars**
**Evidence from Europe**

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Biologics represent a substantial and growing share of the U.S. drug market. Traditional "small molecule" generics quickly erode the price and share of the branded product upon entry, however only a few biosimilars have been approved in the US since 2015, thereby largely preserving biologics from competition. We analyze European markets, which have had biosimilar competition since 2006. Using our own survey, we analyze how market features and public policies predict biosimilar entry, price, and penetration, finding significant heterogeneity across countries and products. Effective buyer institutions are associated with increased biosimilar penetration. Our estimates can inform ongoing policy discussions.