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In *Biogen v. Serono* (September 28), the Federal Circuit clarified that so-called "product-by-process" language nested within a method of treatment claim should be analyzed in the same manner as product-by-process language in a composition claim – *i.e.,* by treating the process steps as ***not*** limiting the scope of the claimed product.

## Background: Facts & The Issue

Biogen sued Serono for infringement of a patent relating to a method of treatment of viral conditions (among other things) involving administration of "a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule," where at least a portion of the recombinant DNA molecule is capable of hybridizing to DNA of human fibroblast interferon (also known as interferon-β ("IFN-β")).[1]

Serono asserted that the claims were anticipated by two prior art references involving administration of native (*i.e.,* naturally-occurring) IFN-β. Two critical facts were not in dispute:

- Native IFN-β has the same amino acid sequence as the recombinant version; and
- Native IFN-β (harvested from human cells) was used in the prior art to treat viral conditions.

The dispute centered on whether the reference to "a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule" limited the claim to exclude, and thereby prevent anticipation by, the use of the corresponding native polypeptide. The legal issue, then, was whether the "recombinant" claim language limited the scope of polypeptides that would be within the scope of the claim. On general principle one might say, "Of course the language is limiting, it's in the claims !!" But there is a complication: Within the confines of this method of treatment, *as claimed*, the method is not distinguishable either structurally or functionally from administering the native polypeptide.[2]

After a five week trial, the jury found the claims anticipated. But the district court reversed the jury, granting JMOL of no anticipation in favor of Biogen "because treatment in the prior art entailed administration of native IFN-β, which was undisputedly not recombinantly produced." Thus, the district court treated the "recombinant" claim language as typical limiting language defining a characteristic of polypeptide of the claimed invention.

The district court also addressed whether the "recombinant" language invoked the product-by-process rules for claim interpretation, first holding that neither precedent nor policy required application of the product-by-process rules to a method of treatment claim and, second, holding that even if the product-by-process rules applied "the jury lacked substantial evidence that the native IFN-β protein as disclosed in [the prior art] was structurally or functionally identical to the claimed three-dimensional recombinant IFN-β protein."

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[1] For the non-molecular biologists, "hybridization" is simply a way of expressing a relatively high degree of similarity between the recombinant DNA sequence and the DNA encoding native IFN-β. The set of "comparator" DNA sequences were, in essence, *in vitro* versions of DNA encoding for naturally-occurring interferon-β. The hybridization criteria also allow the claims to cover variations of the precise DNA sequence that do not materially affect the final structure or function of the polypeptide. As explained by the patent-at-issue: "The recombinant DNA molecules disclosed herein are characterized by DNA sequences that code for polypeptides whose amino acid sequence and composition are substantially consistent with human fibroblast interferon and which have an immunological or biological activity of human fibroblast interferon." US 7,588,755 at col. 1, lines 19-24. The specification highlights how the invention is not a new form of interferon- β but rather permits the synthetic production of interferon-β in large quantities. *See, e.g.,* US 7,588,755 at col. 6, lines 64-67.

[2] For example, from the perspective of the patient's blood stream and interferon receptors both native and recombinant polypeptides "look" identical, at least to the level of amino acid sequence, and "act" identically, at least as far as anti-viral activity. There is, nevertheless, at least one structural distinction between the recombinant and native versions: The recombinant polypeptide lacks the glycosylation of the native polypeptide. But this distinction is not reflected in claim language and therefore was not at issue.

Serono appealed.

## Background: Relevant Black Letter Law

1. Claim Interpretation – Product-by-Process[3]
   a. *Defined:* A product-by-process claim is "one in which the product is defined at least in part in terms of the method or process by which it is made."[4]
   b. *Policy/Purpose:* Allows inventors to claim "an otherwise patentable product that resists definition by other than the process by which it is made."[5]
      i. Product-by-process claiming therefore prevents an inventor from being foreclosed from the benefits of the patent system simply because a product is difficult to describe in words, or its structure is insufficiently understood.
      ii. But, use of product-by-process language has not been strictly limited to situations in which it is difficult or impossible to describe a product other than by reference to the process of making it.[6]
   c. *Effect:* Product-by-process claim language does ***not*** limit the claimed product to a product made using the recited process.
      i. Policy: "It has long been established that one cannot avoid anticipation by an earlier product disclosure by claiming the same product more narrowly, that is, by claiming the product as produced by a particular process."[7] Also, allowing process limitations in a composition claim impermissibly combines and crosses the patent-eligibility line between the two separate statutory classes of "process" and "composition."[8]
      ii. Validity/patentability: The product itself must be novel and unobvious standing alone without regard to how it was made.
         1) "It has long been the case that an old product is not patentable even if it is made by a new process" and "a new product may be patented by reciting source or process limitations so long as the product is new and unobvious."[9]
         2) "The patentability of a product does not depend on its method of production" and "[i]f the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."[10]
      iii. Infringement: The argument that a product-by-process claim "is only infringed when the process of the claim is used" has been squarely rejected by the Federal Circuit,[11] and claims must be construed the same for validity and infringement.
      iv. Recombinant DNA situations:
         1) *Amgen Inc. v. F. Hoffmann-La Roche Ltd.*:[12] In connection with claims relating to recombinant erythropoietin, the Federal Circuit acknowledged that the claim language "purified from mammalian cells grown in culture" serves to "clearly limit[] the source of the EPO used in the claimed 'pharmaceutical composition,'" but held

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[3] Because this section covers only the black letter law that is relevant to the case, here a litigation determination of invalidity, I do not summarize the PTO's manner of handling examination of product-by-process claims (which involves the broadest reasonable construction of claims and certain presumptions and burden shifting due to the PTO's inability to perform laboratory testing to determine similarities and differences between prior art products and a product claimed by the process of making it).

[4] *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.,* 489 U.S. 141, 158 n. (1989).

[5] *In re Thorpe,* 777 F.2d 695, 697 (Fed. Cir. 1985); *see also Application of Brown,* 459 F.2d 531, 535 (CCPA 1972).

[6] *E.g., Smithkline Beecham Corp. v. Apotex Corp.,* 439 F.3d 1312, 1315 (Fed. Cir. 2006) ("Today, however, product-by-process claims are used by inventors even if the invention could have been described independent of the process"); *see also Gen. Elec. Co. v. Wabash Appliance Corp.,* 304 U.S. 364, 373, (1938)("[I]n some instances a claim may validly describe a new product with some reference to the method of production...."); *In re Luck,* 476 F.2d 650, 653 (CCPA 1973) ("[I]t is well established that product claims may include process steps to wholly or partially define the claimed product."); *Amgen Inc. v. F. Hoffmann-La Roche Ltd.,* 580 F.3d 1340 (Fed. Cir. 2009)("a new product may be patented by reciting source or process limitations so long as the product is new and unobvious").

[7] *Smithkline Beecham,* 439 F.3d at 1317 (Fed. Cir. 2006).

[8] *See In re Thorpe,* 777 F.2d at 698 (explaining that Congress can change the rules to allow product claims to be limited to a particular process of manufacturing).

[9] *Amgen Inc. v. F. Hoffmann-La Roche Ltd.,* 580 F.3d 1340, 1366 (Fed. Cir. 2009).

[10] *In re Thorpe,* 777 F.2d at 697.

[11] *In re Thorpe,* 777 F.2d at 698.

[12] 580 F.3d 1340 (Fed. Cir. 2009).

that it was necessary to determine whether "the production of EPO by recombinant technology resulted in a new product, so that claim 1 was not anticipated by the urinary EPO of [the prior art]."

d. *Inconsistency or Aberration:* One Federal Circuit case[13] held that process steps in a product-by-process claim ***do*** serve as claim limitations, at least in the infringement context.

   i. Citing precedent that "has repeatedly stated that infringement requires the presence of every claim limitation or its equivalent," this case explains that "ignoring the claim limits of a product-by-process claim would clash directly with basic patent principles" and holding that "process terms in product-by-process claims serve as limitations in determining infringement."[14]

   ii. However, multiple dissents in this case assert that the majority opinion is wrong and contrary to Federal Circuit precedent.[15]

**What *Biogen v. Serono* Adds or Changes:**

The Federal Circuit reversed the district court's JMOL and determined that the claims were anticipated under existing precedent, clarifying that product-by-process language nested within a method of treatment claim should be analyzed in the same manner as product-by-process language in a composition claim.

*Application of Precedent.*

The Federal Circuit explained that the "key question for anticipation here, as in *Amgen*, is thus whether the recombinant product is identical to the prior art product – not whether the prior art product was made recombinantly." As to the claims here, the court reasoned:

- The claimed recombinant IFN-β polypeptide must distinguish over the prior art native IFN-β polypeptide. "As in Amgen, the recombinant origin of the recited composition cannot alone confer novelty on that composition if the product itself is identical to the prior art non-recombinant product."
- The "recombinant" limitations do not limit the structure of the claimed IFN-β polypeptide. "The requirements that the claimed polypeptide is 'recombinant' and 'produced by a non-human host transformed by a recombinant DNA molecule' . . . describe the process by which the product, *i.e.,* the "polypeptide," is formed. These are not additional structural limitations."
- Accordingly, "the district erred in concluding that the mere absence of recombinantly produced IFN-β in the prior art was sufficient to grant JMOL of no anticipation."

*"Nested" Product-by-Process Limitations.*

Biogen argued that *Amgen* was "limited to composition claims and is not applicable to the method of treatment claims at issue here." The Federal Circuity did not agree, holding that a composition limitation drafted in product-by-process language nested within a method of treatment claim must be analyzed just like a stand-alone composition claim drafted in product-by-process language:

- "There is no logical reason why the nesting of a product-by-process limitation within a method of treatment claim should change how novelty of that limitation is evaluated."
- "If the novelty of the recombinant IFN-β composition requires comparing its structure to the structure of native IFN-β, as *Amgen* requires, it would defy all reason to excuse that analysis for a method of administration claim using that composition."

*Manufacturing Advantages Not Relevant.*

The Federal Circuit criticized the district court for relying on the advantages of manufacturing – *i.e.,* recombinant technology allowing production of large quantities of IFN-β. Although the manufacturing point

[13] *Atlantic Thermoplastics Co., Inc. v. Faytex Corp.*, 970 F.2d 834 (Fed. Cir. 1992).

[14] *Atlantic Thermoplastics,* 970 F.2d at 846-47.

[15] *Atlantic Thermoplastics Co., Inc. v. Faytex Corp.*, 974 F.2d 1279 (Fed. Cir. 1992)(dissents filed in connection with denial of re-hearing *en banc*).

"may well be relevant in considering the novelty of the recombinant *process,* . . . a new process, regardless of its novelty, does not make an old product created by that process novel."

*Three-Dimensional Structure Not Relevant.*

The Federal Circuit also criticized the district court for relying on the three-dimensional of recombinant IFN-β peptide to distinguish the prior art as relating to unclaimed limitations:

- "The 'product' administered in the claimed method is the 'polypeptide.'"
- Biogen's patent explicitly defined "polypeptide" as a "linear array of amino acids connected one to the other by peptide bonds between the α-amino and carboxy groups of adjacent amino acids."
    - Thus, the "polypeptide" structure was "defined by reference to its 'linear' array [of amino acids], without regard to its [three-dimensional] folded protein structure."
- The district court charged the jury with an instruction consistent with Biogen's chosen claim drafting and lexicography, and Biogen neither objected nor offered a jury instruction relating to three-dimensional structure.
- Moreover, nothing in the claim requires any particular three-dimensional structure. Although Biogen argued that the claim language regarding therapeutic effectiveness and anti-viral activity implicitly brought three-dimensional structure into the claim, the Federal Circuit disagreed:
    - First, "Biogen's argument fails to give effect to Biogen's explicit definition of 'polypeptide' in the specification," which defined "polypeptide" merely in terms of a sequence of amino acids without reference to three-dimensional structure, and "[w]e must respect this lexicographic choice."
    - Second, although "an amino acid sequence alone cannot give rise to antiviral activity," it is equally true that every linear sequence of [amino acids] will fold into some three-dimensional configuration." Thus, Biogen drafted its claims such that the "claimed antiviral activity can arise from the administration of any three-dimensional protein with a linear amino acid sequence identical to the claimed recombinant 'polypeptide.'"
    - Third, "Biogen did not ask for a jury instruction on anticipation that required comparing the three-dimensional protein structures of prior art IFN-β and the claimed recombinant IFN-β."

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Closing thoughts:

- Perhaps the Federal Circuit will take this case up *en banc* and revisit the issues in *Atlantic Thermoplastics* or perhaps the Supreme Court will grant *certiorari*. It's not crazy to want all claim limitations to have effect, but there are the underlying issues of combining multiple statutory classes into one claim (a form of claiming that Congress has not yet approved) and of allowing prior art products to be claimed anew based on a new manufacturing process (which could trigger a large volume of expensive, complex patent litigations delving into sensitive – and often trade secret – manufacturing processes without a lot of benefit over the current system of keeping compositions and processes in separate "bins").
    - Biogen needs to consider the possibility that the *en banc* Federal Circuit and/or the Supreme Court decide that product-by-process claim language is flawed and unsupportable unless and until Congress expressly permits it.
- Why didn't Biogen request a jury instruction on three-dimensional structure (or object to the lack of such an instruction)? Two ideas come immediately to mind:
    - It might have been a tactical move to avoid giving Serono an appeal issue if Biogen succeeded in convincing the jury that the claims were not anticipated. The district court likely would have given that instruction, since it relied on that issue in granting JMOL. But that would have been dangerous on appeal, providing a vulnerability Biogen thought it could avoid (presumably because it thought the jury would decide the anticipation question in Biogen's favor).
    - Biogen might also have been concerned that there was insufficient evidence adduced at trial to support a "no anticipation" decision by the jury based on three-dimensional structure (or insufficient evidence to support a claim construction that brought three-dimensional structure into the claim) and Biogen was thinking ahead about how the Federal Circuit would handle the claim construction and substantial evidence issues.