2019-1133

United States Court of Appeals for the Federal Circuit

BIOGEN MA INC.,

Plaintiff-Appellee,

– v. –

EMD SERONO, INC., PFIZER INC.,

Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC., NOVARTIS PHARMACEUTICALS CORPORATION,

Defendants.

On Appeal from the United States District Court for the District of New Jersey in No. 2:10-cv-02734-CCC-MF Hon. Claire C. Cecchi

PETITION FOR PANEL REHEARING AND REHEARING *EN BANC* FOR PLAINTIFF-APPELLEE

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OCTOBER 28, 2020

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 19-1133

Short Case Caption Biogen MA Inc. v. EMD Serono, Inc.; Pfizer Inc.

Filing Party/Entity Biogen MA Inc.

Instructions: Complete each section of the form. In answering items 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance. **Please enter only one item per box; attach additional pages as needed and check the relevant box**. Counsel must immediately file an amended Certificate of Interest if information changes. Fed. Cir. R. 47.4(b).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 10/28/2020

Signature: /s/ Nicholas Groombridge

Name: Nicholas Groombridge

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☑ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Biogen MA Inc.		Biogen Inc.

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

☐ None/Not Applicable ☐ Additional pages attached

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5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

☐ None/Not Applicable ☐ Additional pages attached

The present case on appeal as between Biogen MA Inc. against EMD Serono, Inc. and Pfizer Inc. was part of a previously consolidated case of Bayer HealthCare Pharmaceuticals Inc. v. Biogen Idec Inc. (Civ. No. 10-cv-02734) and Biogen Idec MA Inc. v. EMD Serono, Inc.; Pfizer, Inc.; Bayer Healthcare Pharmaceuticals Inc.; and Novartis Pharmaceuticals Corp. (Civ. No. 10-cv-02760). On October 27, 2017, the case against EMD Serono, Inc. and Pfizer Inc. was severed from the case against Bayer HealthCare Pharmaceuticals Inc. and Novartis Pharmaceuticals Corp. The case against Bayer HealthCare Pharmaceuticals Inc. and Novartis Pharmaceuticals Corp. is currently pending in the District Court for the District of New Jersey before Judge Claire C. Cecchi.

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

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STATEMENT OF COUNSEL

Based on my professional judgment, I believe the panel decision is contrary to at least the following precedent of this Court: *Amgen Inc. v. Hoffman-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009).

Based on my professional judgment, I also believe this appeal requires an answer to the following precedent-setting question of exceptional importance:

1. Whether an anticipation analysis comparing a prior art product to a claimed product-by-process requires considering all of the physical, structural differences between the prior art product and the product that results from the claimed process.

/s/ Nicholas Groombridge
ATTORNEY OF RECORD FOR
PLAINTIFF-APPELLEE

POINTS OF LAW AND FACT OVERLOOKED OR MISAPPREHENDED BY THE COURT

Pursuant to Federal Circuit Rule 35(e)(1)(F) and Federal Rule of Appellate Procedure 40(a)(2), Biogen respectfully identifies these points of law or fact overlooked or misapprehended in the panel decision.

1. The panel misapprehended the requirement of *Amgen Inc. v. Hoffman-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), that the composition that is the product of the claimed process be compared to the prior art compositions, including all their structural features. The district court correctly performed that comparison in granting JMOL of no anticipation, tracking the analysis approved in *Amgen*. Appx22–29 (JMOL Op.).

2. The panel misapprehended the structure of the "polypeptide" produced by the claimed process, wrongly equating it with the amino acid *sequence* of the molecule and ignoring the sugars that are part of those amino acids. This led the panel to disregard the district court's finding that, on the record evidence, no reasonable jury could conclude that the product of the claimed process—recombinant interferon-beta—was identical to the prior art native, human interferon-beta.

3. The panel misapplied Third Circuit precedent governing review of a district court decision conditionally granting a new trial. *See Lind v. Schenley Indus., Inc.*, 278 F.2d 79, 89 (3d Cir. 1960). As a result, the panel overrode the

district court's discretion to weigh the presentation of Appellants' anticipation defense in the overall setting of a lengthy trial, during which that defense received scant attention.

INTRODUCTION

The '755 Patent claims treatment of diseases by administering a composition comprising a recombinant polypeptide that has the biological activity of native, human interferon-beta. This invention led to use of recombinant interferon-beta as the first successful therapy for multiple sclerosis.

Following a five-week trial, the jury found that Appellants infringe the '755 Patent, and it rejected the obviousness, written-description, and enablement defenses that were the centerpieces of Appellants' defense. The jury rendered a verdict, however, that the claimed treatment with recombinant interferon-beta was anticipated by prior-art uses of native, human interferon-beta. After trial, the district court granted judgment as a matter of law of no anticipation, finding that "[t]he evidence presented at trial demonstrates that native interferon-β and recombinant interferon-β are not structurally identical." Appx23 (JMOL Op.). Given its review of the evidence and the minimal attention paid to Appellants' anticipation defense during the five-week trial, the court also conditionally granted a new trial on anticipation.

A panel of this Court reversed. Answering an open question of law, the panel held that product-by-process law should apply to the patent's method-of-treatment claims and that its recombinant-host "source limitations" must therefore be ignored in assessing anticipation. The panel ruled that the proper analysis is whether the product of the recited process is itself found in the prior art.

Biogen does not challenge those rulings. Biogen seeks rehearing because the panel *failed to apply* the test for novelty it announced.

The panel's decision breaks new ground in a startling direction. It permits a jury to find anticipation where the claimed composition that is the product of the claimed process did not exist in the prior art.

The panel's decision also impinges on the broad discretion afforded district courts to conditionally certify a new trial on issues that received short shrift before the jury. As the district court found, "[t]he jury spent the vast majority of the trial hearing fact and expert testimony on issues other than anticipation." Appx36 (JMOL Op.). Indeed, Appellants did not even mention anticipation in closing argument. The district court set out findings that fully support its exercise of discretion to order a new trial on anticipation should the judgment of no anticipation be reversed. The panel decision summarily dismissed those findings. If the Court declines to grant rehearing, it should reinstate the district court's grant of a new trial on anticipation.

BACKGROUND

Interferon-Beta

To fend off viruses, the human immune system makes proteins called "interferons." *See, e.g.*, Appx77873 (24:3–18); Appx77323 (13:10–21). The protein relevant here, interferon-beta, exists in only infinitesimal amounts in human cells. *See, e.g.*, Appx119 (4:49–55); Appx66143. Dr. Fiers, the inventor of the '755 Patent, was the first to recombinantly express interferon-beta-like proteins and to demonstrate that they have the biological activity of native, human interferon-beta such that they could be made in sufficient amounts and used therapeutically. *See* Appx136–140 (37:18–46:37). In 1980, that was unprecedented. The jury found Dr. Fiers' invention not obvious, a finding Appellants do not challenge.

Like all proteins, interferon-beta is made of amino acid building blocks. Appx77878 (29:2–13). Interferon-beta consists of 166 amino acids, connected end-to-end in a linear array. Appx77878 (29:19–22). In human beings, interferon-beta is a "glycoprotein," *i.e.*, one of its amino acids includes a branched structure of sugar groups. Appx77882 (33:9–25). The sugar branches can vary from protein to protein, even when made within the same cell. Appx28 (JMOL Op.).

Where human glycoproteins are made recombinantly in non-human hosts, the amino acids can include different sugar branches, or none at all. *E. coli*, for

example, does not glycosylate proteins. Appx79094 (47:12–21); Appx80514–80515 (100:5–101:2). Chinese Hamster Ovary ("CHO") cells, in turn, glycosylate proteins but differently than human cells do. Appx23744 ('930 Appl., 3/24/97 Amendment); Appx24315 ('843 Appl., 4/4/96 Amendment); Biogen Br. at 21.

That is a critical difference here. In native, human interferon-beta, the sugar groups are part of the amino acid asparagine at position 80 in the polypeptide. When made in *E. coli*, that asparagine is physically different, lacking any glycosylation, and when made in CHO cells it is physically different because the glycosylation is different than when made in human cells. Appx24–25 (JMOL Op.); Appx79094 (47:1–21); Appx80514–80515 (100:5–101:2); Biogen Br. at 23–26. The '755 Patent itself explains that changes in glycosylation result in changes *to the amino acids themselves*:

> The structure of the polypeptide depicted in FIG. 4 for the composite fragment, of course, does not take into account any modifications to the polypeptide caused by its interaction with in vivo enzymes, e.g., glycosylation. Therefore, it must be understood that the amino acid sequence depicted in FIG. 4 may not be identical with HuIFN-β produced in vivo.

Appx130 (26:49–54).

The Asserted Claims of the '755 Patent

The '755 Patent discloses that therapeutic use of native, human interferon-beta was known in the prior art, Appx118–119 (2:53–4:22), and describes how compositions of native, human interferon-beta had been prepared, Appx119–120

(4:49–5:3). Its claims were limited to a method of treatment with "a therapeutically effective amount of a composition," said composition comprising a *recombinant* interferon-beta-like polypeptide made in a *non-human host* transformed by certain DNA sequences. Appx142 (49:59–50:12). During prosecution of a sister application, Biogen explained that the "non-human" host limitation was added for the purpose of distinguishing recombinant interferon-beta from native interferon-beta:

> As amended, the claims expressly recite production in non-human cells. . . . This is not semantics. IFN-β produced in human cells is glycosylated and has a particular type and content of sugar groups. The claimed polypeptides do not have the identical type or content of sugar groups. They cannot have. They are produced in non-human cells whose ability to post-translationally modify proteins is different from that of human cells.

Appx24315 ('843 Appl., 4/4/96 Amendment).

ARGUMENT

I. The Court Should Grant Panel Rehearing or Rehearing En Banc

The panel's anticipation decision suffers from three key errors, each warranting rehearing. First, the panel failed to apply this Court's precedent in *Amgen*, because it did not compare the structure of the composition administered in the claimed method of treatment to the structure of compositions used in the prior art. Second, based on scientific errors that led to a misunderstanding of the structure of interferon-beta, the panel wrongly equated the "polypeptide" of the asserted claims—a physical thing that is the product of the recited process—with an abstract listing of amino acids in a sequential order, and then concluded that the amino acids in native and recombinant interferon-beta are identical despite the uncontroverted evidence, and the district court's express finding, that they are different. Third, the panel misunderstood the jury instructions to have required the jury "to decide anticipation based on the linear amino acid sequence," whereas the jury was actually instructed to determine whether the "identical invention" was made, used, or disclosed before.

Unless corrected by the Court, the panel decision will fundamentally alter the anticipation analysis for product-by-process claims to permit litigants to ignore structural differences between prior art products and the products of a claimed process.

A. The Panel Decision Failed To Apply *Amgen*, Which Requires Comparing the Prior Art Composition to the Composition that Results from the Process of the Asserted Claims

The panel held that product-by-process law applies to the asserted claims and that, under *Amgen*, ascertaining "the novelty of the recombinant IFN-β *composition* requires comparing its structure to the structure of native IFN-β." Op. 14 (emphasis in original). Whether product-by-process law applies to method-of-treatment claims was a question of first impression in this appeal, and Biogen does not seek rehearing of that question. But the panel then failed to apply the product-by-process law it adopted.

The claims are directed to a method of administration of a "composition comprising a recombinant polypeptide" that is produced according to the process recited in the claims, which requires production of the recombinant polypeptide in a non-human host. Appx142 (49:59–50:12). It is undisputed that the amino acids that make up recombinant interferon-beta produced according to the process of the claims include sugar groups when made in a variety of non-human mammalian cells, such as CHO cells. Appx79720 (86:2–15); Serono Principal Br. at 36. Because sugar branches can vary from polypeptide to polypeptide—even when made within the same host—the claimed composition contains a mixture of many polypeptides with many different glycosylation patterns. Appx28 (JMOL Op.). It

is the structure of *this* composition that must be compared to prior art compositions under the *Amgen* test on which the panel relied.

The panel undertook no such comparison. It began by stating that "the key question for anticipation is whether the native 'polypeptide' is identical to the '*polypeptide' 'produced by' the recited recombinant process*." Op. 16 (emphasis added). But the panel did not answer this question. Instead, it ruled that because "[t]he *sequential order* of the amino acid residues for native IFN-β is the same as the sequential order of the amino acid residues for recombinant IFN-β," the "native IFN-β polypeptide and the claimed recombinant polypeptide are identical for purposes of the instant claim." Op. 17 (emphasis added). In so ruling, the panel disregarded the district court's independent, alternative basis for JMOL of no anticipation, set out in a separate section of the opinion entitled "JMOL Of No Anticipation Is Appropriate Even Applying Product-By-Process Law." Appx22 (JMOL Op.). There, the district court applied what the panel held is the proper factual and legal analysis, *i.e.*, comparing the physical polypeptides themselves. As the district court found, "the record evidence shows that the proteins differ structurally in terms of their attached carbohydrates (or sugar) groups, also referred to as glycosylation patterns." Appx23 (JMOL Op.). Appellants' own expert testified that "[t]here were minor differences in the structures of the sugars" of

recombinant and native interferon-beta, such that he "*wouldn't call them identical*." Appx79721–79722 (87:3–88:7) (emphasis added).

The panel's failure to consider the structure of the recombinant polypeptide that was the actual *product* of the claimed process, the test articulated in *Amgen*, was error. If not corrected it will profoundly change product-by-process law. The Court should grant rehearing to correct the panel's error and clarify that in assessing the novelty of a method of treatment using a product claimed as a product-by-process, the factfinder must compare *all* the prior art product's structural features with *all* the structural features of the claimed product produced by the recited process.

B. The Panel Decision Improperly Equated the "Linear Array" of Amino Acids with a List of Amino Acids

In its discussion of the "polypeptide" of the claimed composition, the panel misapprehended the evidence and ignored the structural modifications imparted by the process by which the polypeptide is made. The panel believed it was constrained by the '755 Patent's definition of a "polypeptide" as a "linear array of amino acids connected to one another by peptide bonds between the α-amino and carboxy groups of adjacent amino acids." Appx121 (8:62–64). On that basis, the panel ruled that to assess novelty, only the "sequential order of the amino acid residues" in the polypeptide mattered. Op. 17. This was error. Every polypeptide is a linear array of amino acids, but that linear array is a physical thing made up of

physical things, and the structure of the same amino acid can vary from polypeptide to polypeptide. The panel replaced this physical structure with an abstract idea—an amino acid sequence—and then held that because the '755 Patent would encompass administration of a polypeptide consisting of the same 166 amino acid residues found in the native protein, in the same sequential order, the "polypeptide" of the claim necessarily is identical to prior-art polypeptides. Op. 17.

What matters for novelty, however, is not only whether native and recombinant interferon-beta each consist of 166 amino acids with a methionine in position 1, a serine in position 2, a tyrosine in position 3, on through to an arginine in position 165 and an asparagine in position 166 (the '755 Patent sets forth this sequence in Figure 4). What matters equally is whether the methionine in position 1 in the recombinant protein *is the same as* the methionine in position 1 in the native protein, etc.

As the district court found, the record evidence showed that the amino acids themselves *are not the same* in recombinant and native interferon-beta. Appx24 n.11 (JMOL Op.). The panel's decision overlooks the process of post-translational modifications, by which different hosts modify amino acids in different ways when the amino acids are linked together to form a polypeptide. Appx24315 ('843 Appl., 4/4/96 Amendment); Appx79094 (47:12–21);

Appx80514–80515 (100:1–101:2). Thus, whereas the asparagine at position 80 in native interferon-beta includes one or more glycosylation groups, Appx51643 (Kagawa); Appx77882–77883 (33:9–34:6); Appx79680–79681 (46:17–47:3), the cognate asparagine in *recombinant* interferon-beta either does not include glycosylation groups at all (if made in *E. coli*, for example) or includes glycosylation groups *different from* human glycosylation groups (if made in CHO cells, for example). Appx28 (JMOL Op.); Appx51643, Appx51646 (Kagawa). The district court expressly found that "the record evidence shows that the proteins differ structurally in terms of their attached carbohydrate (or sugar) groups, also referred to as glycosylation patterns." Appx23 (JMOL Op.).

The panel appears to have misunderstood this, because it mistakenly cited the district court as having stated that "the attached carbohydrate groups in native IFN-β protein were glycosolated, and the attached carbohydrate groups in recombinant IFN-β were *not* glycosolated." Op. 8 (emphasis in original). To be clear, the carbohydrate (sugar) groups are not themselves glycosylated; the carbohydrate groups *are* the glycosylation, and the amino acids *are* glycosylated. Appx23 (JMOL Op.).

That matters, because, while the panel found that the amino acids are the same, it did so only by ignoring the sugar groups that are *part of the amino acids*. The '755 Patent itself explains, in referring to the amino acid sequence in Figure 4,

that "[t]he structure of the polypeptide depicted in FIG. 4 for the composite fragment, of course, does not take into account any modifications to the polypeptide caused by its interaction with in vivo enzymes, e.g., glycosylation." Appx130 (26:49–52).

As the district court found, there was no record evidence from which a reasonable jury could find that the amino acids in recombinant interferon-beta are identical to the amino acids in native, human interferon-beta. Appx22 (JMOL Op.). In rejecting the district court's JMOL findings, the panel misapplied the law and misapprehended the facts.

C. The Panel Decision Misstated the Relevant Jury Instructions

In ignoring the undisputed differences in sugar groups, the panel relied on the jury having been instructed "to decide anticipation based on the linear amino acid sequence." Op. 18. Respectfully, the panel was mistaken. The instruction to which the panel referred did not concern anticipation; it appeared in a separate section explaining the meaning of technical terms with which a lay jury would not be familiar. Appx47651 (Final Jury Instructions). The anticipation instructions contain no reference to "polypeptide" or to comparing the "sequential order of amino acid residues" in recombinant interferon-beta and native interferon-beta. Rather, the jury was instructed, in accordance with the Federal Circuit Bar Association pattern anticipation charge, that "inventions are new when the

identical invention has not been made, used, or disclosed before." Appx47665 (Final Jury Instructions). The invention here is based on the novelty of the "composition" being administered, which undisputedly was not found in the prior art.

The Verdict Form confirms the charge to the jury. Its anticipation question, Question 12, read:

> Do you find, by clear and convincing evidence, that the claims of the '755 patent are invalid as anticipated by prior art uses of native human interferon-beta?

Appx68295 (Verdict Form). Thus, nowhere was the jury asked to decide anticipation by comparing "linear amino acid sequences"; it was instructed to determine whether the "identical invention" was made, used, or disclosed before. Appx47665 (Final Jury Instructions).

When the district court reviewed the evidence post-trial, it expressly found that the structure of native, human interferon beta was not identical to the structure of recombinant human interferon beta. The panel did not review this finding for clear error, as *Amgen* would require. Just as in *Amgen,* the product of the recombinant process claimed in the '755 Patent was a product having sugar groups that were different from the sugar groups of the prior art products (or no sugar groups at all). Appx23 (JMOL Op.); Biogen Br. at 23–26. And just as in *Amgen,*

there was no error in the district court's grant of JMOL of no anticipation on this basis.

II. The District Court's Finding that a New Trial on Anticipation Is Warranted Should Be Reinstated

If the Court declines to grant rehearing, it should reinstate the district court's conditional order of a new trial on anticipation. As the Supreme Court has explained, "[t]rial judges have the 'unique opportunity to consider the evidence in the living courtroom context,' while appellate judges see only the 'cold paper record.'" *Gasperini v. Ctr. for Humanities, Inc.*, 518 U.S. 415, 438 (1996) (citations omitted). That is especially true here, where the district court presided over a "long and complicated" five-week trial "noticeably focused on issues other than anticipation, and involv[ing] scientific concepts that are not the 'subject matter . . . lying within the ordinary knowledge of jurors.'" Appx36 (JMOL Op.).

The district court supported its conditional grant of a new trial with extensive findings, including that "[t]he jury spent the vast majority of the trial hearing fact and expert testimony on issues other than anticipation; indeed, in contrast with their other invalidity theories, Defendants did not mention anticipation or Question 12 of the Verdict Form once in their summation." Appx36 (JMOL Op.). Taken together, these findings fully support the district court's exercise of its discretion to grant a new trial.

The panel set aside the district court's findings in a single sentence: "None of the additional considerations noted by the district court in support of its conditional grant of a new trial are independently sufficient to support its decision." Op. 19. That is the wrong standard. The proper inquiry under Third Circuit law is to view the verdict in "the overall setting of the trial," *Lind*, 278 F.2d at 89, not to analyze individual considerations in isolation. *See also Wilburn v. Maritrans GP Inc.*, 139 F.3d 350, 354, 363–64 (3d Cir. 1998) ("trial judge observes the witnesses and follow[s] the trial in a way that we cannot replicate by reviewing a cold record.").

This case shows why district courts may grant new trials conditionally: in the context of the overall trial, Appellants' anticipation evidence was slight at best. The district court, exercising its discretion, concluded that if its grant of JMOL were reversed, a new trial was warranted. The panel's decision negates district courts' ability to manage their trial dockets and assure that verdicts reflect the weight of the evidence. If the Court declines to grant rehearing on the merits of the panel's ruling, it should at the very least reinstate the district court's grant of a new trial on anticipation.

CONCLUSION

For the reasons set forth above, this Court should grant panel rehearing, en banc rehearing, or reinstate the district court's grant of a new trial on anticipation.

Dated: October 28, 2020

Respectfully submitted,

/s/ Nicholas Groombridge

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ADDENDUM

United States Court of Appeals for the Federal Circuit

BIOGEN MA INC.,
Plaintiff -Appellee

v.

EMD SERONO, INC., PFIZER INC.,
Defendants-Appellants

BAYER HEALTHCARE PHARMACEUTICALS INC., NOVARTIS PHARMACEUTICALS CORPORATION,
Defendants

2019-1133

Appeal from the United States District Court for the District of New Jersey in No. 2:10-cv-02734-CCC-MF, United States District Judge Claire C. Cecchi.

Decided: September 28, 2020

NICHOLAS P. GROOMBRIDGE, Paul, Weiss, Rifkind, Wharton & Garrison LLP, New York, NY, argued for plaintiff-appellee. Also represented by PETER SANDEL, ERIC ALAN STONE, JENNY CHIA CHENG WU, JOSEPHINE YOUNG; DAVID J. BALL, JR., Washington, DC; JOHN D. TORTORELLA, KEVIN H. MARINO, Marino Tortorella & Boyle, PC, Chatham, NJ.

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Before NEWMAN, LINN, and HUGHES, *Circuit Judges*.

LINN, *Circuit Judge*.

This appeal arises from a suit filed by Biogen MA, Inc. ("Biogen") against EMD Serono, Inc. and Pfizer, Inc. (collectively "Serono") in the District of New Jersey.[1] The suit alleged contributory and induced infringement of Biogen's U.S. Patent Number 7,588,755 ("'755 patent") by the sale and marketing in the United States of Rebif, a recombinant interferon-ß ("IFN-ß") product used for the treatment of Multiple Sclerosis ("MS"). After a five-week trial, a jury found that the '755 patent claims were anticipated by two references teaching the use of native IFN-ß to treat viral diseases: Kingham *et al.*, *Treatment of HBsAg-positive Chronic Active Hepatitis with Human Fibroblast Interferon*, 19(2) Gut 91 (1978) ("Kingham") and Sundmacher *et*

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[1] Biogen also asserted infringement claims against Bayer Healthcare Pharmaceuticals Inc. ("Bayer") and Novartis Pharmaceuticals Corp. ("Novartis"). The actions against Bayer and Novartis were severed from those giving rise to this appeal. Order Granting Bayer's Motion to Sever, Oct. 27, 2017, ECF No. 743. Bayer filed an amicus brief here.

al., *Human Leukocyte and Fibroblast Interferon in a Combination Therapy of Dendritic Keratitis*, 208(4) Albrecht von Graefes Archiv für Klinische & Experimentelle Opthalmologie 229 (1978) ("Sundmacher"). The jury also held the asserted claims not invalid for lack of enablement or written description, or for obviousness. Finally, the jury held that patients and prescribers directly infringed the asserted claims and that Serono contributorily infringed the claims but did not induce infringement thereof.

On cross-motions, the district court granted judgment as a matter of law ("JMOL") of no anticipation in favor of Biogen and conditionally granted a new trial on anticipation. *In re Biogen '755 Patent Litig.*, 335 F. Supp. 3d 688 (D.N.J. 2018) ("*Biogen I*"). The district court also ruled in favor of Biogen: sustaining the jury's verdict of no invalidity based on written description or enablement; overturning the verdict of no induced infringement; sustaining the verdict of contributory infringement; and holding that the '755 patent claims were not patent ineligible. *Id.* Serono appeals the district court's JMOL rulings on anticipation, written description, enablement, contributory infringement, induced infringement and patent eligibility. We have jurisdiction under 28 U.S.C. § 1295(a).

Because a reasonable jury could find the claims of the '755 patent anticipated on the record presented in this case, we reverse the district court's JMOL of no anticipation and its conditional grant of new trial on that ground. We remand with instructions to reinstate the jury verdict of anticipation. We need not and do not address the other grounds asserted on appeal.

I

The '755 patent is directed to a method of treating a viral condition, a viral disease, cancers or tumors, by administration of a pharmaceutically effective amount of a recombinant polypeptide related to human interferon-ß ("IFN-ß"). The human immune system naturally produces

IFN-ß in small amounts, and it is undisputed that IFN-ß harvested from human cells ("native IFN-ß") was used in the prior art to treat viral conditions. *See* '755 patent, col. 2, l. 53–col. 4, l. 22.

Representative claim 1 of the '755 patent reads:

> 1. A method for immunomodulation or treating a viral condition[ ], a viral disease, cancers or tumors comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of a composition comprising:
>
> a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:
>
> (a) DNA sequences which are capable of hybridizing to any of the DNA inserts of G-pBR322(Pst)/HFIF1, G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and G-pBR322(Pst)/HFIF7 (DSM 1793) under hybridizing conditions of 0.75 M NaCl at 68° C. and washing conditions of 0.3 M NaCl at 68° C., and which code for a polypeptide displaying antiviral activity, and
>
> (b) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a);
>
> said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule.

'755 patent, col. 49, l. 59–col. 50, l. 12. Dependent claim 2 replaces the "capable of hybridizing" limitation with a selection from two particular DNA sequences, one of which is the DNA sequence of human interferon-beta. *Id.* at col. 50, ll. 13–52. Claims 1 and 2 thus define the claimed polypeptide by reference to the DNA sequence inserted into the host during the recombinant manufacture of the polypeptide. Claim 3, dependent from claim 1, limits the polypeptide to a particular linear polypeptide sequence. Because the claimed IFN-ß DNA and polypeptide sequences are derived from human IFN-ß, it is indisputable that native human IFN-ß is capable of hybridizing with the DNA sequences in claim 1, is produced by one of the DNA sequences laid out in claim 2, and comprises the amino acid sequence set out in claim 3. *See* J.A. 47784 (Fiers Aff. to the Canadian Patent Office, indicating that the recombinant IFN-ß was derived from human IFN-ß cDNA); J.A. 77897 (Dr. Green Test., testifying that the sequences claimed in claim 1 are "DNA that will hybridize to one of the four human beta interferon clones"); J.A. 77904 (Dr. Green Test., testifying that accused-product Rebif is capable of hybridizing to one or more of the DNA inserts because the DNA sequence it used is identical to the published sequence of human IFN-ß). For purposes of this opinion, we refer to "recombinant IFN-ß" as shorthand for the recombinant protein that meets these claim limitations.

During *Markman*, the district court held that claim 1 covers a "one-step method of 'administering' to a patient in need the specified recombinant HuIFN-ß." Markman Opinion at 17, Mar. 28, 2016, ECF No. 403. The district court considered the claimed "produced" and "transformed" steps "merely descriptive of the recombinant polypeptide to be administered," i.e. merely source limitations. *Id.* at 15. The district court also held that it was "unclear that [the] method of treatment claim can be treated as a product-by-process claim," and that it was "aware of no binding

precedent requiring method of treatment claims to be treated as product-by-process claims in the claim construction context." *Id.* at 14. The district court did not construe "polypeptide," "therapeutically effective amount," or "antiviral activity," and neither party asked the court to consider whether the claims covered the linear sequence of amino acids or the three-dimensional structure of the protein.

Biogen, Serono, and Bayer all moved for summary judgment. Before Bayer was severed, Bayer argued that it was entitled to summary judgment of anticipation because the claimed recombinant IFN-ß and the prior art native IFN-ß shared the same linear amino acid sequence. The district court denied Bayer's motion, holding, *inter alia*, that the claims require the polypeptide to have "antiviral activity" and be administered in a "therapeutically effective amount." Summary Judgment Opinion at 28, Jan. 9, 2018, ECF No. 892. The district court concluded that those requirements necessitate that the polypeptide "be folded into its appropriate three-dimensional structure," and that Bayer was therefore not entitled to summary judgment of anticipation by merely showing that the amino acid sequence of recombinant IFN-ß and the amino acid sequence of native IFN-ß were identical. *Id.*

After a five-week trial, Biogen and Serono both moved for JMOL under Federal Rule of Civil Procedure 50(a). The district court deferred ruling until the jury verdict. Among other issues, the court submitted anticipation, obviousness, enablement, written description, and contributory and induced infringement to the jury. In its charge on anticipation, the district court told the jury that "[t]he term 'polypeptide' means '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,'" and that the jury "must accept my definition of these words in the claims as correct." Final Jury Instructions at 17, Feb. 21, 2018, ECF No. 968. Biogen did not object to these

instructions and did not request any instruction defining the polypeptide in terms of its three-dimensional structure or requiring identity of the three-dimensional structures of native IFN-ß and recombinant IFN-ß proteins to establish anticipation.

The jury held, *inter alia*, that all claims in the '755 patent were invalid as anticipated by native IFN-ß; not invalid for obviousness, lack of enablement or lack of written description; and that Serono was liable for contributory infringement but not induced infringement. Jury Verdict Form at 1–6, Feb. 23, 2018, ECF No. 977.

Both parties renewed their JMOL motions. As relevant here, the district court granted Biogen's motion of no anticipation as a matter of law. *Biogen I*, 335 F. Supp. 3d at 713. In a comprehensive opinion, the district court held that no reasonable jury could find anticipation under Serono's reading of the claims. First, applying a structural reading of the recombinant limitations, the district court held that Serono had not identified any prior art that disclosed "treatment with a 'therapeutically effective amount' of a composition comprising a 'recombinant' interferon-ß polypeptide produced in a 'non-human host' that had been 'transformed by a recombinant DNA molecule.'" *Id.* at 704. **[JA21]**. The district court reasoned that because treatment in the prior art entailed administration of native IFN-ß, which was undisputedly not recombinantly produced, no reasonable jury could find anticipation. *Id.* at 705. The district court cited but did not distinguish *Amgen Inc. v. Hoffman-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), which analyzed anticipation of a claimed recombinant erythropoietin ("EPO") by prior art urinary (i.e. natural) EPO. *Biogen I*, 335 F. Supp. 3d at 1367. The district court declined to apply a product-by-process analysis to a product-by-process limitation contained within a method of treatment claim, concluding that no precedent required such an analysis and that the policy informing product-by-process claims—to enable an inventor to claim an

otherwise difficult-to-define product—was inapplicable to the instant method of treatment claims. *Id.* at 712–13.

In the alternative, the district court held that no reasonable jury could have found anticipation even applying a product-by-process analysis. *Id.* at 705–11. The district court explained that because the claims required administration of a "therapeutically effective amount" of a recombinant polypeptide that "displays antiviral activity," the product resulting from the claimed recombinant process is defined by the folded three-dimensional structure of the protein. *Id.* at 705 (discussing Summary Judgment Opinion at 28, Jan. 9, 2018, ECF No. 892). The district court held that the jury lacked substantial evidence that the native IFN-ß protein as disclosed in Kingham and Sundmacher was structurally or functionally identical to the claimed three-dimensional recombinant IFN-ß protein. *Id.*

With respect to structural identity, the district court emphasized that whereas the attached carbohydrate groups in native IFN-ß protein were glycosolated, the attached carbohydrate groups in recombinant IFN-ß were *not* glycosolated, and that this change affected the three-dimensional structure of the protein. *Id.* The district court—relying on expert testimony by Serono's expert, Dr. Lodish, and statements found in a post-priority date reference created by InterPharm Laboratories Ltd. entitled "Comparative Biochemical Analysis of Native Human Fibroblast lnterferon and Recombinant Beta Interferon Expressed by Chinese Hamster Ovary Cells" ("InterPharm")—concluded that native and recombinant IFN-ß were not *identical* but merely very similar. *Id.* at 706–07. The district court opined that the structural differences alone preclude anticipation. *Id.* at 710–11 (relying primarily on this court's decision in *Amgen*, 580 F.3d at 1367–69, in which we affirmed a holding of no anticipation based on structural differences). Finally, the district court discounted the conclusion in the InterPharm study that recombinant IFN-ß and

native IFN-ß were identical. It held that there was no substantial evidence that the generic "native IFN-ß" analyzed in the InterPharm study and found to be identical to recombinant IFN-ß was the same native IFN-ß taught in the prior art. *Id.* at 708.

As for functional identity, the district court held that the relative ease of manufacture of recombinant IFN-ß in large quantities functionally distinguished it from native IFN-ß. *Id.* at 709–10.

For these reasons, the district court granted JMOL of no anticipation. *Id.* at 713. The district court also conditionally granted Biogen's motion for a new trial on anticipation "[f]or the same reasons the Court grants Biogen's JMOL motion." *Id.* The district court added that the trial was complex and was "noticeably focused on issues other than anticipation," such that that the jury verdict deserved close scrutiny. *Id.*

Serono appeals. We have jurisdiction under 28 U.S.C. § 1295.

II

We review the grant of JMOL and the grant of new trial under the law of the regional circuit. *Uniloc USA, Inc. v. Microsoft Corp.*, 632 F.3d 1292, 1301, 1309 (Fed. Cir. 2011). The Third Circuit reviews the grant of JMOL for a fact question de novo, affirming "only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability." *Lightning Lube, Inc. v. Witco Corp.*, 4 F.3d 1153, 1166–67 (3d Cir. 1993); *Garzier ex rel. White v. City of Phila.*, 328 F.3d 120, 123 (3d Cir. 2003) ("A district court should grant such a motion only if, viewing all the evidence in favor of the nonmoving party, no reasonable jury could find liability on a particular point."). The Third Circuit reviews the conditional grant of a new trial against the

weight of the evidence for an abuse of discretion, "unless the court's denial is based on the application of a legal precept, in which case the standard of review is plenary." *Lightning Lube*, 4 F.3d at 1167.

III

A claim is anticipated only if "each and every [limitation] is found within a single prior art reference." *Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1294 (Fed. Cir. 2015). Anticipation is a factual question and thus within the ordinary provenance of the jury. *Lighting Ballast Control LLC v. Phillips Elecs. N. Am. Corp.*, 790 F.3d 1329, 1340 (Fed. Cir. 2015).

In evaluating the evidentiary record presented to the jury on the question of anticipation, the district court: (1) declined to apply a product-by-process analysis to the claimed recombinant IFN-ß source limitation; and (2) in its alternative ground analysis, required identity of three-dimensional structures not specifically recited in the claims rather than the claimed and lexicographically defined "polypeptide." Both of these determinations led to an erroneous conclusion on anticipation.

A. The Recombinant Source of the Polypeptide

The district court, focusing on the process of making recombinant IFN-ß, concluded that it need not analyze whether native IFN-ß and recombinantly produced IFN-ß were identical because neither Kingham nor Sundmacher prior art reference taught a method of treatment *using recombinant IFN-β*. *Biogen I*, 335 F. Supp. 3d at 704. It categorized the "produced" and "transformed" limitations as meaningful "source limitations." *Id.* at 711–12. The district court was convinced that because the recombinant source limitations here overcame the shortcoming of the prior art—namely, the unavailability of native IFN-ß in sufficient quantity to facilitate practical treatment—the recombinant nature of the claimed IFN-ß "lies at the heart

of the benefit of this invention" [and] should be given "force and effect in the anticipation analysis.'" *Id.* (quoting Biogen's statements at JMOL hearing, Trial Tr. 6/6/18 at 12:7–10). The district court reasoned that no binding precedent required it to apply a product-by-process analysis to a limitation contained in a method of treatment claim, and held that the rationale underlying the use of product-by-process claims—to allow claiming of an otherwise difficult-to-define invention, *see SmithKline*, 439 F.3d at 1315—did not apply to the claims here because the "product" itself was sufficiently described. *Biogen I*, 335 F. Supp. 3d. at 713. The district court thus concluded there could be no anticipation, regardless of whether Serono had shown the identity of native IFN-ß and recombinant INF-ß.

Serono contends that Biogen has waived any argument that the recombinant source of the IFN-ß can alone confer novelty because Biogen's pre-verdict JMOL motion only argued that native IFN-ß and recombinant IFN-ß were not identical. We find no waiver. The source limitation was one of the bases for Biogen's argument of non-identity and was considered by the district court at Summary Judgment and in its opinion on JMOL.

On the merits, Serono asserts that a source limitation alone cannot confer novelty unless the product itself is novel. Serono argues that the district court erred by holding that the lack of a recombinantly produced IFN-ß product in the prior art compelled a finding of no anticipation. Biogen argues that the source of the IFN-ß matters is an independent limitation.

We agree with Serono. The district court's refusal to consider the identity of recombinant and native IFN-ß runs afoul of the longstanding rule that "an old product is not patentable even if it is made by a new process." *Amgen,* 580 F.3d at 1366. *See also Gen. Elec. Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938) ("[A] patentee who does not distinguish his product from what is old except by

reference, express or constructive, to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced."); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884) ("While a new process for producing [an old product] was patentable, the product itself could not be patented, even though it was a product made artificially for the first time."); *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1317 (Fed. Cir. 2006) ("It has long been established that one cannot avoid anticipation by an earlier product disclosure by claiming the same product . . . as produced by a particular process.").

In *Amgen*, we explained that a claim to a recombinant EPO composition must be analyzed for novelty by comparing the recombinant EPO to the prior art urinary EPO. We further explained that simply because prior art urinary EPO was not made recombinantly was not enough to avoid anticipation as a matter of law.[2] 580 F.3d at 1370 ("To prove invalidity, Roche had to show that recombinant EPO was the same as urinary EPO, *even though urinary EPO was not made recombinantly*.") (emphasis added). The key

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[2] The key claim in *Amgen* read: "A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, wherein said erythropoietin is purified from mammalian cells grown in culture." 580 F.3d at 1364. An additional independent claim in a related patent read: "A non-naturally occurring glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin said product possessing the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells." *Id.* In relevant part, we applied the same analysis to both claims.

question was "whether the production of EPO by recombinant technology resulted in a new product," *id.* at 1367, or, "[i]n other words, does the source limitation 'purified from mammalian cells grown in culture' distinguish recombinant EPO from [prior art] urinary EPO?" *Id.*

The nature of the origin or source of the composition recited in the claims at issue in this case is, in all relevant respects, identical to that considered in *Amgen*. 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 requirements that the claimed polypeptide is "recombinant" and "produced by a non-human host transformed by a recombinant DNA molecule" (in the case of Claim 1 of the '755 patent) describe the process by which the product, i.e. the "polypeptide," is formed. These are not additional structural limitations. *See Purdue Pharma L.P. v. Epic Pharma, LLC*, 811 F.3d 1345, 1353 (Fed. Cir. 2016) (holding that because a source limitation of a composition "has no effect on its structure . . . [that] limitation . . . cannot be a structural limitation"). 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.

Biogen argues that *Amgen* is limited to composition claims and is not applicable to the method of treatment claims at issue here. To support this proposition, Biogen relies on general statements in product-by-process cases such as *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) (applying product-by-process analysis for "an otherwise patentable *product*") (emphasis added), and the well-recognized distinction patent law draws between the scope of composition and method of treatment claims. *See, e.g.*, *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 595 (2013) (recognizing the distinct scope for composition and method of treatment claims in the context of 35 U.S.C. § 101).

Biogen's only basis for novelty of the method of treatment claims at issue here is the novelty of the recombinant IFN-ß composition that is administered. That composition is claimed in terms of the process by which it is manufactured. If the novelty of the recombinant IFN-ß *composition* requires comparing its structure to the structure of native IFN-ß, as *Amgen* requires, it would defy all reason to excuse that analysis for a method of administration claim using that composition. Such a rule could have the absurd result that a recombinant composition could be non-novel, the method of administration could be non-novel, but the method of administration of the composition defined by the process of its manufacture would be novel as a matter of law.

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. Indeed, we have previously applied product-by-process analysis to a nested limitation. In *Purdue Pharma*, we interpreted a claim to "an oral dosage form comprising . . . oxycodone hydrochloride active pharmaceutical ingredient having less than 25 ppm 14-hydroxy[ ], wherein at least a portion of the 14-hydroxy [ ] is derived from 8α[ ] during conversion of oxycodone free base to oxycodone hydrochloride" as including a product-by-process limitation; namely, the 14-hydroxy as derived. *Purdue Pharma*, 811 F.3d at 1353 (emphasis omitted). Similar to our analysis here, the court in *Purdue Pharma* held that it was appropriate to focus on the identity of the products of the claimed and prior art processes, and not on the source limitation, in analyzing obviousness. *See id.* at 1353–54. The nesting of the product-by-process limitation within a method of treatment claim does not change the proper construction of the product-by-process limitation itself.

We are also unpersuaded by the district court's and Biogen's reasoning that a product-by-process-type analysis is inappropriate here because the composition was otherwise

capable of definition other than by the process. That argument is precluded by *Amgen*, where the product was also well-defined in the claims: "human erythropoietin . . . wherein said erythropoietin is purified from mammalian cells grown in culture." 580 F.3d at 1364. Furthermore, as noted *supra*, the rule in *Amgen* is a necessary outgrowth of the black-letter legal principle that an old product made by a new process is not novel and cannot be patented. Logic compels extending that rule to the present case; an old method of administration of an old product made by a new process is not novel and cannot be patented.

Biogen is certainly correct that the scope of composition and method of treatment claims is generally subject to distinctly different analyses. But where, as here, the novelty of the method of administration rests wholly on the novelty of the composition administered, which in turn rests on the novelty of the source limitation, the *Amgen* analysis will necessarily result in the same conclusion on anticipation for both forms of claims.

Finally, the district court erred in considering the advantages of the *recombinant process*—the new capability of manufacturing sufficient quantities of IFN-ß through recombinant technology—as a reason not to apply a product-by-process analysis. *See Biogen I*, 335 F. Supp. 3d at 713. That consideration may well be relevant in considering the novelty of the recombinant *process*, but, a new process, regardless of its novelty, does not make an old product created by that process novel. This does not fail to give "force and effect" to the heart of the claimed invention; it protects the public from attempts to excise old products from the public domain.

Because a proper anticipation analysis of the claims in the '755 patent turns not on the source of the claimed polypeptide but on a comparison of the claimed recombinant polypeptide and the prior art native polypeptide, the

district court erred in concluding that the mere absence of recombinantly produced IFN-ß in the prior art was sufficient to grant JMOL of no anticipation.

B. The Three-Dimensional Structure of the Polypeptide

The district court also held that even applying a product-by-process type analysis, no reasonable jury could have found anticipation because the jury lacked sufficient evidence of identity between the claimed recombinant "polypeptide" and the native IFN-ß. In particular, the district court concluded that just because recombinant and native IFN-ß "share the same linear amino acid sequence is not enough for purposes of anticipation." *Id.* at 705. The district court took the position that native polypeptide anticipates the "recombinant polypeptide" only if their respective folded three-dimensional proteins share identical structure and function. *Id.* The district court reasoned that without a disclosure in the prior art of such three-dimensional protein, a showing of the native polypeptide alone would not necessarily produce "antiviral activity" when administered in a "therapeutically effective amount" as recited in the claims. *Id.* (citing Summary Judgment Opinion at 28, ECF No. 892). This was error.

The "product" administered in the claimed method is the "polypeptide." *See* '755 patent, col. 49, ll. 59–64 ("A method . . . comprising the step of administering . . . a therapeutically effective amount of a composition comprising: a recombinant polypeptide produced by a non-human host . . . ."). As noted *supra*, the key question for anticipation is whether the native "polypeptide" is identical to the "polypeptide" "produced by" the recited recombinant process.

Biogen explicitly defined "polypeptide" in the '755 patent:

> Polypeptide—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.

'755 patent, col. 8, ll. 62–64. The "polypeptide" structure is thus defined by reference to its "linear" array, without regard to its folded protein structure. The district court charged the jury with this definition, adding that the jury "must accept my definition of these words in the claims as correct." Final Jury Instructions at 17, ECF No. 968. Biogen did not object to this charge and did not ask the court for a jury instruction requiring identity of the folded protein structures.

As the district court recognized on summary judgment, "Biogen does not dispute that '[t]he sequential order of the amino acid residues for native IFN-ß is the same as the sequential order of the amino acid residues for recombinant IFN-ß.'" Summary Judgment Opinion at 27, ECF No. 892. *See also Biogen Brief* at 19. Thus, the native IFN-ß polypeptide and the claimed recombinant IFN-ß polypeptide are identical for purposes of the instant claim.

Biogen argues that the district court was correct in requiring identity not just of the polypeptide, but also of the folded proteins, because the claims require the administration of "*a therapeutically effective amount* of a composition" and that the DNA sequences in the claims must "code for a polypeptide displaying *antiviral activity*." Biogen asserts that only three-dimensional proteins can be therapeutically effective and have antiviral activity, and therefore that the "product" to be analyzed for novelty is the folded three-dimensional protein, not just the amino acid sequence.

Biogen is incorrect. First, Biogen's argument fails to give effect to Biogen's explicit definition of "polypeptide" in the specification. We must respect this lexicographic choice. *See Edward Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1329 (Fed. Cir. 2009) ("[W]e will adopt a definition that is different from the ordinary meaning when 'the

patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in . . . the specification'" (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366–67 (Fed. Cir. 2002))). Biogen does not attempt to square its theory with the definition in the specification.

Second, Biogen draws the wrong conclusion from the claimed antiviral activity limitation. The claims, in calling for antiviral activity, do not recite any specific folded three-dimensional structure that gives rise to that activity. While it is indisputable that an amino acid sequence alone cannot give rise to antiviral activity, it is also indisputable that every linear sequence of proteins will fold into *some* three-dimensional configuration. 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."

Finally, and importantly, Biogen did not ask for a jury instruction on anticipation that required comparing the three-dimensional protein structures of prior art IFN-ß and the claimed recombinant IFN-ß. Neither Biogen nor the district court can reframe the anticipation inquiry on JMOL to focus on the unclaimed three-dimensional protein structure, where the jury was instructed, without objection, to decide anticipation based on the linear amino acid sequence. *See Finjan, Inc. v. Blue Coat Sys., Inc.*, 879 F.3d 1299, 1306 (Fed. Cir. 2018) ("[I]t is too late at the JMOL stage to . . . adopt a new and more detailed interpretation of the claim language and test the jury verdict by that new and more detailed interpretation." (quoting *Hewlett-Packard Co. v. Mustek Sys., Inc.*, 340 F.3d 1314, 1321 (Fed. Cir. 2003))).

The jury was correctly instructed that "to be entitled to a patent, the invention must actually be 'new.'" J.A. 81262. It is undisputed that the prior art here teaches the administration of native IFN-ß that has a linear amino acid

sequence identical to the linear amino acid sequence of the recited recombinant IFN-β and that shows antiviral activity. *See* '755 patent, col. 3, ll. 4–14. The jury thus had sufficient evidence to find that native IFN-β polypeptide is identical to recombinant IFN-β polypeptide, was administered in therapeutically effective amounts, and showed antiviral activity in the prior art. The district court thus erred in granting JMOL of no anticipation.[3]

IV. Conditional Grant of New Trial

The district court also conditionally granted a new trial on anticipation. The district court's grant of a new trial was based on the same legal errors supporting its grant of JMOL. *Biogen I*, 335 F. Supp. 3d at 713 ("For the same reasons the Court grants Biogen's JMOL motion, the Court conditionally orders a new trial on anticipation."). None of the additional considerations noted by the district court in support of its conditional grant of a new trial are independently sufficient to support its decision. We therefore reverse the district court's grant of a conditional new trial on anticipation.

CONCLUSION

For the reasons discussed above, we reverse the district court's grant of judgment as a matter of law of no anticipation and the conditional grant of a new trial on anticipation. We remand with instructions to reinstate the jury verdict on anticipation. We need not and do not address the several other issues raised by the parties on appeal.

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[3] Because the proper construction of the claims does not require comparison of the three-dimensional structure of prior art native IFN-β and recombinant IFN-β, we need not consider the parties' contested readings of the Inter-Pharm study or the evidence or lack thereof of structural identity.

REVERSED AND REMANDED

United States Court of Appeals for the Federal Circuit

October 9, 2020

ERRATA

Appeal No. 2019-1133

BIOGEN MA INC.,
Plaintiff -Appellee

v.

EMD SERONO, INC., PFIZER INC.,
Defendants-Appellants

BAYER HEALTHCARE PHARMACEUTICALS INC., NOVARTIS PHARMACEUTICALS CORPORATION,
Defendants

Decided: September 28, 2020
Precedential Opinion

Please make the following change:

On page 18, line 13, change "linear sequence of proteins" to —linear sequence of amino acids—.

FORM 19. Certificate of Compliance with Type-Volume Limitations **Form 19**
July 2020

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATIONS

Case Number: 19-1133

Short Case Caption: Biogen MA Inc. v. EMD Serono, Inc.; Pfizer Inc.

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