IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA

REGENERON PHARMACEUTICALS, INC.,

Plaintiff/Counter-Defendant,

v. **CIVIL NO. 1:22-CV-61 (KLEEH)**

MYLAN PHARMACEUTICALS INC.,

Defendant/Counter-Claimant.

ORDER ON CLAIM CONSTRUCTION

INTRODUCTION

The patents now before the Court with terms requiring construction are: U.S. Patent No. 11,084,865 ("the '865 patent" or the "Formulation Patent") (Dkt. 146, '865 patent); U.S. Patent Nos. 10,888,601 ("the '601 patent") and 11,253,572 ("the '572 patent") (collectively, the "Dosing Patents") (Dkt. 146, '601 patent; Dkt. 146, '572 patent); and U.S. Patent No. 11,104,715 ("the '715 patent" or "the Manufacturing Patent") (Dkt. 146, '715 patent).[1]

[1] Regeneron initially asserted U.S. Patent Nos. 11,053,280, and 11,299,532, (Dkt. 146, MOB at 3, n.3), but has since withdrawn these from the first stage of the litigation.

This Court has examined the disputes over the construction of these claim terms and, on January 24, 2023, held a hearing pursuant to *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996).

GENERAL CONCLUSIONS OF LAW

Claim construction is the process by which the Court gives legal effect to the meaning of the claims of the asserted patents. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 321-22 (2015). "It is not an obligatory exercise in redundancy" and is not required where a term's meaning is apparent from the claim language itself or its scope is not disputed. *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997). "[S]ome line-drawing problems . . . [are] properly left to the trier of fact." *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 806 (Fed. Cir. 2007).

The Federal Circuit's leading authority on how to construe claims, *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc), explains that "the claims of a patent define the invention." *Id.* at 1312 (quotation marks omitted). "[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms" and "the context in which a term is used in the asserted claim can be highly instructive." *Id.* at 1314. This is true for both the claim containing the disputed term itself, as well as all other claims in the patent—whether asserted or unasserted. *Id.*

Indeed, "an independent claim is broader than a claim that depends from it, so if a dependent claim reads on a particular embodiment of the claimed invention, the corresponding independent claim must cover that embodiment as well." *Littelfuse, Inc. v. Mersen USA EP Corp.*, 29 F.4th 1376, 1380 (Fed. Cir. 2022); *see Phillips*, 415 F.3d at 1314 ("Differences among claims can also be a useful guide in understanding the meaning of particular claim terms.").[2]

Together with the claim language, "the specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'" *Phillips*, 415 F.3d at 1315. The specification may define claim terms "expressly," or it may define them "by implication," *i.e.*, "such that the meaning may be found in or ascertained by a reading of the patent." *Id.* at 1321 (quotation marks omitted). But while the specification serves as a resource to understand the words used in the claims, courts must avoid the "cardinal sin[]" of importing language from the specification into the claims. *Id.* at 1320. Indeed, even if every example described in the specification contains a particular element, such uniformity is *not* enough to justify importing that

[2] An "independent" claim is a standalone claim that contains all the limitations that define an invention, whereas a "dependent" claim refers back to, and incorporates by dependency, a previous independent claim and further limits the claim. *See generally* 37 C.F.R. § 1.75.

element into claims whose plain language does not expressly require it. *See id.* at 1323; *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906-07 (Fed. Cir. 2004); *AstraZeneca AB v. Mylan Pharm. Inc.*, 2022 WL 17178691, at *5-6 (N.D. W. Va. Nov. 23, 2022) ("Dependent claims . . . refer to at least one other claim, include all of the limitations of the claim to which they refer, and specify a further limitation on that claim.").

"[A] court 'should also consider the patent's prosecution history.'" *Phillips*, 415 F.3d at 1317. "Yet because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* To find disavowal of the ordinary meaning of a claim term in view of the specification based on statements in the prosecution history, the Federal Circuit requires that the alleged disavowing actions or statements made during prosecution be "both clear and unmistakable." *CUPP Comput. AS v. Trend Micro Inc.*, 53 F.4th 1376, 1382 (Fed. Cir. 2022).

Where the court "reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent's prosecution history), the judge's determination will amount solely to a determination of law." *Teva*, 574 U.S. at 331. However, in

situations where the patent does not provide the meaning for a claim term, a "court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Id.* In those circumstances, the court may "make subsidiary factual findings about that extrinsic evidence." *Id.* at 332. But extrinsic evidence cannot be used to "contradict claim meaning that is unambiguous in light of the intrinsic evidence." *Phillips*, 415 F.3d at 1324. "[A] court should discount any expert testimony that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history, in other words, with the written record of the patent." *Genuine Enabling Tech. LLC v. Nintendo Co.*, 29 F.4th 1365, 1373 (Fed. Cir. 2022) (quoting *Phillips*, 415 F.3d at 1318); *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996) ("[E]xpert testimony ... may not be used to vary or contradict the claim language. Nor may it contradict the import of other parts of the specification." (citation omitted)); *Omega Eng'g, Inc, v. Raytek Corp.*, 334 F.3d 1314, 1332 (Fed. Cir. 2003) ("Yet, Omega submits its expert declarations not to shed light on this field of art, but to rewrite the patent's specification and explicitly provide for the laser splitting

device, lenses, and prisms to strike the center of the energy zone. That we cannot accept."). Accordingly, "where the patent documents are unambiguous, expert testimony regarding the meaning of a claim is entitled to no weight." *Vitronics*, 90 F.3d at 1584.

DISPUTED TERMS

A. The Formulation Patent (The '865 Patent)

a. "Organic Co-Solvent"

The parties agree that a plain and ordinary meaning applies to the term "organic co-solvent." (*See, e.g.*, Dkt. 124, ROB at 3; Dkt. 146, MOB at 9). The specification of the '865 patent is clear that "all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs." (Dkt. 146, '865 patent at 8:23-26).

The scientific literature explains why there is a need for co-solvents:

> Frequently a solute is more soluble in mixtures of solvents than in one solvent alone. This phenomenon is known as *cosolvency*, and the solvents that, in combination, increase the solubility of the solute are called *cosolvents*.

(Dkt. 146, Ex. 50 at 225 (emphasis in original)).

Mylan's expert, who undisputedly is one of ordinary skill in the art, provided the meaning of organic co-solvent to those of ordinary skill: the term "solvent" is well-known in the art (and

commonly defined) as a pharmaceutical excipient (*i.e.*, an ingredient) "[u]sed to dissolve another substance in preparation of a solution." (Dkt. 146, MacMichael Decl. ¶ 52) (internal citations omitted). Dr. MacMichael cites to multiple literature sources from the pharmaceutical formulation art to support this common understanding of a person of ordinary skill in the art. (*Id.* ¶¶ 40-44; *see* Dkt. 269-1, MYL PPP at slides 9-14).[3]

Dr. MacMichael explains that a person of ordinary skill in the art also knows that a co-solvent is a pharmaceutical excipient used in conjunction with a primary solvent to increase the solubility of the substance in question. (Dkt. 146, MacMichael Decl. ¶¶ 52-53; Dkt. 269-1, MYL PPP at slide 15 ("A co-solvent, by definition, changes the overall behavior of the -- of the combined mixtures of the two solvents.")). More specifically, the co-solvent works in conjunction with a primary solvent (*e.g.*, water) to better dissolve the drug substance. (Dkt. 146, MacMichael Decl. ¶ 19). In the '865 patent, the drug substance is the specific

[3] (*See also* Dkt. 146, Ex. 44 at 125 (to prepare solutions, "…one or more solvents are used to dissolve the drug substance"); Dkt. 146, Ex. 49 at 211 (solvent is "the dispersing medium" that dissolves the solute); *id.* at 229 ("A common way to increase drug solubility is through the use of a water miscible organic solvent…. Addition of a cosolvent … thereby improv[es] solubility"); Dkt. 146, Ex. 52 at 1014 ("injectable formulations currently on the market… utilize one or more cosolvents to solubilize the active constituents…. The use of water-miscible cosolvents is by far the most versatile means of increasing the solubility of drugs"); Dkt. 146, Ex. 53 at 912 ("Cosolvents are used to increase the solubility of the poorly soluble drug in water… Water-miscible cosolvents operate on the principle of lowering the dielectric constant property of water, thereby increasing the aqueous solubility of poorly water-soluble drugs.")).

VEGF antagonist fusion protein required by the claims. (*Id.* ¶ 54; *see also* Dkt. 269-1, MYL PPP at slide 8). Dr. MacMichael thus concludes that a person of ordinary skill in the art would understand the phrase "organic co-solvent" in claim 1 to have its plain and ordinary meaning: *an organic substance added to a primary solvent to increase the solubility of [another substance]*. (*See, e.g.*, Dkt. 146, MacMichael Decl. ¶¶ 55, 57).

Regeneron argues that "organic co-solvent" should be given its plain and ordinary meaning, but does not give the Court a different plain and ordinary meaning construction for the term "organic co-solvent." (Dkt. 146, MOB at 11; Dkt. 173, MRB at 3).

This Court "rejects[] at the outset[] the notion that the disputed claim terms … can be construed simply by reference, without explanation, to the 'plain and ordinary meaning.'" *Baxter Healthcare Corp. v. Mylan Lab'ys Ltd.*, 346 F. Supp. 3d 643, 653 (D.N.J. 2016). Regeneron "cannot avoid defining its own claim terms by asserting that its claims have a plain meaning," and effectively appoint itself "arbiter of whether its [own] claims are clear and unambiguous." *Liebel-Flarsheim Co. v. Medrad Inc.*, No. 1:04-CV-607, 2006 WL 335846, at *6 (S.D. Ohio Feb. 14, 2006) (quoting *Moore U.S.A., Inc. v. Standard Register Co.*, 2000 WL 876884, at *3 (W.D.N.Y. 2000)) (internal quotations omitted).

Regeneron proposes that the Court just "acknowledge[e]" that "polysorbate is an organic co-solvent," and need not "consider what additional substances this [organic co-solvent] claim term encompasses." (Dkt. No. 124, ROB at 6). That is not the proper course of action.

First, it has long-been established that "claims are not construed 'to cover' or 'not to cover' the accused device." *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1118 (Fed. Cir. 1985); *see also NeoMagic Corp. v. Trident Microsys., Inc.*, 287 F.3d 1062, 1074 (Fed. Cir. 2002) (same). Second, it will not "resol[ve the] disputed meanings and technical scope [of the claims]" or "clarify… what the patentee covered by the claims." *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997). Mylan challenges the '865 patent claims on both non-infringement and invalidity. (*See, e.g.*, Dkt. 47, Answer at Counterclaim ¶¶ 156-57; *see also* Dkt. 269-1, MYL PPP at slides 22-23 (illustrating the inapplicability of Regeneron's proposal to the prior art)). Claims must be construed similarly for infringement and invalidity. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001); *W.L. Gore Assocs., Inc. v. Garlock, Inc.*, 842 F.2d 1275, 1279 (Fed. Cir. 1988). The term "organic co-solvent" needs a single clear

construction that will apply for both analyses. Only Mylan's claim construction proposal serves that purpose.

Since Dr. MacMichael's description of an "organic co-solvent" is unrebutted, it is adopted as the plain and ordinary meaning of "organic co-solvent."

The intrinsic record, and the role of polysorbates

Regeneron did not provide an actual construction to assist the Court to clarify the meaning of "organic co-solvent" to one of ordinary skill, but Regeneron does ask the Court to confirm that various ingredients ***must always*** qualify as the claimed "organic co-solvent," namely "polysorbate 20, polysorbate 80, polyethylene glycol, or propylene glycol, or a combination thereof." (Dkt. 124, ROB at 5). Regeneron accuses Mylan of wanting to preclude them from being categorized as organic co-solvents. (Dkt. 124, ROB at 5; Dkt. 174, RRB at 6).

Mylan does not dispute that there are ***some formulations*** where a polysorbate ingredient may act as a co-solvent. The specification does label some formulations' polysorbate as a "co-solvent." (*See, e.g.*, Dkt, 146, MacMichael Decl. ¶ 59 (acknowledging that polysorbate may be used as a co-solvent in certain embodiments of the '865 patent)). But deciding whether a particular ingredient in a particular formulation qualifies as an "organic co-solvent" under the claims is premature—that analysis

occurs after claim construction, and during the infringement and invalidity part of the case. (Dkt. 173, MRB at 2-3; Hearing Tr. at 38:19-40:7). Mylan objects to permanently pre-judging ***all*** polysorbates as ***always*** organic co-solvents, irrespective of formulation purpose or amounts, during claim construction. (Dkt. 146, MOB at 9-10; Dkt. 124, MRB at 4; Hearing Tr. at 57:22-60:2).

Regeneron responds that the meaning of co-solvent cannot consider whether a given ingredient is serving a function, role or purpose within the formulation, citing *Ecolab, Inc. v. Environchem, Inc.*, 264 F.3d 1358, 1367 (Fed. Cir. 2001) and *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 731 (Fed. Cir. 2014). (Dkt. 174, RRB at 8-11; Hearing Tr. at 21:8-22:16; Dkt. 268, REG PPP at slide 21).

In *Ecolab*, the district court construed the term "substantially uniform" to require that the claimed alkaline detergent produce a "homogenous cleaning solution … over the life of the cast." *Ecolab*, 264 F.3d at 1364-65. The Federal Circuit disagreed that this latter requirement—staying homogenous over the life of the cast—was required by the "substantially uniform" claim language. *Id.* at 1367. The Federal Circuit *did* agree though that while "there is no claimed functional requirement as to forming a homogeneous wash solution throughout the cast life," the detergent solution *did* have to "contain components capable of 'ware and hard

surface washing.'" *Id.* at 1366. Thus, *Ecolab* does not preclude ensuring that the meaning of "co-solvent" describes what a solvent is supposed to do, *e.g.*, help dissolve something.

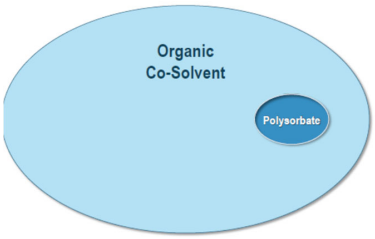
The parties vigorously contested the significance of *GlaxoSmithKline* at the hearing. (Hearing Tr. at 22:4-23:18, 54:11-55:11). *GlaxoSmithKline* involved a Section 112 written description challenge; the Federal Circuit considered this question "***without*** resolving the claim-construction dispute." 744 F.3d at 726 (emphasis added). GlaxoSmithKline's claims were to the drug dutasteride, and "any 'pharmaceutically acceptable *solvate thereof*,'" with solvate referring to a "crystalline" structural arrangement of the atoms of the drug compound. *Id.* at 726-27 (emphasis in original). When the Federal Circuit explained that "solvate" lacked a functional component, it was in the context of differentiating prior *written description* cases where patentees claimed a functional result without a sufficiently supportive specification. *Id.* at 730-31 (reciting cases involving claims to plasmids with a DNA coding sequence broadly defined by its function; claims to all genetic material capable of encoding insulin; claims to an antibody's ability to bind to an antigen, etc.). Even so, when the Federal Circuit discussed the GlaxoSmithKline patent's written description, it noted that a solvate must "originate[] in a 'solution,' which is a mixture of

two substances: a 'solute' dissolved in a 'solvent.'" *Id.* at 727. *GlaxoSmithKline*'s description of a solvent as something that *dissolves* something else is what Dr. MacMichael explained "[p]ersons of skill in the art widely understand": co-solvents are "***used to dissolve*** another substance." (Dkt, 146, MacMichael Decl. ¶ 20) (emphasis added); *see also id.* at ¶ 41 (citing Dkt. 146, Ex. 44; Dkt. 146, Ex. 49; Dkt. 146, Ex. 50; Dkt. 146, Ex. 51; Dkt. 146, Ex. 52).

The function that an ingredient plays in a formulation is not an idle issue. Water is a universally recognized solvent, but in some contexts, does not work as a solvent (*e.g.*, it cannot dissolve sand). (Hearing Tr. at 58:4-14; Dkt 146, Ex. 49 at 211 (noting mixing sand and water only produces a suspension, not a solution)). Polysorbates may in some circumstances—including for some of Regeneron's specification examples or dependent claims—qualify as a co-solvent. But the scientific literature recognizes polysorbate's role in a pharmaceutical formulation as a "surfactant." (Dkt. 173, MRB at 4-6; Hearing Tr. at 45:2-46:15; Dkt. 269-1, MYL PPP at slides 10, 14; MOB Ex. 53 at 11 ("*Surface active agents:* polysorbate 80…")). The terms surfactants and "co-solvents" also are not used interchangeably. *AstraZeneca*, 384 F.3d at 1338-41 (specification recognized that surfactants and co-solvents were different categories of solubilizers); *see also* Dkt.

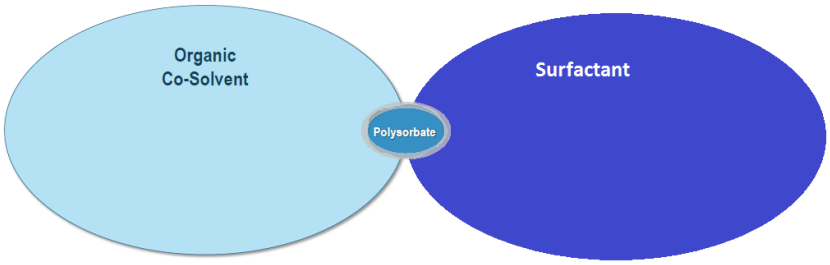
146, Ex. 53 at 917 (three different categories of solubilizers: cosolvents, surface active agents, and complexing agents). Even in this litigation, for other claims, Regeneron calls polysorbate a surfactant.[4]

At oral argument, Regeneron presented a Venn Diagram proposing that the relationship between organic co-solvent and polysorbate looked like this:



(Dkt. 268, RGN PPP at slide 17). The evidence of record suggests this is more accurate:

[4] Regeneron continues to assert, *e.g.*, claim 7 of the '572 Dosing Patent, which requires a regimen that uses aflibercept "formulated with a nonionic surfactant." (Dkt. 146, '572 patent at claim 7). In its pleadings, Regeneron alleges that Mylan infringes the '572 patent claims. (Dkt. 1, Compl. at 32-34, ¶¶ 223-232). Regeneron and its expert assert that the same polysorbate Regeneron wants to call a "co-solvent" for the purpose of the '865 patent *also* meets the "formulated with a nonionic surfactant" element of the '572 Dosing Patent's formulation claims. Regeneron's infringement contentions and expert report regarding infringement are not currently part of the claim construction record, since Regeneron submitted them after the Markman briefing and/or hearing; Mylan is willing to file the relevant evidence if needed by the Court.



(Hearing Tr. at 58:15-60:2). The parties plainly dispute whether, for any given formulation, polysorbate always qualifies as an organic co-solvent; a surfactant; or both. Since Regeneron's contentions accuse polysorbate of being a co-solvent for this patent, and a surfactant for another patent, it is hardly surprising that Mylan's invalidity contentions likewise identify prior art formulations with polysorbates could satisfy the '865 patent's co-solvent element. (Hearing Tr. at 16:16-17:18, 52:8-53:11; Dkt. 268, RGN PPP at slides 19-20). This also indicates that the parties' dispute is more of an infringement/invalidity dispute, not a claim construction dispute, the latter of which must stay focused on what "organic co-solvent" means to one of ordinary skill, having reviewed the intrinsic evidence.

Regeneron's other specification-related arguments also do not justify changing the plain and ordinary meaning of "organic co-solvent" to mandate including all polysorbates.

Regeneron could have used lexicography in the specification to change the plain and ordinary meaning to mandate that organic

co-solvents means polysorbate. *Phillips*, 415 F.3d at 1312–17. But the standard for lexicography is "exacting." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014). Regeneron admits it did not use lexicography here. (*See, e.g.*, Dkt. 174, RRB at 1; Hearing Tr. at 73:18-23, 9:23-10:15). Patentees can disavow claim scope if the specification "describes a feature of the invention" and "criticizes other products" that "lack the same feature." *AstraZeneca*, 384 F.3d at 1340. But there must be a clear "demonstrat[ion of] an intent to deviate from the ordinary and accustomed meaning of a claim term through expressions of manifest exclusion or restriction." *Intellectual Ventures I LLC v. T-Mobile USA, Inc.*, 902 F.3d 1372, 1378-79 (Fed. Cir. 2018) (cleaned up)). Regeneron does not contend disavowal applies. (*See e.g.*, Dkt. 174, RRB at 13-14).

Regeneron suggested that its specification defined "co-solvents" by implication to require polysorbate. (Hearing Tr. at 9:17-10:20). Regeneron insists that "the specification repeatedly confirms that substances like polysorbate ***are*** organic co-solvents," in a "repeated and unequivocal" way. (Dkt. 124, ROB at 5 (emphasis added), 6; *see also* Dkt. 174, RRB at 6).

The specification carefully avoids being so absolute. The specification repeatedly qualifies its polysorbate and polyethylene glycol descriptions. For example, in column 2, the

specification states that "the organic co-solvent ***may be*** polysorbate… polyethylene glycol … or a combination thereof," not 'is" or "must include" one or more of these ingredients. (Dkt. 146, '865 patent at 2:39-42) (emphasis added). Similarly, when column 2 states that the "organic co-solvent is polysorbate and/or PEG," and gives examples of preferred formulations, the immediately preceding text qualifies all of them as reflective of "various ***embodiments***." (*Id.* at 2:49-50) (emphasis added). The same holds true for the formulations with polysorbate in column 3 onwards, which are specific formulation recipes described as "specific preferred embodiment[s]" or "examples." (*Id.* at 3:1-10; *id.* at 3:28-29 ("In another ***embodiment***, the organic co-solvent is selected from one or more of polysorbate…) (emphasis added); *id.* at 7:2-5 ("An ***example*** of a pharmaceutically acceptable liquid formulation comprises … an organic co-solvent ***such as*** polysorbate…"); *see generally* cols. 3-4 (describing formulations with polysorbate as embodiments)). The '865 patent claims also avoid such absolutes, such as by stating "wherein said organic co-solvent ***comprises*** polysorbate." (*Id.* at claims 2-5; Dkt. 269-1, MYL PPP at slide 5); *CIAS, Inc. v. All. Gaming Corp.*, 504 F.3d 1356, 1360-61 (Fed. Cir. 2007) (noting that "comprising" just means "including").

But even assuming the desirability of defining "organic co-solvent" by implication, the '865 patent's specification forecloses that option, reiterating that "the terminology used herein is for the purpose of ***describing particular embodiments only***; [it] ***is not intended to be limiting***." (Dkt. 146, '865 patent at 8:8-13) (emphasis added). The specification emphasizes that the "scope of the present invention ***will be limited only to the appended claims***." (*Id.* at 8:13-14 (emphasis added); *id.* at 5:32-38 (stating that examples and embodiments were non-limiting, and that "the scope of the present invention will be limited only by the appended claims")). Regeneron thus asks the Court for a claim construction to change its claims' parameters based on its particular embodiments, despite its specification reiterating not once, but twice, to ***not*** do that. Regeneron's approach thus conflicts with the specification.

Regeneron alternatively speculates that if proof of an ingredient's "functional" behavior is needed to qualify as a co-solvent, this causes all of the claims to exclude preferred embodiments. (Dkt. 124, ROB at 7; Dkt. 174, RRB at 8-9). The briefing citations and excerpt of Dr. MacMichael's testimony that Regeneron provided at oral argument on claims 2-5 does not support the premise. (Hearing Tr. at 55:12-56:13; Dkt. 268, RGN PPP at slide 27).

The '865 patent has 64 claims. While claim 1 requires a co-solvent, claim 51 does not, even though claim 51 does expressly require using polysorbate in the formulation. (Dkt. 146, '865 patent at claim 51 ("ophthalmic formulation comprising: (a) 40 mg/ml of a glycosylated VEGF antagonist fusion protein" from "SEQ ID NO:4; (b) ***0.03% to 0.1% polysorbate***" and other excipients) (emphasis added)). Claim 51 corresponds to embodiments, *e.g.*, those in column. 2, lines 53 through 57; in Example 3 (40 mg/mL formulation, fusion protein, 0.03% polysorbate 20, and other excipients); and in Example 4 (40 mg/mL formulation, fusion protein, 0.03% polysorbate 20, and other excipients). Example 2 of the '865 patent also is an embodiment of claim 1. (Hearing Tr. at 42:25-43:6). Regeneron thus does have claims that cover its polysorbate embodiments; and its non-polysorbate embodiments. While courts should consider whether a claim construction would exclude all embodiments, "where the patent describes multiple embodiments, every claim does not need to cover every embodiment." *Pacing Techs., LLC v. Garmin Int'l, Inc.*, 778 F.3d 1021, 1026 (Fed. Cir. 2015).

Thus, in view of the intrinsic record, "organic co-solvent" cannot be construed to require covering all polysorbates in all circumstances. *See Conoco, Inc. v. Energy & Env't Int'l., L.C.*, 460 F.3d 1349, 1358 (Fed. Cir. 2006) (finding a specification that

stated an amount of alcohol "may vary widely but it usually forms between about 0 and 70 weight percent of the suspending material" did not limit the claims to between 0 and 70 percent).

Given the above, the Court adopts Mylan's definition of "co-solvent" to have its plain and ordinary meaning to a person of ordinary skill in the art: it is an organic substance added to the primary solvent to increase the solubility of the solute, here a VEGF antagonist. The Court will decide the question of whether a specific formulation with polysorbate 20, polysorbate 80, polyethylene glycol, or propylene glycol satisfies the "organic co-solvent" claim language during the infringement and invalidity part of this case.

b. "Present in Native Conformation"

The parties generally agree that the "native" protein for purposes of the claims here is the original, intact, aflibercept fusion protein, standing alone as a single molecule. (Hearing Tr. at 29:15-17 (Regeneron stating "you have something present in the native conformation. That's the aflibercept by itself."); *id.* at 61:22-24 (Mylan stating "native conformation, Your Honor, is a reference to the protein in its original form and structure, without any degradation.")).

Proteins are complex biologic molecules. The specification recognizes that the nature of proteins' structures present

pharmaceutical formulators with unique issues. Proteins can degrade chemically, through "deamination" reactions, "aggregation," by "clipping of the peptide backbone," and by "oxidation of methionine residues." (Dkt. 146, '865 patent at 5:56-58). Proteins can degrade physically, through "many phenomena, including, for example, aggregation and/or precipitation." (*Id.* at 5:58:60). If aflibercept is chemically changed, it is no longer aflibercept; if it is aggregated or precipitated, it also will no longer be a "single aflibercept molecule by itself." (Hearing Tr. at 28:25 – 30:7).

Plain and ordinary meaning

Dr. MacMichael, consistent with the specification, explained that the "plain and ordinary meaning of the term '[present in] native conformation' requires the VEGF antagonist fusion protein to be present in a form that does not exhibit chemical or physical instability. A POSA would understand that aflibercept '[present in] native conformation' is present in a form that does not exhibit chemical or physical instability." (Dkt. 146, MacMichael Decl. ¶ 21).

Rather than rebut Dr. MacMichael's explanation of how a person of ordinary skill in the art would understand the term "native conformation," Regeneron suggests that the entire claim limitation in which the term appears—i.e., "wherein at least 98% of the VEGF

antagonist is present in native conformation…as measured by size exclusion chromatography"—has a plain and ordinary meaning. (*See, e.g.*, Dkt. 124, ROB at 8-9). That sidesteps the question of what "native conformation" ordinarily means. Regeneron did not give the Court an actual construction of the disputed claim term, "native conformation." Regeneron had to provide its different meaning, if any. *Liebel-Flarsheim*, 2006 WL 335846, at *6; *Baxter,* 346 F. Supp. 3d at 653. It didn't. Mylan's ordinary meaning applies.

The intrinsic record, and concepts of stability

Regeneron argues that "native conformation" cannot consider "all aspects of physical and chemical stability," but "only" the "aspects of stability that are described in the specification and that may be the measured by the specific technique required by the claims," (Dkt. 174, RRB at 11; Dkt. 268, RGN PPP at slide 31), which is just protein "size[], not different oxidation or deamination profiles." (Dkt. 174, RRB at 12). At oral argument, Regeneron's counsel characterized this as a measure of aggregation only. (Hearing Tr. at 30:19-31:7).

Dr. MacMichael's testimony—which is unrebutted—confirms that a person of ordinary skill in the art knows that aflibercept may be able to comply with the claims' size exclusion chromatography (SEC) test, without independently satisfying the "native conformation" standard. (Dkt. 268, RGN PPP at slide 38 (citing

MacMichael Dep. Tr. at 203:8-19)). The '865 patent's specification knew how to discuss aggregation properties; for example, it described and defined "substantially free of aggregates," to mean that "at least 90% of the weight of fusion protein is not present in an aggregate" at the time of formulation. (Dkt. 146, '865 patent at 6:45-55 (also defining "substantially free of contaminants")). Had Regeneron wished to focus solely on the state of protein aggregation, as it proposes to do with its current construction, Regeneron should have used aggregation-specific terms, versus the more general "native conformation" term that those of ordinary skill in the art know is tied to multiple stability considerations.

Regeneron's approach also creates the same problem that Judge Bailey raised in *AstraZeneca AB v. Mylan Pharms., Inc.*, No. 22-35, 2022 WL 17178691, at *6-7 (N.D.W. Va. Nov. 23, 2022): it collapses and subsumes a separate "native conformation" claim term element into what Regeneron calls its aggregate test requirement, which would render the "native conformation" language directed to intact aflibercept superfluous. (Dkt. 174, RRB at 12; Hearing Tr. at 66:5-69:18). These multiple distinct elements can't be rolled into one.

Regeneron proposes that since it used "stable" and "native conformation" in other claims in related patents, "native

conformation" can't involve *any* general stability concepts. (Dkt. 174, RRB at 11-12). The patent it cites, U.S. Patent No. 8,092,803, does not support this premise. The '803 patent's claim 1 applies the term "stable" to the phrase, "liquid ophthalmic formulation," thereby referencing the formulation as a whole. (Dkt. 174, '803 patent at claim 1). The claim applied the term "native conformation" to its description of the VEGF-antagonist, which is the protein within the formulation. (*Id.*) This also differentiates the decision Regeneron relied on, *AstraZeneca*, 2022 WL 17178691, at *6-7: Judge Bailey concluded that the "pharmaceutical composition" could not be construed to be "stable" because other claims in the same family limited the pharmaceutical composition to a stable one. Here, there is nothing inconsistent with a claim requiring the *entire formulation*, which includes both the drug and its excipients, to be stable, while also ensuring that *the protein component* in that formulation independently remains chemically and physically intact in its native conformation.

Regeneron's "stability" argument also conflicts with the prosecution history. Regeneron had claims that lacked the "native conformation" term, which the PTO rejected. (*See* Dkt. 146, Ex. 16 at 2-6). To overcome the rejection, Regeneron added the language "and wherein at least 98% of the VEGF antagonist is present in

native conformation following storage at 5° C. for two months as measured by size exclusion chromatography." (*Id.* at 2). Regeneron represented this element as "relating to the ***stability*** of the protein conformation in storage over a period of time" and represented that this element was "not contained within any of the claims" of the '261 patent that served as the basis for the double-patenting rejection. (*Id.* at 5). The PTO relied on this amendment to withdraw the rejection. (Dkt. 146, Ex. 15 at 2). During prosecution, Regeneron also characterized the "present in native conformation" clause as relating to the general stability of the required protein (*id.* at 2, 5); but now says the term does not involve general stability, rather only purity. (Dkt. 174, RRB at 11-14). Regeneron should be held to its statements to the PTO that "native conformation" relates to the more generalized stability concepts.

Given the above, and both the understanding of those of ordinary skill in the art, as well as the intrinsic record, the term "native conformation" itself is not limited to, and is not only evaluated by, one size exclusion chromatography test, as Regeneron proposes.

Thus, the claim language, "native conformation" is construed to be given its plain and ordinary meaning, which is the original intact form of the VEGF antagonist, which is a form that does not

exhibit chemical or physical instability. The question of whether a given VEGF antagonist in a particular embodiment or formulation meets other claim elements (*e.g.*, percentages following storage at 5°C for two months as measured by size exclusion chromatography), is properly considered during the infringement and invalidity part of the case.

B. "The Treatment Patents" or "Dosing Method Patents" (The '572 and '601 patents)

Independent of the claim constructions above, Mylan argues that neither claim term can be construed to have any patentable weight. The Federal Circuit has identified several reasons why, as a matter of law, language found in patent claims cannot be construed to have patentable weight. This question is properly decided during claim construction. *Praxair*, 890 F.3d at 1033 ("the Board properly addressed the printed matter doctrine during claim construction"); *In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018) (noting that the district court addressed the issue of whether purpose and results claim language was limiting during claim construction).

Claim language that conveys information cannot be construed to have patentable weight.

Claim language is construed to lack patentable weight when it involves subject matter that 35 U.S.C. § 101 treats as unpatentable—such as abstract ideas, information, or mental steps.

Praxair, 890 F.3d at 1032. One doctrine, called the "printed matter" doctrine, historically "referred to claim elements that literally encompassed 'printed' material," but "the doctrine has evolved over time to guard against attempts to monopolize the conveyance of information using any medium." *C R Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1381 (Fed. Cir. 2020). While the original "'printed matter' cases involved the addition of printed matter, such as written instructions, to a known product," the Federal Circuit has found "no principled reason for limiting their reasoning to that specific factual context ... [T]he rationale underlying these cases extends to the situation … wherein an instructional limitation is added to a method … known in the art." *King Pharms. Inc. v. Eon Labs Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010). Method claim language that describes "things to think about" as opposed to, "actions to take," is usually construed to lack patentable weight. *Praxair*, 890 F.3d at 1033-34 (limitation "merely requires a medical provider to *think* about the information claimed" and deserved no patentable weight).

Old methods cannot be made new or different by adding on statements of purpose or result.

In the context of method of treatment claims, an independent but related reason why claim language lacks patentable weight is when language within a claim just describes an old method, without transforming it into something new. This happens when, *e.g.*,

patent claims just add statements of purpose, or proposed results, to the existing old method.

For pharmaceutical treatment methods, the Federal Circuit has explained that when claim language "is only a statement of purpose and intended result," and the language "does not result in a manipulative difference in the steps of the claim," such claim language is non-limiting. *Bristol-Myers*, 246 F.3d at 1376. Even when a patentee argues that the method steps would impact the efficacy of the treatment method, if the claimed process "is not directed to a new use," but "the same use," the claim language lacks patentable weight, because "[n]ewly discovered results of known processes directed to the same purpose[s] are not patentable." *Id.*; *In re Copaxone*, 906 F.3d at 1023 (dependent claims that merely described results or outcomes of claimed method construed to be non-limiting statements of intended effect).

Thus, if claim language "does not change the express dosing amount or method already disclosed in the claims, or otherwise result in a manipulative difference in the steps of the claims," it is "non-limiting" and lacks patentable weight. *In re Copaxone*, 906 F.3d at 1023.

> <u>The exclusion criteria and BCVA scores are information; and neither changes the manipulative steps of the method.</u>

Following the legal analyses above, for method-of-use claims, the key issue is whether the claim language is 1) informational; and 2) functionally related to the substrate—that is, the language changes not mere thoughts or outcomes, but provides ***action steps*** that the method requires. *See C R Bard*, 979 F.3d at 1381 (noting the test for printed matter is whether it "merely informs people of the claimed information, or whether it instead interacts with the other elements of the claim to … ***cause a specific action*** in a claimed process.") (emphasis added); *Bristol-Myers*, 246 F.3d at 1376 (stating that language "is only a statement of purpose and intended result" where its "expression does not result in a ***manipulative difference in the steps of the claim***") (emphasis added); *King,* 616 F.3d at 1279 ("Informing a patient about the benefits of a drug in no way transforms the process of taking the drug …. Irrespective of whether the patient is informed about the benefits, ***the actual method*** … ***is the same.***") (emphasis added).

The claim language, "wherein the exclusion criteria for the patent include…" lacks patentable weight.

Regeneron initially argued that its "exclusion criteria" were intended to "define the population that is to be treated." (Dkt. 124, ROB at 19). A list of exclusion criteria to help doctors identify the patients to treat is informational under *Praxair* claims 1 and 3. *Praxair* claim 1's claim language gave doctors information so that they could "elect to avoid treating one or

more … patients with inhaled nitric oxide" to "avoid putting the one or more patients at risk of pulmonary edema." *Praxair*, 890 F.3d at 1029. Claim 3 instructed doctors to weigh the comparative risks of treatment options "in order to arrive at a decision of whether or not to treat" the patient. *Id.* at 1033. The Federal Circuit characterized such steps as language that "merely requires a medical provider to *think about* the information" before making a treatment decision. *Id.* That is all that happens with exclusion criteria—the criteria list things to think about for the patient groups to potentially treat.

The PTAB agreed in its "exclusion criteria" claim analysis. It characterized the "exclusion criteria" as a "list" that "relays direct information to the practitioner" comparable to "the listing of contraindications included with the packaging of any other drug," and hence "analogous to claim 1 in *Praxair*." (Dkt. 254-2, '601 patent Inst. Decision at 13-14).

At oral argument, Regeneron disputed that its language could be "informational," because "patients don't come to the doctors prescreened," calling it a "gating decision that the physician has to make before continuing and treating those patients that do not have the infection or the inflammation." (Hearing Tr. at 92:4-13, 134:3-13). Mylan pointed out that under *Praxair* claims 1 and 3 this still is "informational" because it merely asks doctors to

think about the question; the information from the "decision" doesn't change the dosing method. (*Id.* at 108:12-18, 110:4-16). The "information" ***is*** the exclusion criteria, because, like a sheet of paper listing contraindications for a drug product, it suggests thinking about whether a patient is in the state of inflammation of infection. (*Id.* at 102:2-116:18, 140:13-141:17). The dose, drug, and schedule that the '572 and '601 patents claim, was known, old, and doesn't change based on the outcome of reading, knowing about, or thinking about any information pertaining to a patient's state of inflammation/infection. (*See, e.g.*, Hearing Tr. at 102:2-104:10; Dkt. 146, MOB at 1 ("Regeneron cannot now recapture claim scope long known")).

The Federal Circuit is clear that for claim instructions to be "informational" it does not require the "information" to be presented as an instruction sheet; "[t]here is no meaningful distinction between claim limitations directed to written information," or "verbal information," or "mentally processed information." *Praxair*, 890 F.3d at 1033-34. Since all that happens here with the exclusion criteria, even under Regeneron's non-clinical trial construction, is that a doctor mentally processes information about the condition of a patient, the "exclusion criteria" claim language is plainly directed to informational content.

Regeneron argued that its exclusion criteria can be salvaged for the same reasons as *Praxair* claim 9. The claims here are simply not structured the same way as *Praxair* claim 9. In *Praxair* claim 9, the doctor started treatment, did an assessment, and if the doctor got a certain result from that assessment, the claims then "***require[d]*** a medical provider to take a specific action, discontinuing treatment." *Praxair*, 890 F.3d at 1035. Thus, in Praxair claim 9, the patients were (a) actually undergoing a treatment regimen; and (b) their medical provider was obligated to *change* the existing treatment regimen's steps upon receiving the information.

Regeneron proposed that its "exclusion criteria" do "prescribe actions," namely "assessing and excluding" the patients. (Dkt. 174, RRB at 19-20; Hearing Tr. at 85:17-21; Dkt. 268, RGN PPP at slide 63). Mylan responds that the "exclusion criteria" language does not "require" a doctor or patient to take any action at all. (Dkt. 146, MOB at 14-17; Dkt. 173, MRB at 18-20; Hearing Tr. at 106:6-108:11). As discussed in Section IV(F)(1)(b)(iii) above, the "action" the doctor may take would preclude using claim 1's method in the first instance. (*See, e.g.*, Dkt. 269-1, MYL PPP at slide 72). This distinguishes the claims here from Praxair claim 9, where the method was required to start, ***then*** it could be modified based on the information. *Praxair*, 890

F.3d at 1035. All that will happen here under Regeneron's proposed construction is that the method will never begin upon prescreening and finding infection/inflammation. That won't change the method of dosing 2 mg aflibercept, on the regimen schedule set forth in the underlying independent claim 1.

The PTAB agreed with Mylan. Even assuming that an "assessment" gets made, as Regeneron suggests, the express language of the "claims do not expressly recite any positive step to be performed" or a "negative step *not* to be performed" once the assessment is made. (Dkt. No. 254-2, '601 patent Inst. Decision at 14). Regeneron's own witnesses also acknowledged that doctors can treat patients with aflibercept or not, even in the face of an ocular infection or inflammation. (Dkt. 269-1, MYL PPP at slide 61 (citing Chu Tr. at 120:21-121:20)). If this knowledge does not force a change in the treatment regimen, then the language is advisory, not mandatory. (Dkt. 254-2, '601 patent Inst. Decision at 13-14; Dkt. 269-1, MYL PPP at slide 60).

District courts are not bound by the PTAB. *Novartis AG v. Noven Pharms. Inc.*, 853 F.3d 1289, 1293-94 (Fed. Cir. 2017). This is because "the PTAB properly may reach a different conclusion based on the same evidence," for the PTAB and district courts function under different evidentiary standards and burdens of proof (preponderance of the evidence before the PTAB, clear and

convincing evidence before the district court). *Id.* at 1294.[5] The Federal Circuit has recognized though that "ideally" both district courts and the PTAB would reach the same results on the same record. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1365 (Fed. Cir. 2012).

Thus, while the PTAB decision is useful persuasive evidence, and Regeneron has indicated it will attempt to develop the record further on this point before the PTAB, (Hearing Tr. at 87:6-88:5), the Court makes its own findings without deference to the PTAB.

The claim language, "wherein the exclusion criteria for the patient include" is written in the passive voice. Even assuming that the doctor or patient secures the results of inflammation or infection screening, and learns the benefits of patients not taking aflibercept when their eyes are not inflamed or infected (which is *Praxair* claim 1); or pauses to weigh the risk of delaying treatment because of infection or inflammation versus the risks of delaying treatment because a patient risks blindness (which is Praxair claim 3)—what changes? The language does not ***require*** any action step to be taken as a consequence. Nothing has "transform[ed] the process of taking the drug" aflibercept in the claimed method—the "actual

[5] The PTAB is scheduled to issue a Final Decision for the '601 patent by January 11, 2024. Under current Federal Circuit precedent, even if this Court were to uphold the validity of the '572 and '601 patent claims being disputed here after trial, the PTAB can independently declare those same claims unpatentable; if the PTAB's judgment is affirmed, Regeneron cannot enforce such claims against Mylan.

method" found in the underlying independent claim, *e.g.*, 2 mg of aflibercept, on the stated dosing schedule, remains the same. *King*, 616 F.3d at 1279 (when claim language did not change the underlying treatment method, it deserved no patentable weight).

Even under Regeneron's "assess and exclude" approach, a patient either never starts the method (and hence the method doesn't change); or, if doctors screened for the information and found no infection or inflammation, the same method proceeds. (Hearing Tr. at 90:1-93:20). This confirms that the "exclusion criteria" are, at best, a non-binding informational "option" for doctors to consider. (*See, e.g.*, Dkt. 254-2, '601 patent Inst. Decision at 15).

Claims that had an actual active step based on the exclusion criteria to be analogous to the *Praxair* claim 9 situation would ***require*** that patients lacking ocular inflammation or infection participate in a modified method (such as a different drug, dose, or schedule); or ***require*** ongoing treatment to stop—but that would only happen if inflammation or infection arises while the method is underway, and Regeneron insists its exclusion criteria are directed to pre-screening *before the method even starts*. (Dkt. 124, ROB at 19-20; Hearing Tr. at 92:4-23, 107:5-109:15, 131:3-25; Dkt. 269-1, MYL PPP at slides 58-60).

As noted in Section IV(F)(1)(b)(iii), above, the specifications of the '601 and '572 patents did discuss action steps involving assessment and administration, or changing dosing regimens based on patient characteristics, but the action words associated with those steps in the specification are missing from the disputed claims, and courts cannot rewrite claims to add them. *See Arlington Indus.*, 632 F.3d at 1255 n.2; *see also Apple*, 757 F.3d at 1297-98 (how a patentee claims their invention is "the claim drafter's choice" and "any resulting risk that emanates from that choice is not a basis for the court to rewrite a claim").

Regeneron, as discussed above, also urges applying the exclusion criteria to patients on an individual basis, not within a clinical trial context. Mylan points out that the failure of the exclusion criteria to modify the underlying dosing method, should an individual patient meet them, also independently renders the claim language non-limiting under *Bristol-Myers*, 246 F.3d at 1376, and *In re Copaxone*, 906 F.3d at 1022-23. (Dkt. 173, MRB at 11-13, 16-18). This is because even assuming that an individual patient is diagnosed with the condition, satisfying the exclusion criteria does not mean doctors will change anything about the underlying method—not the drug, not the dose, not the schedule. (*See, e.g.*, Dkt. 173, MRB at 12-13, 18-19; Hearing Tr. at 103:2, 107:5-108:18; Dkt. 269-1, MYL PPP at slides 62-64, 68).

Consequently, since there is no ***requirement*** to take new action that flows from the "wherein the exclusion criteria for a patient include…" information, in a way that changes the existing treatment method, this claim language is construed to have no patentable weight.

The Best Corrected Visual Acuity claim language also lacks patentable weight.

Mylan reiterates that if Regeneron is given its proposed construction, such that Best Corrected Visual Acuity refers to an individual patient measurement that occurs outside the clinical trial context, then the claim language merely states a test result that a patient may or may not reach after the method is performed. (Dkt. 173, MRB at 11-18; Hearing Tr. at 110:11-113:4, 129:11-130:11). That independently gives the language no patentable weight.

Regeneron has not disputed that under its interpretation of Best Corrected Visual Acuity, all that happens is that a patient is tested to see if their Best Corrected Visual Acuity value meets the claims' test result threshold. There is no change or modification to the underlying dosing regimen if the test result is obtained, or not. Regeneron's witnesses confirmed that if a patient *is not* meeting a particular BCVA threshold, there in fact is no change that doctors can make to the regimen to ensure a given patient achieves a particular BCVA score. (*See, e.g.*, Hearing Tr.

at 112:7-18, 119:11-20, 129:1-10; Dkt. 269-1, MYL PPP at slide 68).

This renders the claims analogous to the claims in *Bristol-Myers*, where the additional claim elements involved tumor regression and reducing patient toxicity, yet the dosing schedule remained the same. *Bristol-Myers*, 246 F.3d at 1375-76. The Federal Circuit explained the added claim language reflected "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim," and thus the language was construed to be non-limiting. *Id.* at 1376.

The BCVA test score result also follows the claim structure of *In re Copaxone*, 906 F.3d at 1023, where the claim language stating that the dosing regimen would reduce a patient's frequency of relapses was "superfluous, [did] not change the claimed method," and thus was construed to be "non-limiting."

The Federal Circuit also explained that merely adding test score outcomes to a method, as was done in *King*, where patient blood AUC and other test measurements did not change the manipulative steps of the claim, also were non-limiting. 616 F.3d at 1277-79.

An old method of treating patients cannot be made new by describing the results that a patient can get from the treatment

method, whether those results involve reducing side effects; alleviating particular symptoms; or achieving certain test results. All that the Best Corrected Visual Acuity claim language does here under Regeneron's approach is measure a letter score result—it does not change the manipulative steps of the claim.

Thus, the Court finds that the phrase, "Best Corrected Visual Acuity (BCVA)" also is informational; does not change the manipulative steps of the claims; and also should be construed to have no patentable weight.

C. Manufacturing Patent or Tustian Patents (The '715 Patent)

a. "Chemically Defined Medium"

Intrinsic evidence – the specification definitional language

The parties agree that the specification uses definitional language for "chemically defined medium." (Dkt. 124, ROB at 24; Dkt. 146, MOB at 23). "When a patentee explicitly defines a claim term in the patent specification, the patentee's definition controls." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009). This definitional language includes the '715 patent at column 30 starting at line 44, and states:

> As used herein, the term "chemically defined medium" or "chemically defined media" (both abbreviated "CDM") refers to **a synthetic growth medium in which the identity and concentration of all the ingredients are defined.** Chemically defined media do not contain bacterial, yeast, animal, or plant

> extracts, animal serum, or plasma, *although individual plant or animal-derived components (e.g., proteins, polypeptides, etc.) may be added*. Chemically defined media may contain inorganic salts such as phosphates, sulfates, and the like needed to support growth. The carbon source is defined, and is usually a sugar such as glucose, lactose, galactose, and the like, or other compounds such as glycerol, lactate, acetate, and the like. … Methods of preparing chemically defined culture media are known in the art, for example, in U.S. Pat. Nos. 6,171,825 and 6,936,441, WO 2007/077217, and U.S. Patent Application Publication Nos. 2008/0009040 and 2007/0212770, the entire teachings of which are herein incorporated by reference.

(Dkt. 146, '715 patent at 30:44-31:5) (emphasis added). This CDM section specifically incorporates WO 217 by reference, (Dkt. 146, '715 patent at cover page, 30:67-31:5, 98:45-49), which makes its specification part of the 715 patent's specification "as if [it] were explicitly contained therein." *Finjan LLC v. ESET, LLC*, 51 F.4th 1377, 1382 (Fed. Cir. 2022) (citation and internal quotation marks omitted).

Both parties agree that the definition must include the bold text above. (Dkt. 124, ROB at 24; Dkt. 146, MOB at 23). Regeneron stops there, but would add the underlined language if the follow-on italicized language also is added. (Dkt. 124, ROB at 24). Mylan's construction included the underlined language, but Mylan would add the italicized text if it has its plain and ordinary

meaning, and *is not* interpreted to add undefined hydrolysates to a CDM. (Dkt. 146, MOB at 23-24).

The Court construes a chemically defined medium to first include the express definition in the specification, where a "chemically defined medium" or CDM means "a synthetic growth medium in which the identity and concentration of all the ingredients are defined. Chemically defined media do not contain bacterial, yeast, animal, or plant extracts, animal serum, or plasma…."

Given this definition, since chemically defined media 1) are defined; and 2) "do not include … yeast … or plant extracts," they cannot include hydrolysates. Hydrolysates are both chemically ***un***defined; and made from the expressly excluded yeast or plant extracts. (Dkt. 146, MOB at 23-24; Dkt. 173, MRB at 21-24). Mylan's expert confirms that those of ordinary skill in the art understand that hydrolysates are "***protein extracts*** derived from plants or yeast" that have been enzymatically digested, rendering them "***undefined*** mixtures of oligopeptides and other unknown components and contaminants." (Dkt. 146, Jungbauer Decl. ¶ 44, 74) (emphasis added). This is outside the scope of the specification's definition, which requires a CDM to be chemically defined. (Dkt. 146, '715 patent at 30:44-31:5; Dkt. 146, WO 217 at [009] (emphasis added); Dkt. 146, Jungbauer Decl. ¶ 74).

The WO 217 publication that column 30's definitional paragraph incorporates by reference highlights the distinction between a chemically defined medium and a hydrolysate one. It explains that cell culture media with "extracts" like "protein hydrolysates derived from plants or yeast" help cells grow efficiently, but come with a downside: "undefined mixtures of oligopeptides and other unknown components and contaminants," will cause "the quality of commercially available lots" to vary "extremely." (Dkt. 146, WO 217 at [003], [006], [009]). WO 217 states that a chemically defined cell culture media that "eliminate[d] … plant and/or yeast derived hydrolysates" and "which do not comprise any added supplementary proteins or oligopeptides," beneficially "increase[ed] the protein and/or virus expression per cell," gave consistent "cell growth" and "increased yield of desired products," and also "obviate[d] the addition of protein hydrolysate to the cell culture medium." (*Id.* at [013] – [016]).

The parties dispute the impact of the italicized text above from column 30 that follows: "*…although individual plant or animal-derived components (e.g., proteins, polypeptides, etc.) may be added*," and specifically, whether this text allows the CDM definition to reinstate hydrolysates. (Dkt. 146, '715 patent at 30:49-51).

Regeneron contends that the "… *although*" language expands CDM's definition to include hydrolysates. (Dkt. 124, ROB at 25). Mylan responds that Regeneron's approach eviscerates the immediately preceding definitional text as follows:

> a synthetic growth medium in which the ~~identity and concentration of all the ingredients are defined. Chemically defined~~ media do not contain bacterial~~, yeast~~, animal, ~~or plant~~ extracts, animal serum, or plasma…."

(*See* Dkt. 268, RGN PPP at slide 73). Specifically, allowing chemically undefined hydrolysates back into the chemically defined medium via the "…*although individual plant or animal-derived components (e.g., proteins, polypeptides, etc.) may be added*" clause would cause the medium to 1) fail the requirement that the identity and concentration of all ingredients be defined (and both parties agree this must be part of the CDM definition); and 2) fail the requirement of not containing "yeast … or plant extracts," because hydrolysates are "protein extracts derived from plants or yeast" that have been enzymatically digested. (Dkt. 146, MOB at 23-24; Dkt. 173, MRB at 21-24; Dkt. 146, WO 217 at [004] – [007]; Dkt. 146, Jungbauer Decl. ¶¶ 44, 72-73). If Regeneron intended to permit hydrolysates in the CDM, it could have simply eliminated the words in its definition rather than adding a new "…*although*" clause. Mylan thus proposes that the "…*although*" language must have a different meaning. Consistent with practice in the field

with supplements, it permits adding an ***individual*** protein or polypeptide (*e.g.*, insulin, a growth hormone), whose composition can be known and defined, and not run afoul of the other definitional requirements. (Dkt. 146, Jungbauer Decl. ¶¶ 74, 78; Dkt. 146, MOB at 26-27, Dkt. 176, MRB at 23-24; *see also* Dkt. 146, '715 patent; Dkt. 146, Ex. 45 at 108 ("A commonly used protein in CHO cell culture is insulin which functions as growth factor in CDM."); Dkt. 269-1, MYL PPP at slide 119).

Regarding the understanding of those of ordinary skill in the art, Regeneron offers no rebuttal testimony to Dr. Jungbauer. Regeneron calls Dr. Jungbauer's declaration improper extrinsic evidence under *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1585 (Fed. Cir. 1996). (Dkt. 174, RRB at 24). But "[e]xperts may be examined to explain terms of art," the "background science" and courts may "mak[e] a factual finding that, in general, a certain term of art had a particular meaning to a person of ordinary skill in the art at the time of the invention." *Teva*, 574 U.S. at 332 (citation and internal quotation marks omitted). Dr. Jungbauer's testimony is directed to that purpose, which is a proper claim construction role for his opinions and testimony. (*See* Dkt. 173, MRB at 26).

Regeneron's interpretation of the "…*although*" text, (Dkt. 174, RRB at 24-25), also conflicts with not just the rest of the

column 30 definition, including the incorporated WO 217 specification; but also several other sections of the '715 patent's specification which clearly distinguish between a chemically defined medium, CDM, and a soy hydrolysate medium.

For example, the '715 patent's specification discusses producing aflibercept:

> using a cell culture medium. ***In one embodiment***, the cell culture medium is a ***chemically defined medium*** ("CDM"). CDM is often used because ***it is*** a ***protein-free***, ***chemically-defined*** formula using no animal-derived components and there is ***certainty as to the composition*** of the medium. ***In another embodiment***, the cell culture medium ***is*** a ***soy hydrolysate medium***.

(Dkt. 146, '715 patent at 2:22-28) (emphasis added). This language is clear that CDM ***is***, without exception chemically defined; has certainty as to the composition; and also is an embodiment that is different from the other embodiment—which ***is*** a soy hydrolysate medium.

Regeneron argues that because its current specification changed language in its original provisional application that read, "A CDM does not include hydrolysate such as, for example, soy hydrolysate," its CDMs can include hydrolysates under *MPHJ Tech. Invs., LLC v. Richo Ams. Corp.*, 847 F.3d 1363, 1368-69 (Fed. Cir. 2017). (*See, e.g.*, Dkt. 124, ROB at 25-26). But as Mylan points out, those skilled in the art know that soy hydrolysates

are undefined yeast or plant extracts, so this is a distinction without a difference. (Dkt. 173, MRB at 21-14; Dkt. 146, Jungbauer ¶¶ 73-74).[6] *MPHJ* also is distinguishable. In *MPHJ*, the provisional application discussed a one step operation; the later-filed application later converted it into a one step ***option***. *MPHJ*, 847 F.3d at 1368-69. The issued patent's specification "contain[ed] no statement or suggestion" that the scope of the invention might be limited to a one step operation, thus those skilled in the art "would reasonably conclude that the inventor intended that single-step operation would be optional, not obligatory." *Id.* at 1369. Here, as just noted above, the '715 patent ***retained*** its CDM specification definition and statements that expressly 1) exclude undefined components derived from plant extracts, 2) require the medium ingredients to be chemically defined; and 3) differentiate between a CDM and a soy hydrolysate medium.

More applicable is *SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187 (Fed. Cir. 2013). SkinMedica's claims involved culturing

[6] Regeneron offers attorney argument via Exhibit 41 at page 19, that Sheff-CHO Plus PF ACF medium qualifies as defined because it lists specific amounts of the minerals calcium, iron and magnesium. (Dkt. 174, RRB at 25). Minerals are only a small subset of a hydrolysate composition, which contains thousands of unknown and undefined compounds. (Dkt. 146, WO 217 at [009]; Dkt. 269-1, MLY PPP at slides 100-101). Further, minerals are a different chemical class than proteins and peptides. Regardless, the legend on page 14 states "PF" refers to "protein free." (Dkt. 174, Ex. 41 at 14). Page 15 differentiates media that is "Defined" from media which is "non-animal hydrolysates," such as "UltraPrep Soy." (*Id.* at 15). Page 18 describes the Sheff-CHO Plus PF ACF medium as having a "various non-animal source," and made from enzymatic digestion. (*Id.* at 18; *id.* (describing ingredient ranges only as "typical")). Each fit the requirements for a non-chemically defined media.

cells in three dimensions in a cell culture medium. *SkinMedica*, 727 F.3d at 1190-91. SkinMedica's specification also disclosed growing cells "in two dimensions" on beads as a "convenient method for preparing, observing and studying cells in culture." *Id.* at 1191. SkinMedica urged its "three-dimensions" claims should cover these cell lines grown on beads. *Id.* at 1193-94. The Federal Circuit disagreed, because the intrinsic record confirmed that the "patentees clearly distinguish[ed] culturing with beads from culturing in three-dimensions." *Id.* at 1197. The specification did this by stating cell lines "grown as a monolayer or on beads, ***as opposed to*** cells grown in three-dimensions, lack the cell-cell and cell-matrix interactions characteristic of whole tissue in vivo"—using disjunctive language between the two terms, and describing their different effects. *Id.* (emphasis added). The '715 patent's specification, like *SkinMedica*'s, likewise uses disjunctive language to discuss chemically defined media ***or*** hydrolysate media; and emphasizes that the two different types of

media will yield significantly different effects.[7] (Dkt. 146, Jungbauer ¶ 79). By "directly contrast[ing] the term it is defining," CDM, with another listed alternative, soy hydrolysate medium, the '715 patent specification "plainly evinces an intent … to classify" the two cell culturing media as distinct. *SkinMedica*, 727 F.3d at 1202; *see also Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1270 (Fed. Cir. 2001) (construing "rate" and "mode" differently when "the patentees, throughout the specification, use the terms 'rate' and 'mode' to refer to separate and distinct concepts"); *Chi. Bd. Options Exch., Inc. v. Int'l Secs. Exch., LLC*, 677 F.3d 1361, 1371 (Fed. Cir. 2012) ("allocating" and "matching" construed to mean distinct processes based on specification).

[7] *See, e.g.*, Dkt. 146, '715 patent at 5:55-57 (protein "can be produced in cell culture medium including a chemically defined medium (CDM) ***or*** soy hydrolysate medium"); *id.* at 69:26-27 ("Anti-VEGF Protein Produced Using CDM"); *id.* at 70:15:34 ("In one embodiment, the anti-VEGF protein [made in CDM] can have a decreased level of fucosylated glycans … ***compared to*** the level of fucosylated glycans in an anti-VEGF protein produced using a soy hydrolysate"); *id.* at 70:35-54 ("the anti-VEGF protein [made in CDM] can have a decreased level of sialylated glycans . . . ***compared to*** the level of sialylated glycans in … protein produced using a soy hydrolysate"); *id.* at 70:55-71:7 (same medium comparison); *id.* at 71:8-27 (same medium comparison); *id.* at 98:56-65 (comparing examples "produced using CDM" 1, 2, or 3 to those "produced using soy hydrolysate"); *id.* at 106:11-16 ("The amount of 2-oxohistidines in MT1 (produced in a CDM) were higher than MT4 (produced in soy hydrolysate), ***suggesting that the media used to express aflibercept can have a significant effect***"); *id.* at 106:18-21 ("the … abundance of the peptide in MT1(CDM produced) was 0.015% ***compared to*** … the peptide in MT4 (soy hydrolysate produced"); *id.* at Table 6-1 (comparing results in a CDM versus soy hydrolysate); *id.* at Tables 6-2 through 6-5 (same); *id.* at 126:17-22 ("The total fucosylation, total sialylation, total galactosylation and mannose-5 observed …. ***These values*** for glycosylation ***differ*** from the glycosylation values obtained using soy hydrolysate") (all emphasis added).

Other claim terms, and the specification's definition of those terms, also support Mylan's proposed construction. Claims 1 and 16 (and the claims that depend upon them), use the term "cumulative concentration," requiring "cumulative concentration" ranges of particular components in the CDM. The specification expressly defines "cumulative concentration" as "the ***cumulative amount*** of a component divided by the volume of liquid in the bioreactor at the beginning of the production batch" and further defines "cumulative amount":

> As used herein, the term "cumulative amount" refers to the ***total amount*** of a particular component added to a bioreactor ***over the course of the cell culture to form the CDM*** …

(Dkt. 146, '715 patent at 31:6-9, 31:32-36). Adding hydrolysate, an undefined mixture of thousands of compounds of unknown identity and concentration, to a medium either before or during the time when the cell medium is in the bioreactor, precludes the bioreactor contents from qualifying as "chemically defined medium"—and render the cumulative concentration standards impossible to calculate, and thus meaningless. (Dkt. 146, MOB at 24, 26; Dkt. 173, MRB at 26-30; Dkt. 146, Jungbauer Decl. ¶¶ 75-79).

Regeneron responds that the cumulative concentration can be calculated at any point in time during the cell culture. (Dkt. 174, RRB at 27). But "any time" is not the same thing as what the specification's definition expressly requires measuring for the

claimed cumulative concentration—the "total amount … added to the bioreactor ***over the course of the cell culture*** to form the CDM." (Dkt. 146, 715 patent at 31:6-9 (emphasis added); Dkt. 146, Jungbauer ¶¶ 75-79).

Viewing the claims and specification as a whole, Regeneron's interpretation of the "…*although*" language to re-introduce hydrolysates invites legal error because it "contradicts the intrinsic record." *Profectus Tech. LLC v. Huawei Techs. Co., Ltd.*, 823 F.3d 1375, 1379 (Fed. Cir. 2016); *see also Phillips*, 415 F.3d at 1324 (noting that a court's construction may not "contradict claim meaning that is unambiguous in light of the intrinsic evidence"). It also conflicts with the specification's rationale for using CDM in the first place: to eliminate undefined media in cell culture, to avoid the "lot-to-lot variability" and "consistency" problems that hydrolysates caused for Regeneron. A more reasonable interpretation that does not conflict with the intrinsic record is that the "…*although*" clause lets an individual chemically defined protein or polypeptide supplement CDM. Whatever that component may be, it won't be the chemically undefined hydrolysates.

<u>The prosecution history: Regeneron expressly differentiated between its claimed CDM and prior art hydrolysates</u>

Regeneron finds it "hard to imagine a record that could more clearly demonstrate Regeneron's intent to define 'CDM' differently from how it is defined in the '635 provisional application," since there it defined CDM to expressly exclude hydrolysates. (Dkt. 174, RRB at 26). Mylan responds that hydrolysates are yeast or plant extracts, thus one of ordinary skill in the art knows that this a superficial and not substantive change—one of ordinary skill in the art knows that there is no *scientific* difference between stating, "CDM does not include hydrolysate" and "Chemically defined media do not contain … yeast … or plant extracts." (Dkt. 146, '715 patent at 30:47-51; Dkt. 174, MRB at 23-24; Dkt. 146, Jungbauer ¶ 74).

Critically, Regeneron relied on the difference between a CDM and an undefined medium with hydrolysates to differentiate the prior art during prosecution. Regeneron presented claims to the PTO that read as follows:

> 18. A method of producing aflibercept harvested from a host cell cultured in a chemically defined medium (CDM), comprising:
>
> (a) providing a host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under conditions suitable in which said host cell expresses said aflibercept; and
>
> (c) harvesting aflibercept produced by said host cell …

(Dkt. 146, Ex. 27 at 5). The Examiner rejected that and other pending claims as anticipated by Regeneron's Johnson reference (U.S. Publication No. 2018/0223249), noting that Johnson taught carrying out the cell culture step "in a chemically defined medium." (Dkt. 146, Ex. 25 at 10-11).

Responding to the Examiner's rejection, Regeneron insisted that the Johnson publication's cell culture media could not anticipate the claimed CDM. While Regeneron acknowledged that Johnson discussed the "general use of cell culture media, including CDM," (Dkt. 146, Ex. 27 at 16), Regeneron argued that Johnson did not disclose the claimed CDM/antioxidant concentration elements, because Johnson used the antioxidants taurine and cysteine only "in serum free media ***which may contain hydrol[y]sates*** and not CDM." (*Id.*) (emphasis added). Regeneron argued this again regarding Johnson's use of cysteine: "the cysteine is not necessarily added to CDM and may instead be used with serum-free media ***containing hydrolysates***." (*Id.* at 17) (emphasis added).[8]

The prosecution history, viewed from the perspective of one of ordinary skill in the art, confirms that Regeneron distinguished between its chemically defined medium and one "which may contain"

[8] Johnson also distinguished between "chemically defined media, which is not only serum-free, but also hydrolysate free," and a cell culture medium which could be "serum free," but also contain "≤ 16 g/L of hydrolysates, such as soy hydrolysate…." (Dkt. 146, Johnson at [0059]).

or "containing" hydrolysates. (Dkt. 146, Jungbauer Decl. ¶¶ 87-89; Dkt. 146, Ex. 27 at 17). If hydrolysate-containing medium, in whole or in part, qualified as the chemically defined medium in the pending claims, then nothing distinguished Johnson's medium containing, *e.g.*, cysteine or taurine, from what the pending claims before the PTO required. *See Personalized Media Commc'ns, LLC v. Apple Inc.*, 952 F.3d 1336, 1340 (Fed. Cir. 2020) ("[A]n applicant's amendment accompanied by explanatory remarks can define a claim term by demonstrating what the applicant meant by the amendment."); *see also Tegal Corp. v. Tokyo Electron Am., Inc.*, 257 F.3d 1331, 1343 (Fed. Cir. 2001) ("In the prosecution history, [Plaintiff] also distinguished over the [prior art] reference by stating that 'the electrodes claimed in the present invention are not the same as those disclosed in [the reference],' which [Plaintiff] described as being spiked electrodes. Accordingly, the term 'electrode' must be construed so as not to cover a spiked electrode."). These clear prosecution history representations thus independently confirm that hydrolysates cannot be included within the scope of the claim term "chemically defined medium."

The Court adopts Mylan's construction. It more correctly adheres to the provided specification definition, as well as the remaining intrinsic evidence of record regarding the scope and

meaning of the claim language, which excludes hydrolysates from the CDM.

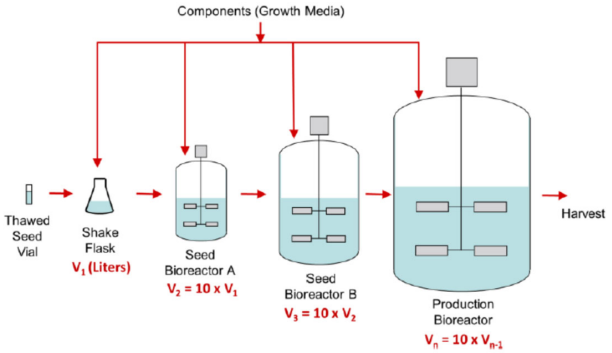
b. "Harvested from a Host Cell Cultured in a Chemically Defined Media (CDM)"

Plain and ordinary meaning

Both Regeneron and Mylan ask the Court to apply the plain and ordinary meaning to the "harvested from a host cell cultured in" CDM claim language.[9] The parties agree that for the phrase's use of the term "chemically defined medium (CDM)," the Court's construction for CDM above applies. Each party differs on what constitutes the ordinary meaning of "harvested from a host cell cultured in" CDM.

One of ordinary skill in the art knows that cell growth will start after "thawing a seed vial into a small container, along with a solution of sugars, amino acids, and other nutrients essential for the cells to survive, grow, and divide." (Dkt. 146, Jungbauer Decl. ¶ 45).

[9] Some now-dropped claims in the Manufacturing Patents also used the phrase, "a clarified harvest of a cell cultured in a chemically defined medium."



Regeneron seemingly agrees that a cell culturing process will involve culturing a cell with a cell culture medium under conditions suitable to the survival, growth, or proliferation of the cell. (Dkt. 268, RGN PPP at slide 77 (citing Jungbauer testimony)). Eventually, cells are transferred to the final bioreactor. After "growing for a period of time, typically a few days, in the largest container, the production bioreactor," the "cells are harvested and the protein they produced is purified, often by chromatography." (Dkt. 146, Jungbauer Decl. ¶ 48). As shown in the diagram above, *harvesting* is at the end of that bioreactor process. (*Id.* ¶¶ 46, 48; Dkt. 146, '715 patent at 2:29-35 (harvesting occurs after the cell culturing process)). Dr. Jungbauer's explanation is consistent with the '715 patent, which recognizes that proteins can be produced inside the cells, or "directly secreted" from the cell "into the [cell culture] medium." (Dkt. 146, '715 patent at 55:38-41). The proteins "may be

harvested" from that medium using various separation techniques, including chromatography. (*Id.* at 55:49-52; *see also id.* at 2:55-57 ("in one embodiment, a clarified harvest sample from a CDM culture comprising aflibercept is subjected to a capture chromatography procedure")).

A person of ordinary skill in the art also understands that to describe a protein as harvested from a host cell cultured in a particular medium, is to convey that the protein was harvested from a process made using only that particular medium. (Dkt. 146, Jungbauer Decl. ¶ 25). This is especially so when describing a protein harvested from a host cell cultured in a chemically defined medium—if the harvesting is not done from host cells cultured *throughout the process* in a chemically defined medium, then that cell culture process and product loses the whole point of being cultured in a way that is "chemically defined." (*Id.* ¶¶ 26, 75-79). The natural reading of the harvest-related claim language is that the harvest was made from a host cell cultured in CDM. (Dkt. 146, MOB at 26; Dkt. 173, MRB at 26-28; Dkt. 269-1, MLY PPP at slides 122, 138).

Regeneron did not put forth any rebuttal or contradictory testimony on the understanding of a person of ordinary skill in the art from anyone who qualifies as a person of ordinary skill in

the art. Mylan's expert testimony is consistent with the intrinsic record.

Thus, the plain and ordinary meaning of "harvested from a host cell cultured in a chemically defined medium (CDM)" generally means that the protein will be harvested from a host cell cultured in CDM throughout; and the cell culture at the time of harvesting will likewise be from cells being cultured in the CDM.

The context of the claims

Regeneron argues that the phrase, "harvested from a host cell cultured in chemically defined medium (CDM)" need not be treated as involving one start-to-finish process, but can be considered piecemeal, so that a host cell need only be "cultured in a chemically defined medium" at "*some point* during the cell culture process," while the "harvesting" step need not use a chemically defined medium at all, but can come from host cells cultured in a bioreactor using a non-chemically defined medium. (Dkt. 124, ROB 27; Dkt. 174, RRB at 26).

Mylan responds that Regeneron's approach improperly rewrites the claims to eliminate both the meaning of harvesting from host cells cultured in the medium, as well as the "chemically defined medium" requirement. Those of ordinary skill do not consider cells cultured in undefined media (even if put at one point in CDM), to

qualify as "harvested from a host cell cultured in a chemically defined medium." (Dkt. 146, Jungbauer Decl. ¶¶ 26, 75-79).

Regeneron admits that under its "for a period of time" construction, the only way to *avoid* its claims would be for a cell culture process to "occur entirely in non-CDM" from start to finish. (Dkt. 174, RRB at 27-28). Regeneron, in essence, seeks to cover *all* cell culture processes, so long as CDM medium is used at one moment in time. While Regeneron makes a purported fairness appeal with regard to Mylan's process to justify this, (*see* Dkt. ROB at 26-28; Dkt. 268, RGN PPP at slides 78-79), the Federal Circuit prohibits using the accused process to drive claim construction, which Regeneron's "at some point" theory transparently attempts to do. *NeoMagic*, 287 F.3d at 1074 (stating that "claims may not be construed by reference to the accused device"). It also conflicts with the ordinary meaning of CDM, harvesting, a natural reading of the claims, and is not supported by the intrinsic record. (Dkt. 173, MRB at 28-30; Dkt. 146, Jungbauer ¶¶ 84-89).

If the claims were to actually cover both CDM-based and non-CDM-based culturing, the claims could simply recite, "…aflibercept from cells cultured in a cell culture medium." But the claims purposefully joined "harvested from" *and* "a host cell" *and* "cultured in a chemically defined medium" together; that cannot be

disregarded just because the word "comprising" is later used in the claim. While "comprising" can permit "additional elements not required by a claim," the term "*does not remove the limitations that are present*." *Power Mosfet Techs., LLC v. Siemens AG*, 378 F.3d 1396, 1409 (Fed. Cir. 2004) (emphasis added).

Since asserted independent claim 16 uses the relevant language identically to the other independent claims, it is representative for purposes of the "harvested from a host cell cultured in a chemically defined medium (CDM)" step, in bold italics below:

> 16. A method of producing aflibercept ***harvested from a host cell cultured in a chemically defined medium (CDM)***, comprising:
> …
> ***culturing said host cell in said CDM*** under conditions suitable in which said host cell expresses said aflibercept …
> and…
> harvesting aflibercept produced by said host cell.

(Dkt. 146, '715 patent at 262:52-263:4, 261:2-23).

Regeneron argues that the term "comprising" after the phrase, "harvested from a host cell cultured in a chemically defined medium (CDM)," justifies breaking the "harvesting" step apart from culturing the host cells in a CDM; and after this partition, they can apply their "at some point in time" meaning, citing *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364 (Fed. Cir. 2003). (Dkt. 124, ROB at 28-29; Hearing Tr. at 149:21-151:10). Mylan

responds that *Invitrogen* does not allow Regeneron to sever the harvesting step from cells cultured in CDM throughout the process range set forth in the claims. (Dkt. 173, MRB at 29).

The *Invitrogen* claim 1 stated as follows:

> 1. A process for producing transformable E. coli cells of *improved competence* by a process **comprising** the following steps in order:
> (a) *growing* E. coli cells in a growth-conducive medium at a temperature of *18° C. to 32° C.;*
> (b) rendering said E. coli cells competent; and
> (c) freezing the cells.

Invitrogen, 327 F.3d at 1366 (bold underline added; italics in original). The specification described the E. coli cell cultivation process as one that involved the claimed steps (a) and (b), but *also* other known growth steps, such as growing "master seeds," which were unclaimed steps. *Id.* at 1368-69. The specification taught that the master seeds had to be further processed "*before* becoming the primary seeds for use in the claimed method." *Id.* The claims also were limited to just one part of the cell growth phase: the "improved competence" process. *Id.* at 1369. The Federal Circuit thus found that the claims had not "addressed or limited" activities that "occurred before steps (a) and (b)." *Id.* at 1368. The description of the process as one for "improved competence" at certain temperatures, could "not preclude growth before the first step" at higher temperatures, such as a

cell growth phase that took place before the claimed improved competence process began. *Id.* at 1369.

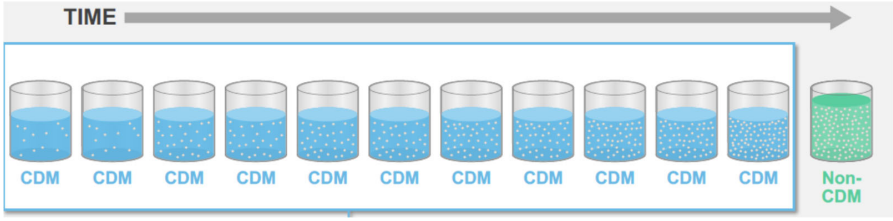
Regeneron argues that just as *Invitrogen* allowed cell culturing to occur at other temperatures, the same reasoning lets its cells use other culture media. (Dkt. 124, ROB at 28-29; Hearing Tr. at 150:23-151:10). Mylan responds that this is an oversimplification and a misapplication of the Invitrogen's reasoning. *Invitrogen*'s steps (a) and (b) expressly limited the claims to a limited "improved competence" cell culture step. The Federal Circuit just declined to expand the claimed "improved competence" temperature limits to different, unclaimed, process phases. *Invitrogen*, 327 F.3d at 1368-69. Here, by contrast, the '715 patent's claims do *not* use language carving up the cell culture process between start and harvest; and do *not* divide the cell culture process into subset steps. Aflibercept must be "harvested from a host cell cultured in a chemically defined medium (CDM)," without exception.

The correct way to apply *Invitrogen*'s analysis to the claims here is to start with *Invitrogen*'s claim 1 preamble, which used the term, "improved competence" and which preceded the term "comprising." *Invitrogen*, 327 F.3d at 1366. The Federal Circuit confirmed that this preamble limited the scope of the claimed process steps; and that all steps within the "comprising" part of

the method had to *also* fulfill the role of being "improved competence" steps. *Id.* at 1368-70. The '715 patent's claim 16 likewise places "harvested from a host cell cultured in a chemically defined medium (CDM)" in the preamble, and *before* the word "comprising":

> 16. A method of producing aflibercept **harvested from a host cell cultured in a chemically defined medium (CDM), comprising**: …

(Dkt. 146, '715 patent at 262:52-54) (emphasis added). Under *Invitrogen*, "harvested from a host cell cultured in a chemically defined medium" limits all of the steps in the claimed process; and likewise, all of the steps that are listed after "comprising" must be a part of the process of "harvested from a host cell cultured in a chemically defined medium (CDM)." *Invitrogen*, 327 F.3d at 1368-69. Thus, this scenario Regeneron presented at oral argument:



is not something that *Invitrogen* lets the '715 patent claims do, because this chops up one unified "host cell cultured in a" CDM preamble requirement into multiple sub-culture and media steps that fall outside it. (Dkt. 268, RGN PPP at slide 78).

Regeneron argues that requiring the full process from cell culturing to harvest to be in a chemically defined medium would either improperly add or remove claim limitations. (Dkt. 124, ROB at 28-29; Dkt. 174, RRB at 28). It does not. This approach applies and upholds the existing placement, scope, and order of the claim terms, and adheres to the intrinsic record.

Regeneron argued that re-using the host cell and chemically defined medium terms after "comprising" was good enough to convert the method steps into an open-ended process that creates multiple cell cultures to permit non-CDM culturing and harvesting. (Hearing Tr. at 149:4-20; Dkt. 268, RGN PPP at slides 80-81). The '715 patent's claim 16 does have steps after "comprising" involving aflibercept, host cells, and the medium; but they are not truly open-ended. The claim language states, "***said*** aflibercept," "***said*** host cell" and "***said*** CDM":

> 16. A method of producing ***aflibercept*** harvested from a ***host cell cultured in a chemically defined medium (CDM)***, comprising: …
> culturing ***said host cell*** in ***said CDM*** under conditions suitable in which ***said host cell*** expresses ***said aflibercept*** … and …
> harvesting aflibercept produced by ***said host cell***.

(Dkt. 146, '715 patent at 262:52-263:5) (emphasis added). As in *Invitrogen*, once claim 1 preceded the terms "aflibercept," "host cell" and "CDM" with the word "said," that language tied the terms'

scope to their limiting antecedent preamble phrase, "aflibercept harvested from a host cell cultured in a chemically defined medium (CDM)." *Invitrogen*, 327 F.3d at 1368 (Step (b) was limited to only those cells that "immediately result from Step (a) … Step (b) conveys this by stating 'rendering *said* E. coli cells competent' (emphasis added)."); *see also Traxcell Techs., LLC v. Nokia Sols. & Networks Oy*, 15 F.4th 1136, 1144 (Fed. Cir. 2021) ("it would defy the concept of antecedent basis" for claims that used "said first computer" to not be "tied to all those functions" the claims imposed on the first computer). The cell culture steps can't be further split into different media.

Dippin' Dots, Inc. v. Mosey, 476 F.3d 1337 (Fed. Cir. 2007), also rejects Regeneron's open-ended construction theory here. In *Dippin Dots*, the patentee argued that the term "comprising" at the beginning of the claim rendered its later steps open ended, so that a specified method step—freezing a composition into a bead shape—covered a process that made both bead-shaped spheres *and* irregular particles. *Dippin' Dots*, 476 F.3d at 1343. Regeneron similarly argues that its listed process step of aflibercept harvested from a host cell cultured in a CDM includes cell cultures produced in CDM *and* non-CDM. (Dkt. 124, ROB at 28-30; Dkt. 174, RRB at 28-30; Dkt. 268, RGN PPP at slides 78-79). The Federal Circuit reiterated that comprising is not a "weasel word" that

abrogates claim limits. *Dippin' Dots*, 476 F.3d at 1343. It does not "render every word and phrase" in the recited steps open-ended; *recited* steps must be practiced as-recited. *Id.* The district court in *Dippin Dots* thus correctly construed the step of freezing the composition into a bead shape to mean a beads-only process, not a step that permitted a combination of beads ***and*** other particles. *Id.* Similarly, here the recited step of "culturing said host cell in said CDM" cannot be opened up to mean multiple culture steps occurring in non-CDM; the cell culturing process can only allow CDM.

Thus, the term "comprising" cannot expand the claims to allow host cells to be cultured in CDM only "at some point in time," or have aflibercept be harvested from non-CDM.

<u>The context of the specification</u>

Regeneron's "at some point in time" approach via the word "comprising" also conflicts with the specification. The term "comprising" does not let patentees capture subject matter that is contrary to the written description. *Trading Techs. Int'l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1354-55 (Fed. Cir. 2010).

Mylan reiterates that Regeneron's interpretation is scientifically inconsistent, and conflicts with the specification. (Dkt. 146, MOB at 27-29; Dkt. 174, MRB at 25-26). The main focus of the '715 patent was to establish a cell culture process that

eliminated non-defined media entirely, to produce "certainty as to the composition" and to avoid the "reproducibility/consistency" and "lot-to-lot variability" issues that arose with Regeneron's use of hydrolysate in earlier processes. (Dkt. 146, '715 patent at 2:24-27; Dkt. 146, Ex. 12 at [0046], [00164]; Dkt. 269-1, MYL PPP at slide 102). Regeneron's "at some point" theory would include in the process the very undefined ingredients that the specification says to avoid; and reintroduces the reproducibility, consistency, and lot-to-lot variability problems that the specification and intrinsic record say using CDM is supposed to solve.

Regeneron also objects to the premise that the cells are in CDM at the time of harvesting, (Dkt. 124, ROB at 27-30; Dkt. 174, RRB at 26-30), and suggested at oral argument that just like its proposal that its one cell culturing step can be broken apart into multiple cell culturing steps, harvesting is an ongoing process, not an event that happens at the end, (Hearing Tr. at 148:5-151:10). Nothing in the specification supports that view.

The '715 patent confirms that proteins can be produced inside the cells, or "directly secreted" from the cell "into the [cell culture] medium." (Dkt. 146, '715 patent at 55:38-41). But when the proteins "may be harvested" from that medium, it requires using various separation techniques. (*Id.* at 55:49-52; *see also* at 2:55-

57 ("In one embodiment, a clarified harvest sample from a CDM culture comprising aflibercept is subjected to a capture chromatography procedure.")). No mention is made of splitting the culturing and harvesting steps, let alone into different media at different times, or switching media at harvesting time.

The specification is consistent with using CDM for the whole process. For example, Example 1 of the '715 patent discusses "Using a Chemically Defined Medium" for a "Cell Source and Harvest" process. (Dkt. '715 patent at 99:36-39). This process uses an "aflibercept producing cell line," which was "cultured ***and*** harvested using chemically defined media (CDM)." (Dkt, 146, '715 patent at 99:37-43); *see also id.* at 123:44-46 ("A clarified ***harvest using each of the CDM*** was prepared by centrifugation followed by 0.45 um filtration.") (all emphasis added).[10]

The specification also is clear that harvesting secreted proteins is an end-stage process where the proteins are separated from both the medium and cells by using *e.g.*, a concentration filter, or centrifugation followed by depth filtration and

[10] *See, e.g.*, Dkt. 146, '715 patent at 62:54-57 ("compositions can be obtained ***from*** the clarified ***harvest made using CDM***"); *id.* at 63:27-28 ("compositions can be obtained ***from*** a clarified harvest ***made using CDM***"); *id.* at 63:64-66 (same); *id.* at 64:14-17 (same); *id.* at 71:57-62 ("This invention includes culturing a host cell in a modified CDM under suitable conditions in which the cell expresses a recombinant protein of interest followed by harvesting a preparation of the recombinant protein of interest produced by the cell. Such a modified CDM can be used to produce the compositions as described above…."); *id.* at 71:63-72:13 (harvesting from the CDM once the CDM achieved particular cumulative concentrations) (all emphasis added).

affinity capture. (Dkt. 146, '715 patent at 55:45-52 (discussing harvesting process generally); *id.* at 76:53-60 (process with "a host cell in a CDM," where "protein is secreted from the host cell into the medium and a clarified harvest is obtained" has "biological sample obtained from the harvest" loaded onto chromatography column); *id.* at 123:44-46 ("A clarified harvest using each of the CDM was prepared by centrifugation….")).

The specification in *Invitrogen*, which Regeneron relies on, made clear distinctions between cell culture steps that were not part of the claimed method (*e.g.*, storing and processing master seeds); and culturing primary cells during the claimed "rendering competent" step. *Invitrogen*, 327 F.3d at 1368-69. *Invitrogen*'s Example 3 used different temperatures for unclaimed process steps, including for ancestral growth, before reducing the temperature to the claimed range for the full "rendering … competent" step (b) stage. *Id.* at 1369. This showed a deliberate intent to carve that earlier step out of the claims' more limited temperature range.

By contrast here, the '715 patent's specification nowhere describes either host cell culturing or aflibercept harvesting involving CDM to be an "at some point" or even in any mixed-media process. Rather, it uniformly states that "compositions can be obtained from the ***clarified harvest made using CDM***." (Dkt. 146,

'715 patent at 62:54-55) (emphasis added).[11] The specification, including all examples, describe cultures and harvests either from CDM from start to harvest finish; or from a different culture from start to harvest finish. (Dkt. 146, Jungbauer Decl. ¶¶ 84-86). The '715 patent has *no* examples or other written description of switching or mixing the media during culturing, or by the time of harvesting. *See* 35 U.S.C. § 112 (specification must disclose the manner and process of making and using the invention "in such full, clear, concise, and exact terms" to permit the person of ordinary skill to understand what was invented).

When the specification does refer to a harvest's cell culture in a manner that is not specific as to the type of medium being used, it used language such as, "harvested cell culture fluid." (Dkt. 146, '715 patent at 54:44-45). The claims do not use this more general non-media specific term; the claims call for harvesting aflibercept from a host cell cultured in CDM.

Thus, the specification conveys that the host cell culturing, and aflibercept harvesting, both occur in the chemically defined medium (CDM) throughout.

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[11] *See also id.* at 63:27-28 ("compositions can be obtained ***from a clarified harvest made using CDM…***"); *id.* at 63:50-51; *id.* at 63:64-65 ("clarified harvest made using CDM"); *id.* at 64:14-15 (same); *id.* at 71:57-62 ("This invention includes ***culturing a host cell in a modified CDM*** under suitable conditions in which the cell expresses a recombinant protein of interest ***followed by harvesting a preparation*** of the recombinant protein of interest produced by the cell. Such a modified ***CDM can be used to produce the compositions*** as described above….") (all emphasis added).

The prosecution history

During prosecution of the 715 patent, Regeneron sought claims as follows:

> 1. A method of producing aflibercept having a reduced amount of aflibercept variants expressed in a host cell cultured in a chemically defined medium (CDM), comprising:
> (a) providing said host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under conditions suitable in which said host cell expresses said aflibercept to produce an aflibercept sample; and
> (c) harvesting protein produced by said host cell, …
>
> 18. A method of producing aflibercept harvested from a host cell cultured in a chemically defined medium (CDM), comprising:
> (a) providing a host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under conditions suitable in which said host cell expresses said aflibercept; and
> (c) harvesting aflibercept produced by said host cell, …
>
> 23. A method of increasing production of aflibercept harvested from a host cell cultured in a chemically defined medium (CDM) and reducing aflibercept sample color, comprising:
> (a) providing said host cell genetically engineered to express aflibercept;
> (b) culturing said host cell in said CDM under suitable conditions in which said host cell expresses aflibercept;
> (c) harvesting aflibercept produced by said host cell forming a harvest comprising aflibercept wherein: …

(Dkt. 146, Ex. 27 at 3, 5, 7; *see also* Dkt. 146, Ex. 25 at 11).

The PTO rejected these and other claims "as being anticipated by Johnson et al. (US Publication No. 2018/0223249 published 8/9/2018)." (Dkt. 146, Ex. 25 at 11). The PTO explained that the claim 1 above was directed in part to "a method of producing aflibercept by culturing a CHO host cell that expresses aflibercept in a chemically defined medium (CDM)," claim 18 above was directed in part to "a method of producing aflibercept produced by a host cell that expresses aflibercept wherein said host cell is cultured in a CDM that comprises an anti-oxidant," while pending claim 23 above was directed in part to "a method of increasing the production of aflibercept harvested from culturing a host cell that expresses aflibercept, wherein the host cell is cultured in a CDM that comprises an anti-oxidant…." (*Id.*)

The PTO observed that "Johnson et al. teach a method" of producing proteins such as aflibercept in a CHO host cell, "wherein said culturing is carried out in a chemically defined medium," and where antioxidants are used. (Dkt. 146, Ex. 25 at 11).

In response, Regeneron argued that:

> *Johnson* does not disclose ***producing and harvesting aflibercept in CDM*** having a target value of aflibercept variants…. Likewise, *Johnson* does not disclose ***producing and harvesting aflibercept in CDM*** having a target value of aflibercept variants that can be obtained by adding anti-oxidants where the cumulative concentration for all anti-oxidant in the CDM does not exceed 30 mM, as recited in some of the pending claims.

(Dkt. 146, Ex. 27 at 17) (emphasis added).

Regeneron thus clearly described its claimed process, and argued that it was different from Johnson's, because the steps of both producing ***and*** harvesting aflibercept, *i.e.*, the entire process, occurred ***in CDM***. Likewise, as noted in ¶¶ 180-182 above, Regeneron differentiated Johnson because Johnson used "serum free media which may contain hydrol[y]sates and not CDM." (Dkt. 146, Ex. 27 at 16). Regeneron thus explicitly foreclosed even the option of its claims using a medium that "may contain" hydrolysates at some point.

This again differentiates the prosecution history in *Invitrogen*. There, during prosecution the patentee replaced the original step (a)'s claim language "less than 37°C" with the amended and issued 18° C to 32° C temperature range; this "did not disclaim all growth above 32° C" for all steps, but rather "emphasized the advantages of growth at 18° C to 32° C [in step (a)] immediately before rendering the E. coli competent [in step (b)]." *Invitrogen*, 327 F.3d at 1369. Here, Regeneron emphasized that it was both producing in ***and*** harvesting from ***only CDM***, and that this CDM production and harvesting differentiated its claims from Johnson.

Regeneron's arguments before the PTO are analogous to those the patentee made in *Amgen Inc. v. Coherus BioSciences Inc.* that

were construed as limiting. 931 F.3d 1154, 1159-61 (Fed. Cir. 2019). In *Amgen*, the PTO rejected Amgen's claims to a pharmaceutical formulation; and Amgen responded that the PTO's prior art Holtz reference did not disclose "the particular combinations of salts recited" in Amgen's claims. *Id*. at 1158 (internal quotation marks omitted). Likewise here, the PTO rejected Regeneron's claims over Johnson; and Regeneron responded that Johnson did not disclose the particular CDM-only culturing and harvesting step. The Federal Circuit confirmed in *Amgen* that this was a "clear and unmistakable surrender" of a broader meaning for salts, and held the claims limited. *Id*. at 1161. The same is true here: Regeneron cannot secure coverage to a "partial" CDM process once it represented and confirmed to the PTO that its process was different from the prior art processes because culturing ***and*** harvesting occurred ***only in CDM***.

Regeneron points to a different part of the prosecution history where the PTO rejected a claim that read, a "method of producing aflibercept, comprising: (a) binding aflibercept from a clarified harvest cultured in a chemically defined medium to a Protein A resin…" as indefinite. (*See* Dkt. 124, Ex. 21 at 3; Dkt. 124, Ex. 20 at 3). The PTO pointed out the phrase lacked a proper antecedent basis, "because the claim does not state what is cultured in the CDM." (Dkt. 174, Ex. 20 at 3). The PTO pointed

out that "a harvest is typically the product of a culturing step rather than the substance which is cultured." (*Id.*)

In response, Regeneron amended the claims. Regeneron argues that its amendment made clear "that it was the cells, not the harvest, that must be 'cultured in a chemically defined medium (CDM).'" (*See* Dkt. 124, ROB at 30; Dkt. 124, Ex. 21 at 3). First, that is not at all how Regeneron phrased it to the PTO—what Regeneron stated is that the purpose of the amendment was "to clarify the use of the chemically defined medium and address the antecedent basis rejection for claim 27." (Dkt. 124, Ex. 21 at 7). Second, that doesn't change the premise that the entire cell culturing process must occur only in CDM.

Moreover, in the final claims that issued, the antecedent basis for what is cultured in the CDM is the language that was preserved in the preamble: "aflibercept harvested from a host cell cultured in a chemically defined medium (CDM)." (Dkt. 146, '715 patent at 262:52-263:4). And, what Regeneron's cited text from the prosecution history did not change, modify, or repudiate, was its clear representation that its claims differed from Johnson because it was ***producing and harvesting aflibercept in CDM*** only.

Regeneron argues that "[n]othing in the prosecution history suggests that the word 'comprising' in the Manufacturing Patents should be read to exclude cell culture processes having an

unrecited, non-CDM culturing step." (Dkt. 174, RRB at 30). To the contrary, the PTO's repeated rejections under 35 U.S.C. § 112 evidences the PTO's concern that Regeneron had not properly linked its claimed steps to their proper antecedent basis. (*See, e.g.*, Dkt. 146, Ex. 25 at 4-10). Further, Regeneron's unequivocal representation to the PTO regarding what it considered the scope of its claims, and that of the prior art, confirms that it intended its claims to cover "***producing and harvesting aflibercept in CDM***." (*See, e.g.*, Dkt. 146, Ex. 27 at 17).

Nothing in the intrinsic record justifies Regeneron's request to have the term harvesting from a cell cultured in CDM lose its ordinary meaning, or the repeated discussion that that the entire process will occur in CDM through harvest. Regeneron's "at some point in time" construction conflicts with the ordinary meaning, conflicts with the intrinsic record (the claims; the specification; and its representations made to the PTO), and also conflicts with the *Invitrogen* decision upon which Regeneron's "comprising" analysis was based.

Thus, the Court adopts Mylan's construction of this claim element, and rejects that "harvested from a host cell cultured in a chemically defined media (CDM)" could mean harvested from a host cell that "at some point in time" was cultured in a CDM.

c. "Anti-Oxidants"

Mylan originally identified the term "anti-oxidants" as needing construction and proposed that term be limited to "taurine, hypotaurine, glycine, thioctic acid, glutathione, choline chloride, hydrocortisone, Vitamin C, Vitamin E and combinations thereof." Regn. Ex. 26 at 7. Regeneron contends that the term is not so limited, and Mylan has refused to stipulate to Regeneron's position. Dkt. 102 at 7-9; Regn. Ex. 15 (Nov. 16, 2022 Mylan Email).

Claim 1 of the '715 refers to "anti-oxidants," without further limitation. By contrast, claim 3 of the '715 patent, which ultimately depends from claim 1, limits the set of anti-oxidants for that dependent claim to the following: "taurine, hypotaurine, glycine, thioctic acid, glutathione, choline, hydrocortisone, Vitamin C, Vitamin E or combinations thereof."

The specification of the '715 patent discloses "[n]on-limiting examples of the antioxidant," which include chemicals such as "S-carboxymethyl-L-cysteine" and "chelating agents" like "aurintricarboxylic acid" and "citrate." '715 patent, 23:64-24:3. Those exemplary anti-oxidants are excluded from Mylan's proposed construction of "anti-oxidants." At his deposition, Mylan's expert agreed that "anti-oxidants" are not limited to Mylan's list. Jungbauer Dep. 157:4-14.

The parties have a dispute over claim scope that the Court "must resolve." *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008); *see also Baxter Healthcare Corp. v. Mylan Labs. Ltd.*, 346 F. Supp. 3d 643, 653 (D.N.J. 2016). The doctrine of "claim differentiation" presumes that an independent claim has a different, broader scope than its dependent claim, *see Hill-Rom Servs.*, 755 F.3d at 1374, such that subject matter within the scope of a dependent claim necessarily is within the scope of an independent claim from which it depends, *see Littelfuse*, 29 F.4th at 1380 (Fed. Cir. 2022) ("By definition, an independent claim is broader than a claim that depends from it, so if a dependent claim reads on a particular embodiment of the claimed invention, the corresponding independent claim must cover that embodiment as well."). The presence of Mylan's list of anti-oxidants in dependent claim 3 gives rise to the strong presumption that claim 1—and the term "anti-oxidant" itself—is not so limited. *See id.; see also Intamin Ltd. v. Magnetar Techs., Corp.*, 483 F.3d 1328, 1335 (Fed. Cir. 2007); *AstraZeneca*, 2022 WL 17178691, at *5.

Mylan's proposed construction would also render claim 3 superfluous. Such a construction is "highly disfavored." *See Intel*, 21 F.4th at 810. Mylan's proposed construction also violates the fundamental rule that a construction that "most naturally aligns with the patent's description of the invention

will be, in the end, the correct construction." *Phillips*, 415 F.3d at 1316 (quoting *Renishaw,* 158 F.3d at 1250). Mylan's construction would exclude, without any basis, exemplary antioxidants recited by the specification. Therefore, the Court rejects Mylan's proposed construction and adopts Regeneron's proposal instead.

The Clerk is directed to forward a copy of this Order to all counsel of record.

DATED: April 19, 2023

Tom S Kleeh

THOMAS S. KLEEH, CHIEF JUDGE
NORTHERN DISTRICT OF WEST VIRGINIA