United States Court of Appeals for the Federal Circuit

REGENERON PHARMACEUTICALS, INC.,
Plaintiff-Appellant

v.

MYLAN PHARMACEUTICALS INC., AMGEN USA, INC., BIOCON BIOLOGICS INC., CELLTRION, INC., FORMYCON AG, SAMSUNG BIOEPIS CO.,
Defendants

AMGEN INC.,
Defendant-Appellee

2024-2351

Appeal from the United States District Court for the Northern District of West Virginia in Nos. 1:22-cv-00061-TSK-JPM, 1:23-cv-00089-TSK-JPM, 1:23-cv-00094-TSK-JPM, 1:23-cv-00097-TSK-JPM, 1:23-cv-00106-TSK-JPM, 1:24-cv-00039-TSK-JPM, 1:24-cv-00053-TSK, 1:24-md-03103-TSK-JPM, Chief Judge Thomas S. Kleeh.

Decided: March 14, 2025

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Before MOORE, *Chief Judge*, LOURIE and STARK, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Regeneron Pharmaceuticals, Inc. ("Regeneron") appeals from a decision of the United States District Court for the Northern District of West Virginia denying Regeneron's motion for a preliminary injunction. *In re Aflibercept Pat. Litig.*, No. 1:24-md-3103, 2024 WL 4958308 (N.D. W. Va. Oct. 1, 2024) ("*Amgen Decision*").[1] For the following reasons, we affirm.

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[1] The case generating this appeal is *Regeneron Pharmaceuticals, Inc. v. Amgen, Inc.*, No. 1:24-cv-39 (mistakenly identified as 1:23-cv-39 in the district court case caption), which is part of a consolidated multi-district litigation, No. 1:24-md-3103.

BACKGROUND

The district court denied Regeneron's motion because it failed to establish a likelihood of success in showing that Amgen Inc. ("Amgen") infringed its U.S. Patent 11,084,865 ("the '865 patent"). Regeneron's '865 patent is directed to pharmaceutical formulations of a fusion protein known as aflibercept, claimed by its amino acid sequence. The '865 patent is asserted to cover a vial containing Regeneron's biologic product EYLEA® ("Eylea") and is listed in the FDA's Purple Book[2] under Regeneron's Biologic's License Application ("BLA") 125387 for Eylea.

Regeneron obtained FDA approval to commercially market Eylea for administration in a vial presentation on November 18, 2011.[3] *Amgen Decision*, at *1. Eylea is an ophthalmic drug product used to treat angiogenic eye disorders, associated with uncontrolled blood vessel growth in the retina, that can cause vision loss or even blindness. *Id.* When administered intravitreally, it controls excessive blood vessel growth by inhibiting a growth factor known as vascular endothelial growth factor ("VEGF"). *Id.* at *2. The Eylea formulation contains 40 mg/ml aflibercept (the active ingredient), 10 mM sodium phosphate, 40 mM sodium chloride, 0.03% polysorbate 20, and 5% sucrose, and has a pH of 6.2. *Id.* Examples 3 and 4 of the '865 patent disclose that formulation. *Id.*

Amgen filed abbreviated Biologics License Application 761298 ("Amgen's aBLA") at the FDA on August 23, 2023, seeking to market ABP 938, a biosimilar of Eylea now branded as "Pavblu." *Id.* at *2–3; *see also* J.A. 26703-09. Amgen's aBLA, approved a year later, states that ABP

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[2] The FDA's Purple Book is a searchable online database that lists all FDA-approved biological products.

[3] Regeneron received FDA approval for its pre-filled syringe presentation in August 2019. Amgen Br. 9.

938's formulation is different from Eylea's formulation. *Id.* at *3. Relevant here, while ABP 938's formulation contains a version of the fusion protein aflibercept, it does not contain a separate buffer component. *Id.* That is because Amgen had discovered a way to prepare and formulate the active ingredient, aflibercept, in a manner that eliminates the need for a separate buffer component—*i.e.*, the aflibercept itself provides sufficient buffering capacity to stabilize the formulation. *See id.*; Amgen Br. 2. Unlike Amgen's biosimilar ABP 938, other aBLA filers, including Mylan, Formycon, Samsung Bioepis, and Celltrion, proposed biosimilar versions of Eylea that do contain a separate buffer component. *Amgen Decision*, at *3.

On January 10, 2024, Regeneron filed an action against Amgen in the U.S. District Court for the Central District of California, alleging infringement of various Regeneron patents based on Amgen's aBLA for ABP 938. *Id.* at *4. After Regeneron's action was consolidated with other aBLA-filer actions by the Joint Panel on Multidistrict Litigation ("JPML"), Regeneron filed a motion for a preliminary injunction against Amgen, based on allegations that Amgen's filing of its aBLA for ABP 938 infringed claims 2, 3, 27, and 28 ("the asserted claims") of the '865 patent. *Id.* at *1.

The asserted claims depend from claims 1 and 26 of the '865 patent. Claim 1 is representative and recites:

> 1. A vial comprising an ophthalmic formulation suitable for intravitreal administration that comprises:
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> *a vascular endothelial growth factor (VEGF) antagonist*,
>
> an organic co-solvent,
>
> *a buffer*,
>
> and a stabilizing agent,

> wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4; 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.

'865 patent col. 19 ll. 29–41 (emphases added). Because we have held that "[t]here can be no literal infringement where a claim requires two separate structures and one such structure is missing from an accused [product]," *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1255 (Fed. Cir. 2010), the primary dispute before the district court was "whether the asserted claims require that the 'VEGF antagonist' [*i.e.*, aflibercept] and the 'buffer' be separate and distinct components of the claimed formulation." *Amgen Decision*, at *8 (cleaned up).

Amgen opposed the motion for a preliminary injunction, arguing that "the asserted claims require that the claimed 'VEGF antagonist' and the claimed 'buffer' be separate components" and therefore that ABP 938 could not infringe the asserted claims. *Id.* at *9 (cleaned up). Regeneron disagreed and argued that "the VEGF antagonist can also satisfy the limitation of the claimed buffer." *Id.* Specifically, Regeneron argued that the asserted claims were not so limited by pointing to two passages from the specification allegedly explaining that (1) the claimed formulation's components could embody multiple functions, and (2) all scientific terms should retain their ordinary meanings. *Id.* at *15. To support the latter allegation, Regeneron relied on extrinsic evidence, including various references and expert testimony, to show that "using aflibercept as a buffer was so 'well known in the art' such that no description in the specification was necessary for a [person of ordinary skill in the art] to understand that the

claimed VEGF antagonist can serve as the separately claimed 'buffer.'" *Id.* at *17.

The district court began its claim construction analysis by reciting well-established claim construction principles, including that "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Id.* at *11 (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (en banc)). Consistent with such principles, the district court applied our precedent in *Becton* and its progeny to assess the claims. *Amgen Decision*, at *11 (citing *Becton*, 616 F.3d at 1254). Specifically, the district court evaluated the applicability and effect of the claim construction principle, reiterated in *Becton*, that explains "[w]here a claim lists elements separately, *the clear implication* of the claim language is that those elements are distinct components of the patented invention." *Id.* (emphasis added); *see Becton*, 616 F.3d at 1254 (quoting *Gaus v. Conair Corp.*, 363 F.3d 1284, 1288 (Fed. Cir. 2004)).

The district court acknowledged that the "parties d[id] not dispute that the asserted claims separately list the claimed 'VEGF antagonist' and the 'buffer.'" *Amgen Decision*, at *12 (citing the '865 patent at claims 1 and 26) (cleaned up). It therefore determined that there was no dispute that "the separate listing of these elements establishes a presumption the claimed 'VEGF antagonist' and 'buffer' are distinct components." *Id.*

The district court next considered whether the evidence overcame "the clear implication" of separateness under *Becton*. *See id.* at *12–23. It determined that it did not. Specifically, the district court determined that neither the intrinsic nor extrinsic evidence rebutted the implication of separateness and, in fact, only reinforced the implication that the "VEGF antagonist" and "buffer" must be separate components of the claimed formulation. *Id.* at *17

("Here, neither the claims nor the specification of the '865 patent explain or suggest that the VEGF antagonist can serve as the buffer, or vice versa, or that these components can overlap in function. Rather, the claims and the specification further support and confirm that they cannot be one and the same."); *id.* at *19 (considering the extrinsic evidence).

As part of its analysis, the district court explained that the claim construction issue in this case had yet to be determined, notwithstanding the district court's earlier construction of the term "buffer," in separate Regeneron litigation asserting the same '865 patent, as "a substance that resists changes to pH upon addition of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component, including, for example, histidine, phosphate, and proteins like aflibercept." *Id.* at *8; *see In re Aflibercept Pat. Litig.*, No. 1:23-cv-97, 2024 WL 3423047, at *15–17 (N.D. W. Va. July 9, 2024) ("the *Formycon Decision*").[4] Because the claim construction issue before the district court in this case was different from the issue presented in the *Formycon Decision*, the district court explained that its earlier decision "did not address the claim construction issue that Amgen raises in this case" and proceeded to

[4] Prior to its decision in this case, the district court granted Regeneron's motion for a preliminary injunction against Formycon based on Formycon's biosimilar product, FYB203, which contains a separate histidine buffer. *Amgen Decision*, at *8. Formycon had argued that it did not infringe the '865 patent because, in its view, the term "buffer" was limited to a phosphate buffer. *Formycon Decision*, at *15. The district court rejected that construction. *Id.* That issue was not raised on appeal, and we otherwise affirmed. *See Regeneron Pharms., Inc. v. Formycon AG*, No. 2024-2009, 2025 WL 324288 (Fed. Cir. Jan. 29, 2025).

determine whether the "buffer" was a distinct component of the claimed formulation under *Becton* and its line of cases. *Id.* at *8.

Ultimately, the district court "construe[d] the asserted claims to require that the claimed 'VEGF antagonist' be a separate component from the claimed 'buffer.'" *Id.* at *9 (cleaned up). And because Amgen's ABP 938 product does not contain a separate buffer, the district court determined that Amgen had raised a substantial question of noninfringement and thus that Regeneron had not demonstrated a likelihood of success on the merits for its infringement action. *Id.* The district court therefore denied Regeneron's motion for a preliminary injunction. *Id.* at *27.

Regeneron timely appealed and we have jurisdiction under 28 U.S.C. §§ 1292(a)(1) and 1292(c)(1).

DISCUSSION

Regeneron's appeal challenges the district court's claim construction, and specifically whether the district court erred in applying *Becton*. In Regeneron's view, *Becton* is inapplicable here and, even if it were applicable, the evidence overcomes the clear implication, recited in *Becton*, that separately listed components of a claimed invention are distinct. We address each argument in turn.

I

We first address the applicability of *Becton*. As explained below, because the plain language of the claim recites a formulation comprising four separately listed components, *Becton* applies.

"We review claim construction based on intrinsic evidence de novo and review any findings of fact regarding extrinsic evidence for clear error." *Promptu Sys. Corp. v. Comcast Corp.*, 92 F.4th 1372, 1377 (Fed. Cir. 2024). Claim terms are generally given their plain and ordinary meaning, which is the meaning that one of ordinary skill in the

art would ascribe to a term when read in the context of the claims, specification, and prosecution history. *See Phillips*, 415 F.3d at 1313–17.

We have held that "where a claim lists elements separately, the clear implication of the claim language is that those elements are distinct components of the patented invention." *Becton*, 616 F.3d at 1254 (quoting *Gaus*, 363 F.3d at 1288) (cleaned up); *see, e.g.*, *Kyocera Senco Indus. Tools Inc. v. Int'l Trade Comm'n*, 22 F.4th 1369, 1382 (Fed. Cir. 2022) ("The asserted claims list those elements separately" and "there is, therefore, a presumption that those components are distinct."); *see also Schindler Elevator Corp. v. Otis Elevator Co.*, 593 F.3d 1275, 1282 (Fed. Cir. 2010) (explaining that "the term 'information transmitter' itself suggests that the transmitter is a thing, separate and apart from an 'elevator user'").[5]

Here, claim 1 plainly recites a pharmaceutical formulation, comprising four separately listed components, which include a "VEGF antagonist" and "a buffer." '865 patent col. 19 ll. 29–34. As we determined in *Becton*, the plain language of the claim therefore establishes a "clear implication" that the VEGF antagonist and buffer

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[5] As we recently reiterated in *Google LLC v. Ecofactor, Inc.*, 92 F.4th 1049, 1058 (Fed. Cir. 2024):

> [Our] cases do not create a *per se* rule that separately listed claim elements are distinct components, regardless of the intrinsic record. . . . Rather, we have explained that there is a "presumption" that separately listed claim limitations may indicate separate and distinct physical structure, but that presumption may always be rebutted in the context of a particular patent.

components are distinct components of the claimed formulation. *Becton*, 616 F.3d at 1254. *Becton* therefore applies.

Regeneron's arguments otherwise are misplaced. Regeneron argues that "[t]he district court fundamentally erred in applying the *Becton* line of precedent." Regeneron Br. 35; *see also* Regeneron Reply Br. 2–8. Regeneron argues that "claim construction must 'begin' with, not evade, the claim language's ordinary meaning," Regeneron Reply Br. 12 (citing *Phillips*, 415 F.3d at 1313), and that the district court failed to heed that established principle of claim construction, *see id.* ("The fundamental error in the district court's construction is that it failed to address what 'buffer' means."). Specifically, Regeneron argues that because the district court in *Formycon* had previously construed the term "buffer" in a way that "encompasses what the patent recites in a different limitation, the implication of separateness under *Becton* is simply inapplicable." Regeneron Br. 35–37 (relying on *Formycon Decision*, 2024 WL 3423047, at *16–17). Stated otherwise, Regeneron argues that because the district court previously construed the claimed buffer as covering "proteins like aflibercept," *Becton* does not apply. *Amgen Decision*, at *39. We disagree.

First, contrary to Regeneron's arguments, the district court did properly engage with the claims, consistent with *Phillips* and established claim construction principles. It did so by evaluating, under *Becton*, whether the implication of separateness applied, which necessarily requires a review of the claims themselves. *See id.* at *11 ("The claims separately list 'a VEGF antagonist' and 'a buffer,' giving rise to a presumption that they are separate and distinct components of the claimed formulation."). Additionally, as discussed in Section II, *infra*, the district court also considered whether the surrounding context, including other claims of the '865 patent, overcomes the implication of separateness. *Id.* at *12–15.

Second, Regeneron's argument that *Becton* does not apply conflates two independent claim construction inquiries. The claim construction inquiry relevant here, under *Becton*, is directed to whether a formulation is claimed in a way that clearly implies it requires distinct components. In contrast, Regeneron's proposed inquiry, relevant in the *Formycon Decision*, asks whether the claimed "buffer" component overlaps in scope with the claimed "VEGF antagonist" component. *Formycon Decision*, 2024 WL 3423047, at *15–17. Because the district court's *Formycon Decision* "did not address the claim construction issue that Amgen raises in this case," *id.* at *8, the district court properly viewed itself as not bound by its earlier construction. Thus, we find Regeneron's related arguments regarding overlapping claim scope unpersuasive.[6]

Because the asserted claims plainly recite a pharmaceutical formulation comprising four separately listed components, including a "VEGF antagonist" and "a buffer," we conclude that "the clear implication of the claim language is that those elements are distinct components of the patented invention." *Becton*, 616 F.3d at 1254 (cleaned up). The district court therefore correctly applied *Becton*.

II

We next address whether the evidence overcomes the implication of separateness under *Becton*, such that a formulation comprising a self-buffering VEGF antagonist, like Amgen's ABP 938, may infringe the claims even in the absence of a separate buffer component. Because the claims and specification of the '865 patent only reinforce that the claimed components are distinct, we agree with

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[6] We note that the *Formycon* construction was also preliminary in nature and non-binding, as it was determined at the preliminary injunction stage of a separate litigation to which Amgen is not a party.

the district court that the implication of separateness has not been overcome, and the claimed "VEGF antagonist" and "buffer" are distinct limitations.

A claim "can be defined only in a way that comports with the instrument as a whole." *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 389 (1996). Consistent with this principle, to overcome *Becton*, there must be evidence that shows that the impliedly distinct components, instead, can be satisfied by a single component. *Compare Google*, 92 F.4th at 1058 (overcoming the implication of separateness in part because "the specification contemplates an embodiment in which one claimed input is calculated based on at least one other claimed input"), *with Becton*, 616 F.3d at 1254 (not overcoming the implication of separateness because "[t]he specification . . . *confirms* that the spring means is a separate element from the hinged arm, as the only elements disclosed in the specification as 'spring means' for urging the guard forward are separate structures from the hinged arm and its hinges") (emphasis added). Such evidence may be intrinsic or extrinsic, though it is difficult to envision *Becton*'s clear implication of separateness being overcome without at least a suggestion of non-separateness in the intrinsic evidence. *See generally Intel Corp. v. VIA Techs.*, 319 F.3d 1357, 1367 (Fed. Cir. 2003) (holding that extrinsic evidence may never be used to alter meaning that is clear from intrinsic evidence); *see also Kyocera*, 22 F.4th at 1382 ("The mere fact that there is an alternative embodiment disclosed in [a] patent that is not encompassed by a claim construction *does not outweigh the language of the claim*, especially when the court's construction is supported by the intrinsic evidence." (cleaned up) (emphasis added) (quoting *TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.*, 529 F.3d 1364, 1373 (Fed. Cir. 2008))).

Having addressed the showing required to overcome the implication of separateness under *Becton*, we now turn to whether Regeneron has made such a showing. For the

following reasons, the district court correctly determined that the record evidence failed to overcome the implication of separateness under *Becton*. *See Amgen Decision*, at *16 ("[T]he intrinsic evidence is clear and uniform that the 'VEGF antagonist' and the 'buffer' are separate components.").

"[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms." *Phillips*, 415 F.3d at 1314. Moreover, "[o]ther claims of the patent in question, both asserted and unasserted, can [] be valuable sources of enlightenment as to the meaning of a claim term." *Id.* For instance, "[d]ifferences among claims can [] be a useful guide in understanding the meaning of particular claim terms." *Id.* Here, the district court identified that all of the claims of the '865 patent treat the "VEGF antagonist" as separate from the "buffer." *Amgen Decision,* at *13. Specifically, as the district court explained, "[t]he components are listed with different concentrations and *different units of measurement*." *Id.* (emphasis added). The district court therefore concluded that "[t]he clear implication of the claims' use of different units of measurement for these two components is that the components are separate and distinct." *Id.* We agree.

Certain dependent claims use different units of measurement to recite the claimed concentrations of each component, respectively. For example, where claim 2 recites a "concentration of said VEGF antagonist fusion protein [that] is 40 *mg/ml*," claim 7 recites a concentration of buffer that is "5-25 *mM*." *Compare* '865 patent col. 19 ll. 21–43 (claim 2), *with id.* at col. 19 ll. 53–54 (claim 7) (emphases added). Put simply, one component is measured in milligram per milliliter (mg/ml) units and the other in millimolar units (mM). The dependent claims therefore provide "a useful guide in understanding the meaning of particular claim terms," *Phillips*, 415 F.3d at 1314, and such context reinforces that the two components are different.

We next consider whether the specification overcomes the implication that the claimed buffer and VEGF antagonist are separate components. And again, we agree with the district court that "[l]ike the claims, the specification of the '865 patent uniformly describes the 'VEGF antagonist' and the 'buffer' as separate and distinct components of the formulation." *Amgen Decision*, at *14.

"The importance of the specification in claim construction derives from its statutory role," requiring that "the specification describe the claimed invention in 'full, clear, concise, and exact terms.'" *Phillips*, 415 F.3d at 1316 (citing 35 U.S.C. § 112, para 1). The specification is therefore "always highly relevant to the claim construction analysis," "is the single best guide to the meaning of a disputed term" and can "make[] plain what the [patentee] did and did not invent." *Id.* at 1315 (cleaned up). "Thus claims must be construed so as to be consistent with the specification, of which they are a part." *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 347 F.3d 1367, 1371 (Fed. Cir. 2003).

The specification explains that a "VEGF antagonist is a compound capable of blocking or inhibiting the biological action of [VEGF], and includes fusion proteins capable of trapping VEGF." '865 patent col. 6 ll. 27–30. The specification further describes how "the buffering agent, may be, for example, phosphate buffer." *Id.* col. 2 ll. 45–48. And as the district court correctly identified, "[t]he specification does not suggest that the VEGF antagonist can be a buffer or vice versa," and "Regeneron has not identified any such disclosure." *Amgen Decision*, at *14. More to the point, the specification explains that "[p]referably, the liquid formulation comprises a pharmaceutically effective amount of the *VEGF antagonist* . . . [and] *can also comprise* one or more pharmaceutically acceptable carriers, *buffers*, tonicity agents, stabilizers, and/or excipients." '865 patent col. 6 l. 65–col. 7 l. 2 (emphases added). That is, the specification describes a formulation containing a VEGF antagonist plus a distinct buffer component. And that understanding

is reinforced consistently throughout the specification, which "includes eight example formulations and twenty-two (22) embodiments, each of which describes the VEGF antagonist (aflibercept) plus a buffer." *Amgen Decision*, at *14 (cleaned up) (citing '865 patent col. 2 l. 33–col. 4 l. 62, col. 8 l. 32–col. 12 l. 26).

Regeneron does not seriously dispute the overwhelming evidence from the specification reinforcing the implication that the claimed "VEGF antagonist" and "buffer" are distinct components of the claimed formulation. Instead, Regeneron argues that "[t]he patent did not need to list known or unknown buffers in order for 'a buffer' to overlap with the 'VEGF antagonist' limitation and rebut any presumption from *Becton*." Regeneron's Br. 51. Regeneron explains that is so because there is no "requirement to repeat what is known." *Id.* To support that argument, Regeneron relies on the *Formycon* construction, arguing that it proves that "proteins like aflibercept . . . were known buffers or categories of buffers." *Id.* (citing *Formycon Decision*, 2024 WL 3423047, at *16). It continues, "[j]ust as the patent undisputedly did not have to list ingredients like histidine in order for them to be within the scope of 'buffer,' . . . it also did not have to list proteins as buffers where, as the experts agreed, proteins like aflibercept that contain histidine residues were understood to act as buffers." *Id.* at 51–52 (citing *Formycon Decision*, 2024 WL 3423047, at *16). We disagree.

Again, Regeneron unduly relies on the preliminary claim construction in *Formycon*. Regardless, Regeneron's avoidance of the specification's disclosures, or lack thereof, is telling and is an apparent concession that the "specification, moreover, confirms that the [buffer] is a separate element from the [VEGF antagonist], as the only elements disclosed in the specification as [being a buffer] are separate structures from the [VEGF antagonist]." *Becton*, 616 F.3d at 1254. Further, like the patent at issue in *Becton*, "[n]othing in the specification indicates" that the

VEGF antagonist "might" also satisfy the distinct "buffer" component. *Id.* at 1255. In fact, all eight examples and twenty-two other embodiments disclose a VEGF antagonist "*plus*" a separate buffer. *Amgen Decision*, at *14 (emphasis in original) (citing '865 patent col. 2 l. 33–col. 4 l. 62, col. 8 l. 32–col. 12 l. 26). And every embodiment either describes the buffer as a phosphate buffer or provides a concentration range for a buffer that does not overlap with the converted concentration range for the VEGF antagonist. *Id.*

Despite acknowledging that the specification nowhere gives an example of a single component performing both functions (*e.g.*, a self-buffering protein), Regeneron argues that "[t]he patent does not disavow the ordinary meaning of 'buffer.'" Regeneron Br. 67 ("Although the specification only explicitly discloses phosphate buffer, it contains no 'expressions of manifest exclusion or restriction' as to non-excipient buffers."). It adds that "[t]he patent did not need to list known or unknown buffers," *id.* at 51, and that "[t]he evidence was unequivocal that proteins containing histidine were known buffers," *id.* at 52.

But here, the claims recite the "VEGF antagonist" and "buffer" as distinct components, and the specification only reinforces that understanding. The specification makes clear what "the inventors actually invented and intended to envelop," *Phillips*, 415 F.3d at 1316, and that is, a formulation containing a VEGF antagonist *plus* a distinct buffer. While Regeneron argues "that the [person of ordinary skill] would have understood in the context of the '865 patent that proteins containing histidine were buffers," like Amgen's ABP 938 product, it says so without identifying any support from the specification. Regeneron Br. 63. That lack of specification-based support is revealing because the claims "do not have meaning removed from the context from which they arose." *Netword, LLC v. Centraal Corp.*, 242 F.3d 1347, 1352 (Fed. Cir. 2001). And the claims here "arose" from a specification that clearly and

repeatedly describes the "VEGF antagonist" and "buffer" as distinct components and does not explain or suggest that one can stand in as the other. *See* '865 patent col. 2 l. 33–col. 4 l. 62, col. 8 l. 32–col. 12 l. 26.

Similarly, the fact that the term "buffer" was left undefined in the specification without any clear disavowal, does not mean that the term is divorced from what is so clearly implied by the claims and the specification alike. *See Sequoia Tech., LLC v. Dell, Inc.*, 66 F.4th 1317, 1324 (Fed. Cir. 2023) ("[T]he use of a term denoting a non-exhaustive list does not eviscerate our obligation to construe terms in the context of the entire patent."). Accordingly, and because the *Becton* presumption applies, the district court correctly concluded that the only reasonable construction of the claim language, in light of the specification (which does nothing to rebut the presumption of separateness), is that the "VEGF antagonist" and "buffer" are distinct components.

We turn next to the district court's consideration of extrinsic evidence and Regeneron's argument that the district court clearly erred by "concluding that extrinsic evidence was irrelevant to whether claim terms could overlap under *Becton*." Regeneron Br. 53. For the following reasons, we conclude that the district court did not clearly err in finding that "none of the extrinsic evidence discloses that aflibercept can function as a buffer in a pharmaceutical formulation" as of the effective filing date of the '865 patent. *Amgen Decision*, at *19.

As the district court correctly noted, "while extrinsic evidence can shed useful light on the relevant art, it is less significant than the intrinsic record in determining the legally operative meaning of claim language." *Id.* at *18 (cleaned up) (citing *Phillips*, 415 F.3d at 1317). The district court also correctly recognized that "it need not consider this extrinsic evidence for claim construction where, as here, the intrinsic evidence is clear and unambiguous." *Id.*

at *19 (*citing Seabed Geosolutions (US) Inc. v. Magseis FF LLC*, 8 F.4th 1285, 1287 (Fed. Cir. 2021) ("If the meaning of a claim term is clear from the intrinsic evidence, there is no reason to resort to extrinsic evidence.")). The district court accordingly determined that "the claims and specification are clear and uniform in supporting that the asserted claims require separate components such that the buffer must be separate and distinct from the VEGF antagonist." *Id.* (cleaned up). Nevertheless, the court considered the extrinsic evidence "for completeness" and found "that the evidence supports the construction that the claims require the VEGF antagonist and buffer to be separate and distinct components." *Id.* We see no clear error in the district court's analysis.

Regeneron argues that "the court erred in disregarding the . . . extrinsic evidence." Regeneron Br. 54; *see also* Regeneron Reply Br. 23–28. In Regeneron's view, "[t]he [extrinsic] evidence was unequivocal that proteins containing histidine were known buffers," and that "[t]here was no dispute that proteins have been known for decades to be buffers or have buffering capacity." Regeneron Br. at 52. It also contends the district court, "in alternatively considering the extrinsic evidence, . . . legally erred in disregarding [International Patent Application Publication WO 2006/138181 ("Gokarn")] as irrelevant to claim construction." *Id.* at 55. Gokarn, it argues, "undisputedly predated the filing of the '865 patent, and so it unquestionably confirmed to the [person of ordinary skill in the art] that 'biopharmaceutical proteins' could 'be formulated in self-buffering compositions.'" *Id.*

We are unpersuaded. Indeed, as already noted, the district court did not need to consider the extrinsic evidence given the overwhelming evidence in the intrinsic record. But the district court nevertheless considered both experts' testimony as well as the references submitted by Regeneron and found that evidence too "supports the construction that the claims require the VEGF antagonist and

buffer to be separate and distinct components." *Amgen Decision*, at *19. Additionally, it was reasonable for the district court to determine that, given the proximity of Gokarn's publication date to the '865 patent's filing date, the reference actually supports Amgen's contention that self-buffering proteins were not well known and that "Gokarn advanced the art over the '865 patent precisely by disclosing certain buffer-free formulations in which the therapeutic protein is itself capable of maintaining pH stability." Amgen Br. 51. We therefore conclude that the district court's findings regarding the extrinsic evidence are not clearly erroneous. *See Genentech, Inc. v. Sandoz Inc.*, 55 F.4th 1368, 1376 (Fed. Cir. 2022) ("Where there are two permissible views of the evidence, the fact-finder's choice between them cannot be clearly erroneous.").

In light of the foregoing, and given the undisputed fact that Amgen's ABP 938 product does not contain a buffer separate from the VEGF antagonist, there is at least a substantial question of noninfringement. Regeneron has therefore not established a likelihood of success on the merits of its infringement allegations and the district court did not abuse its discretion in denying its motion for a preliminary injunction. *See Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1364 (Fed. Cir. 1997) (holding that if an alleged infringer "raises a 'substantial question' concerning validity, enforceability, or infringement (*i.e.,* asserts a defense that [the patentee] cannot show 'lacks substantial merit')[,] the preliminary injunction should not issue").

III

Amgen, during oral argument, waived its right to a remand for a calculation of damages from the temporary injunction. *See* Oral Arg. at 25:13–48, Appeal No. 24-2351, *available at* https://oralarguments.cafc.uscourts.gov/default.aspx?fl=24-2351_01142025.mp3.

CONCLUSION

We have considered Regeneron's remaining arguments and find them unpersuasive. For the foregoing reasons, we affirm.

AFFIRMED