Fed. Circ. Ruling Reaffirms Listing Elements Separately Is Key

By **Roshan Shrestha and Andrew Alul** (April 1, 2025)

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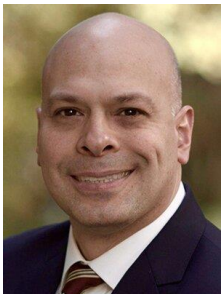

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The U.S. Court of Appeals for the Federal Circuit's March 14 decision in Regeneron Pharmaceuticals Inc. v. Mylan Pharmaceuticals Inc. reaffirmed a critical principle in patent law: When a claim lists elements separately, the clear implication is that they are distinct elements.[1]

This case affirmed an almost identical issue and opinion reached in the Silvergate v. Bionpharma decision in 2021, which was presided over by one of the panel judges in Regeneron, U.S. Circuit Judge Leonard Stark, during his tenure as a district court judge on the U.S. District Court for the District of Delaware.[2]

In Regeneron, the dispute centered around U.S. Patent No. 11,084,865, which covers a pharmaceutical formulation for aflibercept containing a vascular endothelial growth factor antagonist and a buffer. Regeneron previously obtained a preliminary injunction against other biosimilars.[3]

In this case, Regeneron was seeking the same relief against Amgen's biosimilar. But the lower court found a reasonable likelihood that Amgen's product was noninfringing because it lacked a separate buffer component, and the Federal Circuit affirmed.[4]

The decision has significant implications for patent claim construction and design-arounds, particularly in pharmaceutical formulations.

Claim Construction in Two District Court Cases

The U.S. District Court for the Northern District of West Virginia, in the Formycon and Amgen cases — both part of In re: Aflibercept Patent Litigation, and both decided in 2024 — used the same construction for the term "buffer."

In Formycon, the court adopted Regeneron's construction, defining a buffer 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."[5]

This explicit construction allowed the term "buffer" to include proteins such as aflibercept. The court then found a likelihood of success on the merits because Formycon's formulation included histidine, which the court found would meet the buffer element, and thus granted Regeneron's preliminary injunction motion.[6]

Key Arguments in Regeneron

In Amgen, the district court acknowledged the same construction for buffer from the Formycon case.[7] But the issue presented in Amgen was the construction of the term "an ophthalmic formulation ... that comprises: a vascular endothelial growth factor (VEGF) antagonist ... an organic co-solvent, a buffer, and a stabilizing agent."

Amgen proposed that this term should be construed to mean "a formulation that comprises four separate components: (1) a VEGF antagonist; (2) an organic co-solvent; (3) a buffer; and (4) a stabilizing agent."

Regeneron, however, argued that the asserted claims permitted a single formulation component category, namely, the "VEGF antagonist," to satisfy multiple claim elements, namely, both the VEGF antagonist and the buffer.[8]

Applying precedent, the Federal Circuit affirmed the district court's ruling that the separate listing of these elements establishes a presumption that the claimed VEGF antagonist and buffer are distinct components.[9]

Thus, the specific construction of the term "buffer" did not matter because the claim required two separate components to meet the claimed limitation — a VEGF antagonist and, separately, a buffer. One component could not satisfy both limitations.[10]

Since Amgen's ABP 938 formulation did not include a separate buffer, the Federal Circuit agreed that Regeneron would not likely succeed in proving that Amgen's biosimilar, which lacked an independent buffer, met the claim limitation.[11]

The Regeneron court also analyzed the specification, the claims and even extrinsic evidence, but came to the same conclusion. First, the court found no evidence supporting the idea that the VEGF antagonist itself could serve as a buffer in the specification.[12]

Second, the court also affirmed that the dependent claims specifying distinct buffer concentrations also reinforced the requirement that the buffer be a separate component. For example, Claim 2 recites a VEGF antagonist concentration of 40 milligrams per milliliter, while Claim 7 recites a different concentration range for the buffer, 5 to 25 millimolar.

The court also affirmed that the claims' use of different units of measurement for these two components implied that they were separate and distinct.[13] The district court's analysis additionally converted the concentration of aflibercept from mg/ml to mM, calculating that 40 mg/ml of aflibercept is equivalent to approximately 0.347 mM.

This converted concentration falls well below the 5 to 25 mM range specified for the buffer in Claim 7.[14] Thus, both the differing units of measurement and the numerical disparity between the concentrations strongly reinforced the conclusion that the VEGF antagonist and the buffer must be construed as separate and distinct components.

Third, though not required, the Federal Circuit also analyzed the extrinsic evidence, but concluded that it did not show that aflibercept was commonly understood to be a buffer in pharmaceutical compositions at the relevant time, and that the district court did not clearly err in its finding.[15]

Combined with the clarity of the intrinsic record, the court held that the claimed VEGF antagonist and the claimed buffer must be separate components.[16]

On appeal, Regeneron also argued that the self-buffering protein formulation patent filed by Yatin Gokarn demonstrated that proteins were known to have buffering capacity.[17] The Federal Circuit disagreed, noting that although Gokarn was filed shortly before the priority date of the '865 patent — June 16, 2006 — it was not published until Dec. 28, 2006.

Rather than reflecting an established understanding, Gokarn's disclosure actually highlighted the novelty of self-buffering protein formulations. The timing and substance of the reference indicated that such formulations were not well known in the art at the time.

The Federal Circuit agreed that Gokarn's discussion of buffer-free protein compositions supported Amgen's position that self-buffering proteins like aflibercept were not commonly understood to function as buffers in pharmaceutical formulations, thereby reinforcing the conclusion that the claims required the VEGF antagonist and buffer to be separate and distinct components.[18]

The Federal Circuit thus affirmed the district court's denial of Regeneron's preliminary injunction, agreeing that under Becton, when claim language separately listed the VEGF antagonist and buffer, the term should be construed to require distinct components.[19]

Comparison to Silvergate v. Bionpharma

An almost identical issue was presented in Silvergate v. Bionpharma, where the Delaware court addressed whether a claimed buffer was a distinct component or could be interpreted more broadly.

Silvergate alleged that Bionpharma's enalapril oral solution infringed its patent, which claimed a formulation containing a buffer system with citric acid and sodium citrate.[20] However, Bionpharma's formulation lacked a separate buffer, and instead relied on inherent pH stabilization mechanisms.[21]

The court ruled for Bionpharma, finding that because Silvergate had listed enalapril and the buffer as distinct elements, the claims "require[d] a separate, independent buffer component," and further, that because Silvergate had also distinguished its claimed buffer system from prior art by emphasizing specific concentrations of citric acid and sodium citrate during prosecution, Silvergate was estopped from later arguing a broader interpretation.[22]

Even accepting Silvergate's argument that the claimed active ingredient, enalapril maleate, could also function as the separately claimed buffer, the court found that Silvergate failed to prove that the enalapril maleate in Bionpharma's product was equivalent to the claimed buffer system, as the alleged buffer concentration from enalapril did not meet the concentration range of a separate buffer component contemplated by the specification.[23]

This issue parallels the Regeneron decision, where the Federal Circuit refused to adopt a broad interpretation allowing a VEGF antagonist to also meet the buffer limitation. Both cases emphasize that when a claim expressly requires a buffer component, a formulation lacking a separate buffer does not infringe.

Key Takeaways for Patent Drafting and Litigation

These cases underscore several critical takeaways for both patent practitioners and generic or biosimilar companies.

For patentees, first, drafting claims with precision is essential. If an element is critical, it should be separately listed — courts will typically interpret separately listed elements as requiring distinct components unless the patent clearly indicates otherwise.

Second, if a single ingredient is intended to serve multiple roles — e.g., a protein or active

ingredient functioning as both the therapeutic agent and a buffer — the specification should expressly support this dual functionality with clear language and illustrative examples.

Third, during prosecution, narrowing amendments and arguments should be avoided when possible, as they may limit later claim scope. Expert declarations can be strategically used to provide scientific context and reinforce the intended breadth of illustrative examples.

Finally, dependent claims should be drafted with care to preserve flexibility without inadvertently supporting a narrower reading of the broader claims — particularly when they introduce specific concentration ranges or diffident units that differentiate one component from another.

Likewise, generic or biosimilar companies must pay close attention to the claim elements of the relevant patents. First, if a particular component or step can be eliminated from a formulation or process without sacrificing performance, this may present a stronger noninfringement position.

Second, developers should closely analyze the intrinsic record — the claims, specification and prosecution history — to determine whether the patentee's interpretation is genuinely supported, as courts give it greater weight than general scientific assertions.

Third, although scientifically less significant, differences in units or numerical concentration ranges — as demonstrated in Regeneron — can serve as persuasive evidence that certain components are intended to be separate.

Finally, extrinsic evidence — particularly references published after the priority date — may support the argument that a scientific principle, such as self-buffering proteins, was not yet understood in the art, reinforcing a noninfringement position.

Conclusion

These cases highlight a clear rule in claim construction: When elements are listed separately, they cannot be satisfied by a single component. These rulings reinforce the principle that each listed claim element is presumed distinct unless the patent clearly states otherwise.

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[1] Regeneron Pharms. Inc. v. Mylan Pharms. Inc., No. 2024-2351, 2025 WL 807962 (Fed. Cir. March 14, 2025) ("Regeneron").

[2] Silvergate Pharms. Inc. v. Bionpharma Inc., No. CV 18-1962-LPS, 2021 WL 1751148, at *1 (D. Del. April 29, 2021), aff'd sub nom. Azurity Pharms. Inc. v. BionPharma Inc., No. 2021-1926, 2022 WL 703903 (Fed. Cir. March 9, 2022).

[3] See, e.g., In re: Aflibercept Pat. Litig., No. 1:23-CV-97, 2024 WL 3423047, at *1

(N.D.W. Va. July 9, 2024) ("Formycon"), aff'd sub nom. Regeneron Pharms. Inc. v. Mylan Pharms. Inc., No. 2024-2009, 2025 WL 324288 (Fed. Cir. Jan. 29, 2025).

[4] In re: Aflibercept Pat. Litig., No. 1:23-CV-39, 2024 WL 4958308, at *1 (N.D.W. Va. Oct. 1, 2024) ("Amgen"), aff'd sub nom. Regeneron Pharms. Inc. v. Mylan Pharms. Inc., No. 2024-2351, 2025 WL 807962 (Fed. Cir. March 14, 2025) ("Regeneron") (denial of preliminary injunction motion affirmed).

[5] Formycon, 2024 WL 3423047, at *15.

[6] Id. at *1.

[7] Amgen, 2024 WL 4958308, at *8.

[8] Id. at *9.

[9] Id. citing Becton, Dickinson & Co. v. Tyco Healthcare Group LP, 616 F.3d 1249, 1254 (Fed. Cir. 2010); Regeneron, 2025 WL 807962, at *4.

[10] Amgen, 2024 WL 4958308, at *11.

[11] Regeneron, 2025 WL 807962, at *4 (holding the application of Becton, "the plain language of the claim therefore establishes a 'clear implication' that the VEGF antagonist and buffer components are distinct component").

[12] Regeneron at *5-6 (noting that the specification consistently reinforces the sperate element because it "includes eight example formulations and twenty-two (22) embodiments, each of which describes the VEGF antagonist (aflibercept) plus a buffer").

[13] Amgen, 2024 WL 4958308, at *13; Regeneron, 2025 WL 807962, at *6.

[14] Amgen at *13.

[15] Regeneron, 2025 WL 807962, at *8; see also, Amgen, 2024 WL 4958308, at *17-19.

[16] Regeneron, 2025 WL 807962, at *8.

[17] Id.

[18] Id.

[19] Id. at *9.

[20] Silvergate, 2021 WL 1751148, at *8.

[21] Id. at *19, *29.

[22] Id. at *19, *29-31.

[23] Id. at *32-33.