UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.
and PFIZER INC.,
Petitioners,

v.

SANOFI-AVENTIS DEUTSCHLAND GMBH,
Patent Owner.

Case IPR2018-01680
Patent No. 9,526,844

PETITIONERS' REPLY TO PATENT OWNER RESPONSE

TABLE OF CONTENTS

I. Introduction

Sanofi's Patent Owner Response ("POR") nowhere contests that claims 21 and 23 are anticipated if Giambattista is prior art. Sanofi argues that Giambattista is not prior art because its GB Application allegedly discloses a broad genus of interchangeable externally- and internally-threaded components. But Sanofi's argument ignores what the GB Application actually discloses: using an internally-threaded ***drive sleeve*** to drive an externally-threaded piston rod, not a leadscrew and not a stinger connected to a drive sleeve. Because Giambattista is prior art, claims 21 and 23 are unpatentable as anticipated.

Despite Sanofi's additional arguments, the remaining claims also are unpatentable. Sanofi's proffered claim construction for "has a circular cross-section" lacks support in the claim language and in the specification. Sanofi's further argument that Giambattista must use the phrase "unit doses" to describe the clicks is contrary to law. Thus, Giambattista anticipates claims 22 and 24-29 too.

Moreover, claims 24-30 are obvious. Sanofi argues that claims 24-30 are patentable because Giambattista must supply the reason for clicks to correspond to unit doses and because Steenfeldt-Jensen merely discloses that doing this was possible. Sanofi is wrong. Steenfeldt-Jensen provides a reason to employ clicks corresponding to unit doses on Giambattista's pen. Sanofi's response for claim 30 also fails because

it improperly reads limitations into claim 30 and relies on an erroneous teaching-away argument.

Sanofi's secondary-consideration arguments are insufficient to diminish the strong obviousness case here. Sanofi does not even attempt to tie any secondary considerations to the additional limitations of claims 22-30, so Giambattista's anticipation of claim 21 alone fatally undermines Sanofi's secondary-considerations case. Furthermore, Sanofi's alleged secondary considerations lack evidentiary support and lack nexus to the claims. Each of claims 21-30 is unpatentable and should be cancelled.

II. Giambattista Is Prior Art

As the petition explained, Giambattista is prior art to claims 21-30 because those claims lack written-description support before May 2016. Pet. 15-18. Sanofi argues in response only that a few specific lines of the GB Application (EX1026, 0007:25-0008:9) "broadly discloses" a genus of interchangeable internally- and externally-threaded piston rods, which Sanofi says could have been combined with a "conventional lead-screw drive mechanism." POR 22-30. Sanofi's argument fails to demonstrate that the GB Application or any parent application leading to the '844 patent justifies the priority claim. *See Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

Petitioners' expert Karl Leinsing applied the correct standard for his opinion that the claims lack written-description support at least before May 2016. Mr. Leinsing testified that the '844 patent does not teach an internally-threaded piston rod to interface "with all the other components" involved in the pen. EX2163, 172:11-173:6; POR 28-29. Sanofi's argument amounts to the assertion that a POSA ***could have had possession*** of what the '844 patent claims if the POSA had abandoned the approach disclosed in the GB Application. This is not the standard for establishing a priority claim. As discussed in detail below, the Board should reject Sanofi's priority argument because it fails to account properly for the GB application's disclosure as a whole.

A. The GB Application Does Not Disclose A Genus of Internally- and Externally-Threaded Piston Rods

Sanofi's "genus" argument fails because it does not read the cited embodiment as a whole. Lines 0007:25-0008:9 of the GB Application do not describe the threaded connections of the piston rod as an abstract form. Instead, they describe them as part of a pen-type injector having various components with numerous requirements. Sanofi's expansive approach to interpreting the GB Application's disclosure infects its entire priority analysis.

Sanofi's priority analysis commits a fundamental error by ignoring the language of the very passage it relies on in the GB Application. The GB Application does not

disclose a generic driving member with generic threading, it discloses a ***drive sleeve***. EX1026, 0007:31-32; EX1095, ¶¶7-15. In the GB Application, it is not a "conventional lead screw" or a "drive screw" that drives the piston rod. Nor is the piston rod driven by a leadscrew or "stinger" having a sleeve disposed concentrically around it. EX1095, ¶¶10, 13; EX1053, 113:9-16, 156:11-19. In the GB Application, ***the sleeve*** that drives the piston rod, not a drive screw connected to a sleeve. EX1095, ¶10. Indeed, Sanofi admits the specification shows that the piston rod "is adapted ***to engage with*** and move rotationally and axially relative to ***the cylindrical bore in the drive sleeve***." POR 32 (emphasis added). Contrary to Sanofi's arguments, neither a leadscrew nor a stinger is a drive sleeve. EX1095, ¶10; *see also* EX1053, 158:6-159:5 ("If it was [hollow], you might call it a threaded sleeve"). In the GB Application, a ***sleeve*** located between the piston rod and the housing drives the piston rod. EX1095, ¶10.

It is clear from the context of the GB Application that the cited text on pages 0007-0008 of the GB Application describes only an externally-threaded piston rod. For example, in the GB Application, the dose-dial sleeve is "located between the housing and the piston rod" and the drive sleeve is "located between the dose dial sleeve and the piston rod." EX1026, 0007:28-30. This means exactly what is uniformly depicted in the GB Application: the piston rod is disposed within the drive sleeve, which is disposed within the dose-dial sleeve, which is disposed within the

housing. EX1095, ¶11. The GB Application thus contemplates that the threaded portions of the piston rod are external threads on the outside surface of the piston rod and that these external threads engage with internal threads on internal surfaces of components (i.e., the "helical groove" on the drive sleeve) disposed radially between the piston rod and the housing. EX1095, ¶11.

Sanofi argues the word "between" could, in other circumstances, refer exclusively to an "axial" placement. POR 24-25. Sanofi's argument relies on a dose-tracking nut feature between two flanges that does not appear in EX1026, 0007:25-0008:13. Sanofi's argument conflates the spatial relationship of two sleeves between a rod and a housing with the spatial relationship of a nut tracking location between two axially-displaced flanges. Accepting *arguendo* Sanofi's argument that "between" means "axially between," the GB Application invented an extremely long pen in which the dose-dial sleeve extends axially from the housing, the drive sleeve extends axially from the dose-dial sleeve, and the piston rod extends axially from the drive sleeve. EX1095, ¶12. In the arrangement Sanofi proposes, the "sleeve" aspect of the components is ignored entirely. Sanofi's axially-disposed sleeve and piston-rod components simply are not what the GB Application discloses.

Sanofi's argument also fails to account for the remainder of the disclosure in the cited portion of the GB Application. For example, the first threaded portion of the piston rod rotates "through" an "insert or radially inwardly extending flange" located

in the housing. EX1026, 0008:1-5. Imagining the piston rod's threaded portions are internal makes no sense when the whole point of the piston rod's threaded portions in the GB Application is to mate with internal threads of components located between the piston rod and the housing. EX1095, ¶13. The GB Application only discloses external threading on both the first and second ends of the piston rod. Pet. 16-18 & n.4; EX1095, ¶13. The Board should reject Sanofi's argument and find that Giambattista is prior art to claims 21-30 of the '844 patent.

B. Sanofi's "Conventional" Leadscrew Argument Ignores the "Drive Sleeve" Requirement of the GB Application's Disclosure

Relying on the alleged disclosure of a genus in EX1026 at 0007:25-0008:9, Sanofi argues that employing a "lead-screw drive mechanism" was conventional. POR 27. Each of the exhibits Sanofi cites discloses using an externally-threaded, motor-driven screw to drive the piston. EX1095, ¶14; EX2169, abstract; EX2170, 6:34-42; EX2171, 2:26-27, 2:55-58; *see also* EX1053, 157:18-24 ("they're not insulin injector pens"). None of these documents discloses engaging a piston rod's internal threads with a drive sleeve's external threads. EX1095, ¶14. In any case, importing "conventional" knowledge to supply missing teachings in the disclosure is contrary to law. *Ariad*, 598 F.3d at 1352 ("a description that merely renders the invention obvious does not satisfy the requirement").

Sanofi errs by reading "conventional" leadscrew-drive mechanisms into the GB Application's disclosure, which does not deal with a conventional leadscrew-drive mechanism. Lines 0007:25-0008:9 of EX1026 do not disclose a generic "driving member." Instead, these lines specifically disclose a "drive sleeve" that uses clutch means to permit rotation between a drive sleeve and a dose-dial sleeve when a button on the dose-dial sleeve is depressed. EX1026, 0008:10-13; EX1095, ¶14. In the GB Application, unlike the "conventional" leadscrew-drive mechanisms Sanofi relies upon, the ***sleeve*** must drive the piston rod into the piston. EX1095, ¶14. A POSA would not look to any of Exhibits 2169-2171 to understand how to implement the drive mechanism disclosed in the GB Application. EX1095, ¶14. The Board should reject Sanofi's proposal to redesign the drive-sleeve mechanism disclosed in the GB Application into a leadscrew-drive mechanism that is nowhere disclosed in the GB Application.

III. Giambattista Anticipated Claim 22.

Claim 22 recites "The drug delivery device of claim 21 where the piston rod has a circular cross-section." Sanofi's POR nowhere disputes that Giambattista's piston rod has a circular cross-section at each end of the piston rod. Sanofi argues instead that the phrase "has **a** circular cross-section" requires that "***the*** cross-section of the piston rod" extending "over its length" be circular and that the piston rod may not be

"rotationally constrained" by a rectangular aperture in the insert. POR 32 (emphasis added). Sanofi's claim construction should be rejected because it attempts to rewrite the claim to include limitations that simply are not present. See *Scanner Techs. Corp. v. ICOS Vision Sys.*, 365 F.3d 1299, 1304 (Fed. Cir. 2004) (presuming "a" includes a plurality absent "a clear intent" to limit to one); EX1095, ¶¶123-125.

The specification also does not support Sanofi's construction. When the specification describes a component's uniform shape over a length, it says so using additional language. For example, the specification describes that "insert 16 is provided with a threaded circular opening 18 ***extending therethrough***." EX1004, 3:60-62 (emphasis added). Sanofi's construction would rewrite claim 22 to recite "where the piston rod has a circular cross-section **extending therealong**." Sanofi's attempt to rewrite claim 22 should be rejected as falling short of the broadest reasonable interpretation in light of the specification.

The specification also uses additional language not used in claim 22 when it refers to the piston rod's overall shape. For example, the specification refers to piston rod 20 in Figures 1-5 as being "of generally circular section." EX1004, 3:65-4:11. Sanofi has conceded that claim 22 does not recite a "generally circular" limitation. POR 33 ("the claim calls for a piston rod with a circular cross section, not a generally circular cross section"). Sanofi's proposed construction of "a circular cross-section" should be rejected as inconsistent with the specification.

Sanofi argues that "Giambattista's leadscrew has a non-circular cross section" because "Steenfeldt-Jensen describes its piston rod as having a 'not round cross-section' and a 'non-circular cross section.'" POR 31 (quoting EX1014). But this does not mean that Giambattista's leadscrew does not also comprise "a" circular cross-section in addition to having a non-circular cross-section, as the petition explained. Claim 22 does not require every cross section along the piston rod's length to be circular.

Even if claim 22 required the piston rod to have circular cross-sections over its entire length, Sanofi's argument would still fail. The central portion of Giambattista's piston rod, while not *perfectly* circular, is still generally circular. EX1095, ¶¶126-27. If Sanofi is suggesting "a circular cross-section" must be perfectly circular along the piston rod's entire length, it ignores that the piston rod disclosed in the '844 patent does not itself have a perfectly circular cross-section along its length, since the threaded portion's cross-sections would have protrusions corresponding to the threads. *Id.* (citing EX1004, 3:65-4:11; Fig. 5 (below left)). Indeed, the '844 specification itself describes its piston rod only as having a "generally circular" cross-section. EX1004, 3:34-36, 3:65-66 & Fig. 5; EX1095, ¶¶126-27. Mr. Leinsing confirmed Giambattista's piston rod likewise has a generally circular cross-section. EX1011, ¶577.

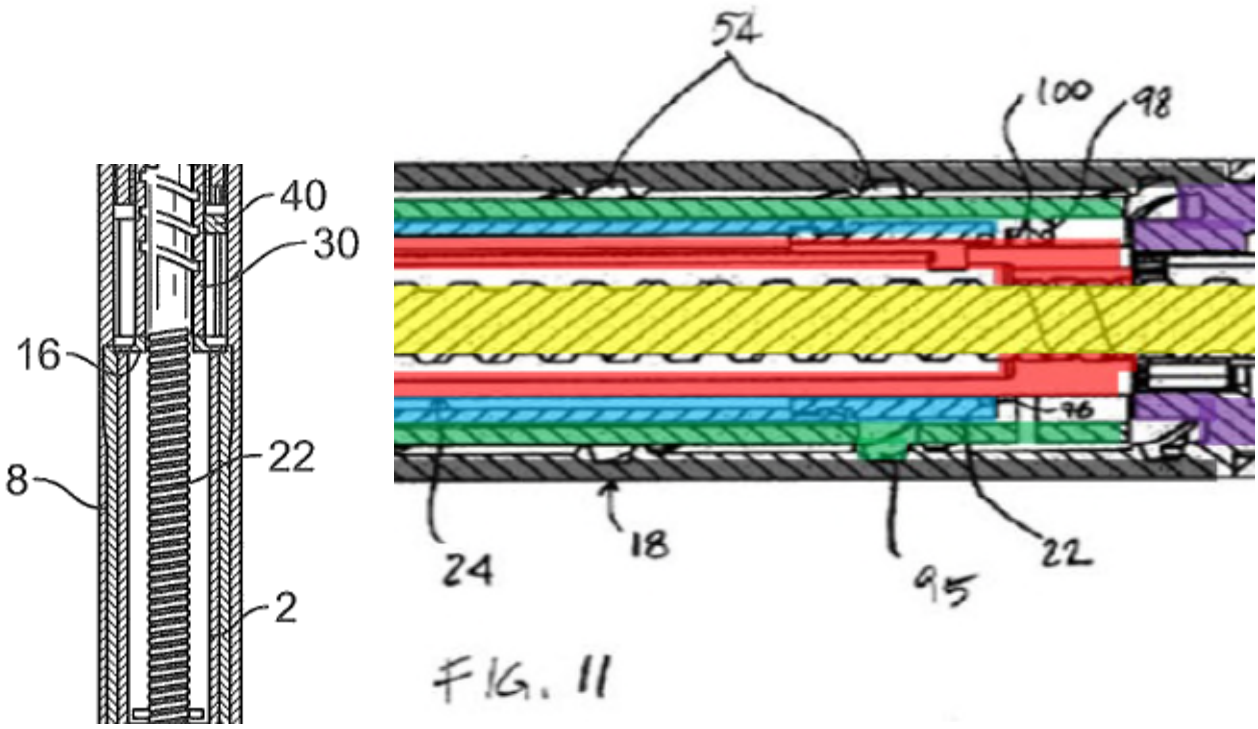


FIG. 11

Sanofi argues that if Giambattista's leadscrew "were to have a circular cross-section, it would not work for its intended purpose." POR 30-31. This argument assumes that claim 22 prohibits the piston rod from having any non-circular cross section along its entire length. As discussed above, however, this is not the case, and Sanofi's construction is incorrect.

Sanofi argues that a piston rod having a circular cross section must be "adapted to engage with and move rotationally and axially relative to the cylindrical bore in the drive sleeve." POR 32. This argument overlooks the fact that Giambattista's leadscrew ***is*** adapted to engage with and move rotationally and axially relative to the cylindrical bore of the driver 24. EX1016, 5:16-24; EX1095, ¶128.

For all of the reasons stated above, as well as those stated in the petition, claim 22 should be cancelled.

IV. Giambattista Anticipated Claims 24-29

Sanofi challenges ground 1 for claims 24-29 solely on the basis that Giambattista's audible- and tactile-click feedback during dose dialing and dose cancelling allegedly is not "indicative of unit doses." POR 33-35.

Sanofi argues that Giambattista cannot satisfy claims 24-29 unless it states that "one click corresponds to one unit dose or, for example, that five clicks correspond to one unit." POR 35. But anticipation does not require language identical to that used in the claim. *See In re Bond*, 910 F.2d 831, 832 (Fed. Cir. 1990) (whether a reference teaches a claim limitation "is not an 'ipsissimis verbis' test"); *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 953 F.2d 1360, 1369 (Fed. Cir. 1991) ("An anticipatory reference…need not duplicate word for word what is in the claims."). Giambattista anticipated claims 24-29 because the tactile and audible feedback in each click equals a dose that qualifies as a unit dose. Pet. 57-60; EX1011, ¶¶ 580-85, 594. Giambattista need not use the word "unit dose" to anticipate.

Sanofi argues that the number of clicks is not indicative of unit doses if it is "based on the number of grooves 76." POR 35. This argument is a red herring. In Giambattista, the ribs 80 and ratchet arms 96 are designed such that the clicks are

equal to unit doses of medicament. Pet. 57-60; EX1011, ¶¶ 580-85, 594. Having "numerous" grooves 76 as compared to the number of teeth 100 (POR 35) does not negate the fact that the interaction of the ribs 80 and ratchet arms 86 provide audible and tactile click feedback that equals unit doses of medicament.

Moreover, Sanofi does not substantiate its argument that the number of ribs 80 derives from the number of grooves 76 or that a specific number of grooves 76 derives from the number of teeth 100. And even if Sanofi were correct that the number of ribs 80 in Giambattista derives from the number of grooves 76, this merely confirms that the ribs 80 are "spaced at equal intervals," EX1016, 3:49-55, thereby confirming that each click corresponds to the same unit dose.

For the reasons discussed above, and in the petition, the Board should reject Sanofi's arguments and find that Giambattista anticipated claims 24-29.

V. Giambattista and Steenfeldt-Jensen Rendered Claims 24-29 Obvious

Sanofi opposes Ground 2 based on two arguments. Sanofi argues first that "Giambattista does not disclose or suggest that its pen could be modified to provide audible or tactile feedback indicative of unit doses." POR 36-37. But reason to modify need not arise from the primary reference. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420 (2007) ("The idea that a designer would ignore Asano because Asano was designed to solve the constant ratio problem makes little sense."). Indeed, "§103 likely

bars" patentability if a POSA "can implement a predictable variation" because the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *Id.* at 416-17.

As the petition discussed, Steenfeldt-Jensen expressly taught that the clicker means' spacing was "appropriately made so that a dose of one unit is set when the protrusion is moved from one depression to the neighboring depression so that the number of clicks heard and felt during the dose-setting rotation corresponds to the size of the set dose." Pet. 66-69. Steenfeldt-Jensen thus provided a POSA with reason to employ Giambattista with each click corresponding to a unit dose. Pet. 67. Sanofi's categorization of Giambattista as a reference attempting to solve the problem of dialing down a dose cannot render Steenfeldt-Jensen and Giambattista non-analogous art or in some other way read Steenfeldt-Jensen out of the prior art.

Sanofi's second argument is that Steenfeldt-Jensen merely demonstrates "that a POSA ***was able to*** make this modification," and provides no "reason ***why*** a POSA would modify Giambattista to arrive at the claim limitation." POR 37. As the petition explained, however, Steenfeldt-Jensen discloses that setting clicks was desirable. Pet. 66-69. Specifically, Steenfeldt-Jensen discloses that this spacing is "appropriate," and permits "the number of clicks heard and felt during the dose-setting rotation" to correspond to the size of the set dose." *Id.*, 67.

For the reasons discussed above, and in the petition, the Board should reject Sanofi's arguments and hold that claims 24-29 were obvious from Giambattista and Steenfeldt-Jensen.

VI. Giambattista and Steenfeldt-Jensen Rendered Claim 30 Obvious

Sanofi argues that Ground 3 fails, alleging, (1) the nut member disposed between dosing ring adapter 28 and dose knob 20 would not satisfy claim 30; and (2) a POSA would not make the modification because of its expected impact on pen width. POR 38. Both Sanofi arguments fail.

A. The Modification Satisfies Claim 30.

Sanofi argues the modification would not satisfy claim 30 because, allegedly, when the nut correctly indicates that all the available medicament has been dialed up, a user would "still dial a dose beyond the amount of medicament remaining in Giambattista's drug cartridge." POR 39-44.

First, Sanofi's argument fails because it mistakes claim 30 as requiring a dose stop. Claim 30 recites the "drug delivery device of claim 21 further comprises a nut that tracks each set dose of medicament delivered." Unlike claim 18, which *does* recite that the nut "further comprises a final dose stop…", claim 30 does not require a dose stop. Sanofi once again attempts to read additional limitations into the claim.

Regardless, Sanofi mistakenly assumes the modification will result in a user unknowingly dialing doses that exceed the remaining medicament available to be delivered. Sanofi argues first that a "snap fit" connection will permit rotation of the dose-ring adaptor 28 in relation to the dose ring 22. POR 41-43. As the petition explained, however, Giambattista discloses that dosing ring 22 and dosing-ring adaptor 28 are movable in concert with each other whether they are formed unitarily as a single piece or are "mounted" together. Pet. 37. Giambattista does not state that snap ring 82 permits rotation between the dosing ring and the dosing-ring adaptor. EX1016, 4:21-28. Sanofi's assumption is simply incorrect. EX1095, ¶¶129-132.

Sanofi argues that a user could still think he was dialing a dose larger than the remaining medicament when the dose-ring adaptor and dose ring are formed unitarily if the "protection against unwanted rearward movement" of the driver provided by its ratchet fingers is overcome by the user. POR 43-44. *Id.* Sanofi's assumptions ignore Giambattista's express statements to the contrary. *See, e.g.*, EX1016, 1:4-45 ("dosing ring non-rotatably disposed on the driver"), 3:44-47 ("dosing ring 22 is mounted on the driver 24 with the splines 86 extending into keyways 74. As a result, the dosing ring 22 cannot be rotated relative to the driver 24."), 3:33-38 ("Preferably, the ratchet teeth 52 and the ratchet fingers 66 cooperate to allow the ***driver 24 to rotate in only one direction*** relative to the body 18.") (emphasis added), 5:31-35 ("In the preferred embodiment, to maintain the spinner 16 position accurately, the interengagement of

the ratchet teeth 52 and ratchet fingers 66 ***prevents undesired rearward rotation*** of the driver 24….") (emphasis added); Figs. 4-5 (ratchet finger 66 and ratchet teeth 52).

As Mr. Leinsing explains, the protection the ratchet fingers provide against unwanted rearward movement would be adequate to prevent over-dialing a dose. EX1095, ¶133. Furthermore, a user would not unknowingly continue to torque the dosing ring beyond the remaining medicament because the audible and tactile feedback would inform the user that the cartridge was empty. *Id.*

Sanofi's argument that the proposed modification would not satisfy claim 30 should be rejected.

B. Pen Width Would Not Have Dissuaded a POSA from Making the Proposed Modification.

Sanofi also argues a POSA would have been dissuaded from implementing a tracking nut in Giambattista because doing so would allegedly make the pen 25% wider and require greater injection force. POR 44-45. This argument fails for several reasons.

First, Sanofi wrongly assumes the width of the pen would necessarily be 25% wider. EX1095, ¶134. Similarly, the force required to inject a dose would not necessarily be higher and could be mitigated, if necessary, through lubrication. EX1095, ¶134. Sanofi's teaching-away argument fails at least because its assumptions are wrong.

Second, the factors Sanofi alleges would not dissuade a POSA from employing the tracking nut. As Mr. Leinsing explains, injection pens of different widths and injection forces were available on the market, were sufficiently ergonomic, and did not impair the user's ability to handle and operate the pen. EX1095, ¶134. A wider pen can actually assist patients with gripping. EX1048, ¶50. Even if Sanofi were correct about an increase in pen width, POSAs would have viewed the minor alleged increase in width and injection force as a reasonable tradeoff for the benefit of tracking doses and would not have been dissuaded from making the proposed modification. EX1095, ¶134.

For the reasons discussed above, and in the petition, claim 30 would have been obvious from Giambattista and Klitgaard.

VII. No Nexus for Alleged Secondary Considerations

Sanofi bears the burden of production for secondary considerations. *Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092, 1101-02 (Fed. Cir. 2015); *Biomarin Pharmaceutical Inc. v. Genzyme Therapeutic Products Lmt. P'ship*, IPR2013-00537, Paper 79, 22 (nexus to "novel element in the claim" required); *see also Ormco Corp. v. Align Technology, Inc.*, 463 F.3d 1299, 1311-12, n.14 (Fed. Cir. 2006). Each of Sanofi's arguments fails for lack of nexus.

Sanofi provides identical secondary consideration arguments without differentiating among claims-at-issue or patents-at-issue. EX1048, ¶¶36-37, Attachment B-1; EX1055, 53:9-12; EX1055, 44:17-45:17, 47:21-25, 48:18-49:19, 50:20-51:24; EX1056, 9:4-7, 18:16-20, 19:18-25, 24:22-25:5, 37:2-6; EX1056, 11:19-14:10. This failure undermines Sanofi's case.

Sanofi argues that Lantus SoloStar practices claims 21 and 30, but Lantus SoloStar is not "the invention" of these claims. For example, the claims do not require Lantus (or insulin at all), an 80-unit cartridge, a particular stroke length or injection force.[1] The "overwhelming consideration" in insulin-prescription decisions is "the insulin itself." EX1048, ¶25; EX2145.008, .015 ("real value…is Lantus itself."), EX2145.022 ("our long term advantage comes from the insulin properties"); EX2146 at 13, 77-78 36; *see also* EX1055, 28:14-29:22, 30:2-6. The patents-at-issue simply are not important. EX1048, ¶¶37-39 (discussing EX2146 at 13, 36, 43, 75, 77-78; EX2145.020-022; EX1045; EX1067; EX1072). Insulin pens are "largely fungible."

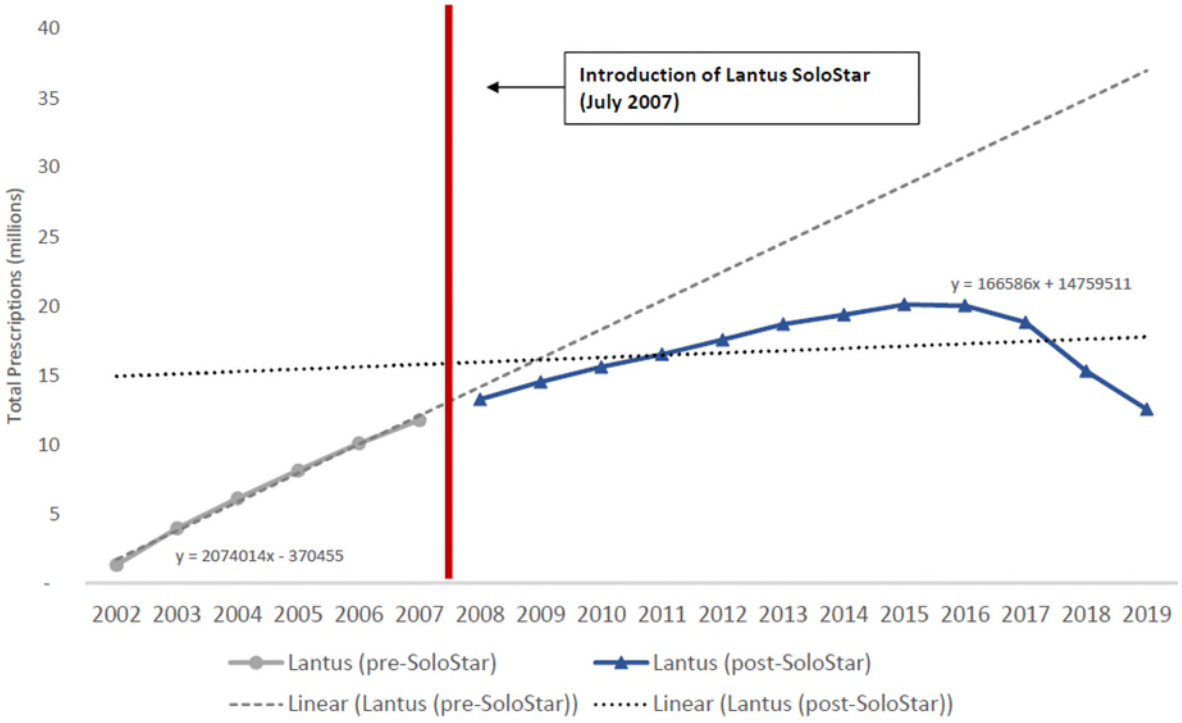
[1] Aside from Lantus, these unclaimed properties do not drive Lantus SoloStar performance. EX1048, ¶¶52-56; *see also* EX1048, ¶¶25, 27-30. The challenged claims essential for any of these properties, nor do they necessarily provide these features. EX1095, ¶156.

EX1048, ¶¶27-28. Sanofi's nexus argument ignores the claims and fails to apportion any secondary consideration to the active ingredient of the commercial product it relies upon for secondary considerations.

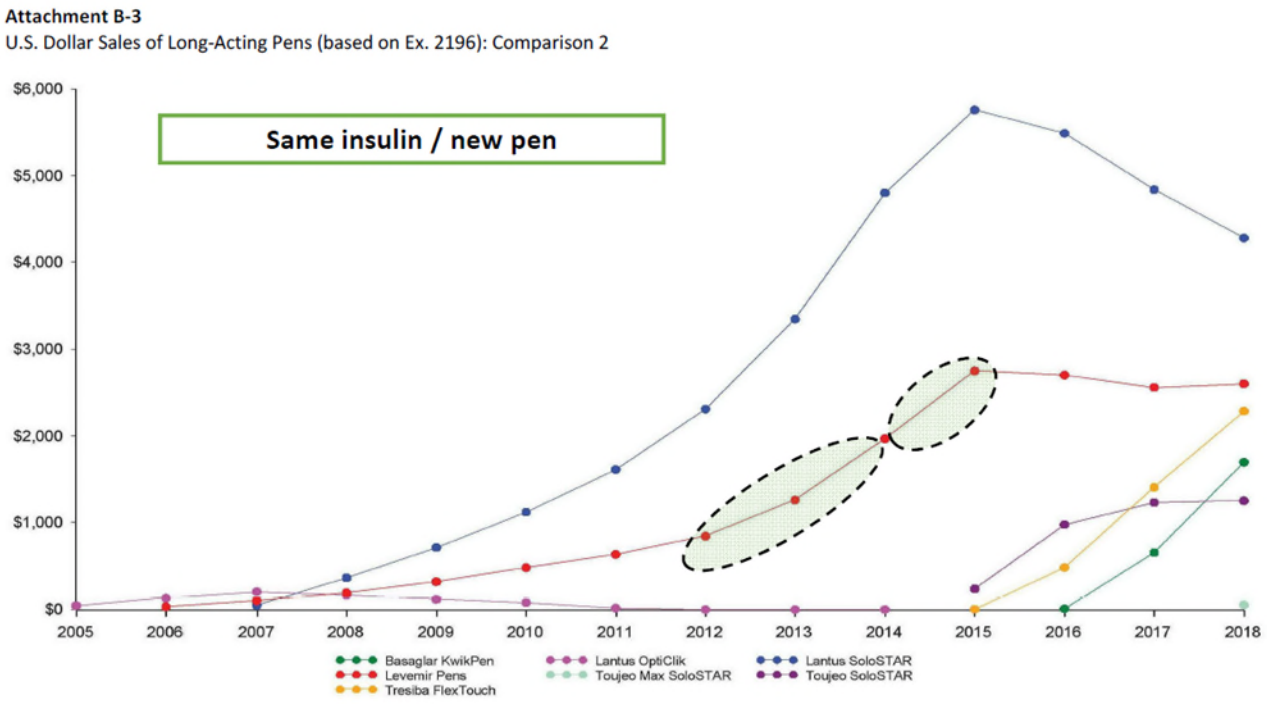
Indeed, Sanofi leveraged its Lantus franchise and years of prior Lantus marketing to drive SoloStar sales. EX1048, ¶¶48-51; EX1056, 69:9-70:10. Sanofi pushed consumers to use SoloStar instead of OptiClik. EX1048, ¶¶46-47; EX2145.008 ("conversion strategy"), EX2145.0099 (OptiClik samples discontinued), EX2145.0099 ("limit competition between portfolio entities"), EX2145.010; EX1055, 125:16-127:6.

The economic evidence confirms that Lantus SoloStar's commercial performance is not driven by any feature unique to the SoloStar pen. EX1048, ¶¶30-35. The Lantus franchise growth rate had already stabilized before SoloStar's introduction. EX1048, ¶¶21. Attachment B-7:

Attachment B-7
Chart of Lantus Franchise Total Prescriptions by Year

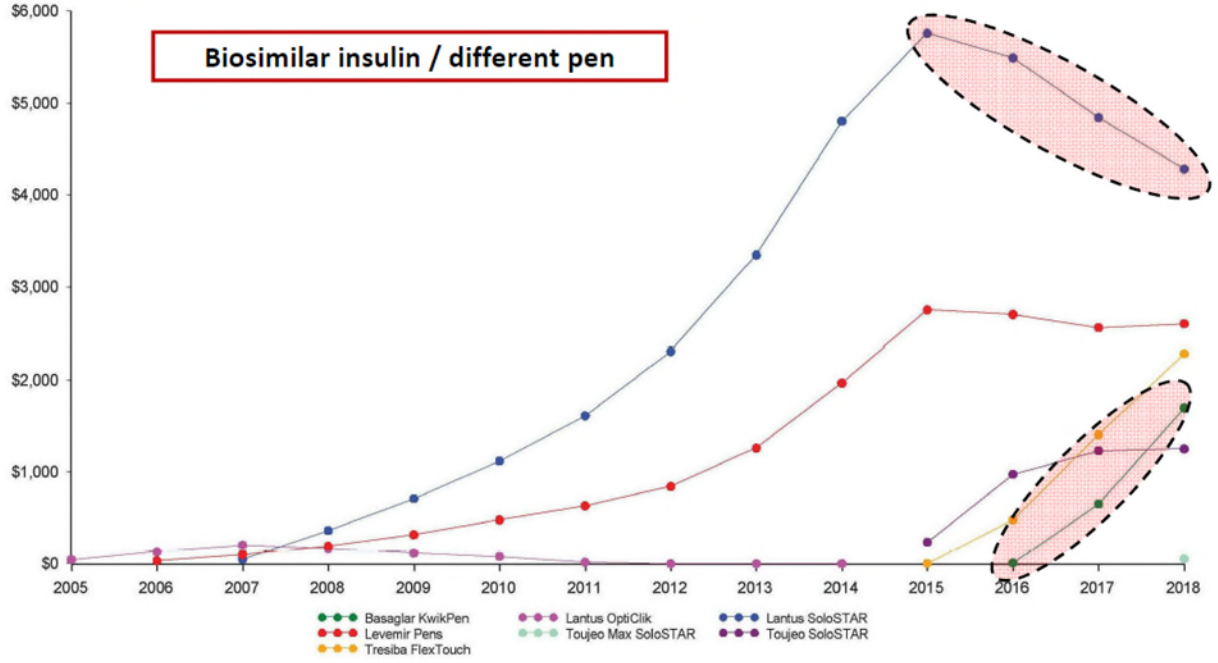


Changes in injector pens (FlexPen to FlexTouch) did not improve performance of Levemir, an existing long-acting insulin competitor to Lantus SoloStar. EX1048, ¶¶30-35, 64, Attachments B-3:

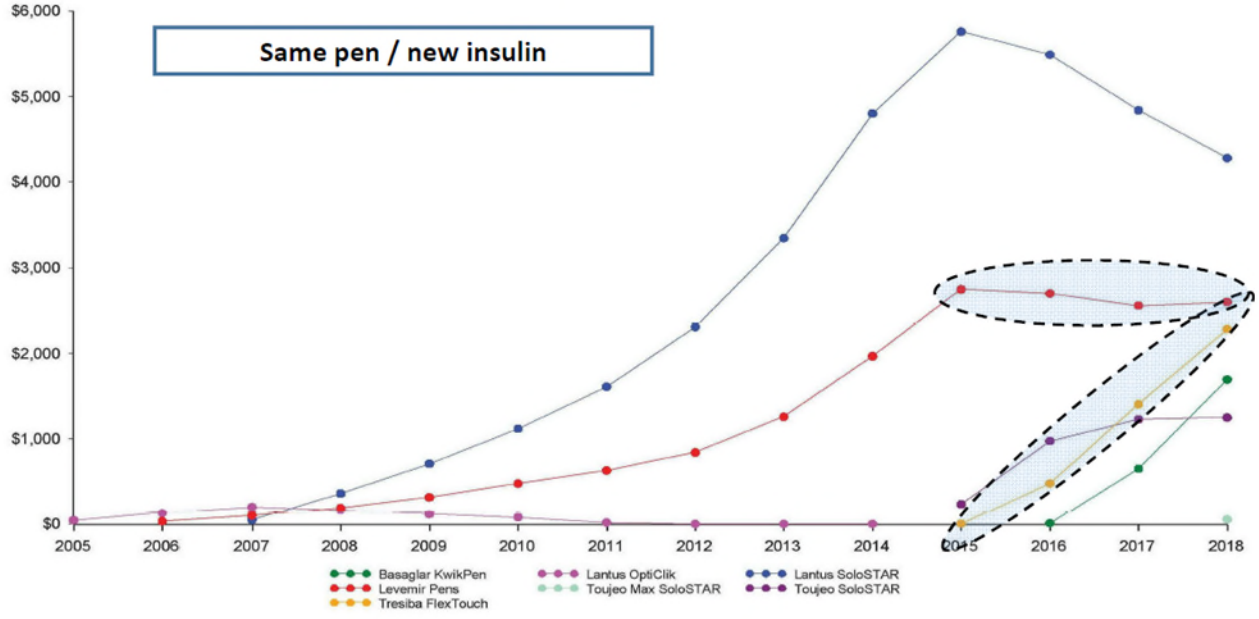


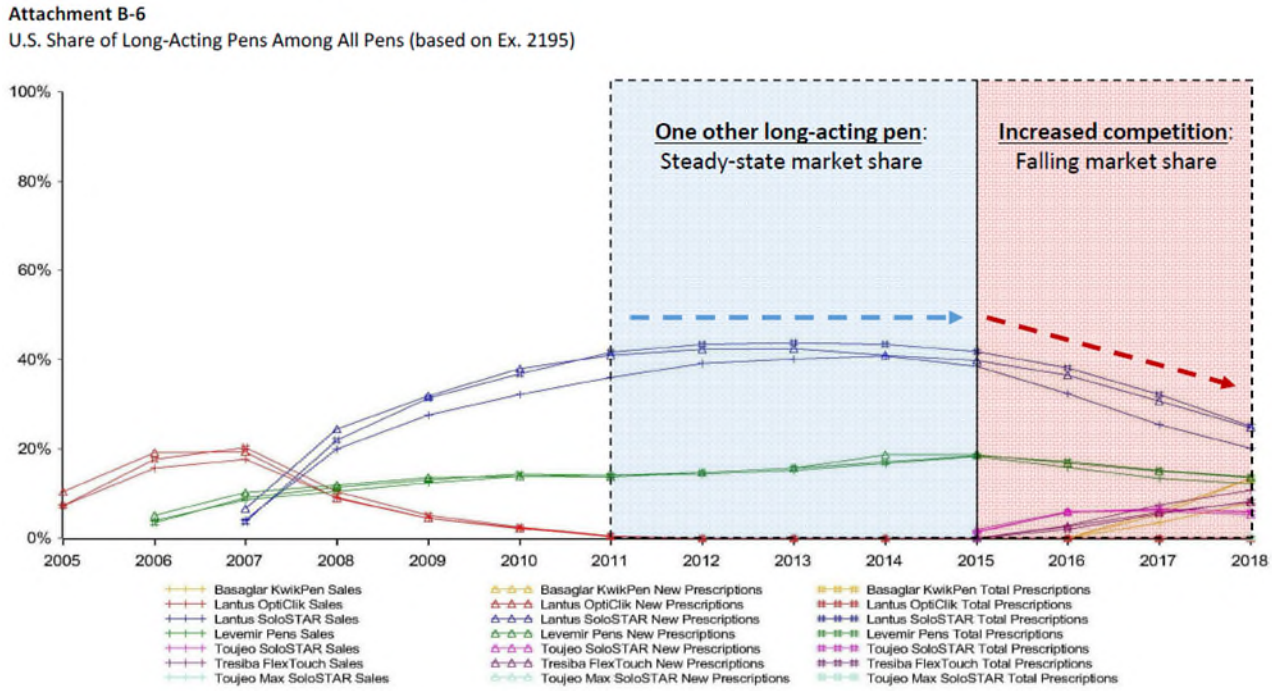
But introducing a competing long-acting insulin (Basaglar or Tresiba) in an existing pen (KwikPen or FlexTouch) had a dramatic impact. EX1048, ¶¶30-35, 64; EX1055, 96:13-20. Attachments B-2, B-4, B-6:

Attachment B-2
U.S. Dollar Sales of Long-Acting Pens (based on Ex. 2196): Comparison 1



Attachment B-4
U.S. Dollar Sales of Long-Acting Pens (based on Ex. 2196): Comparison 3



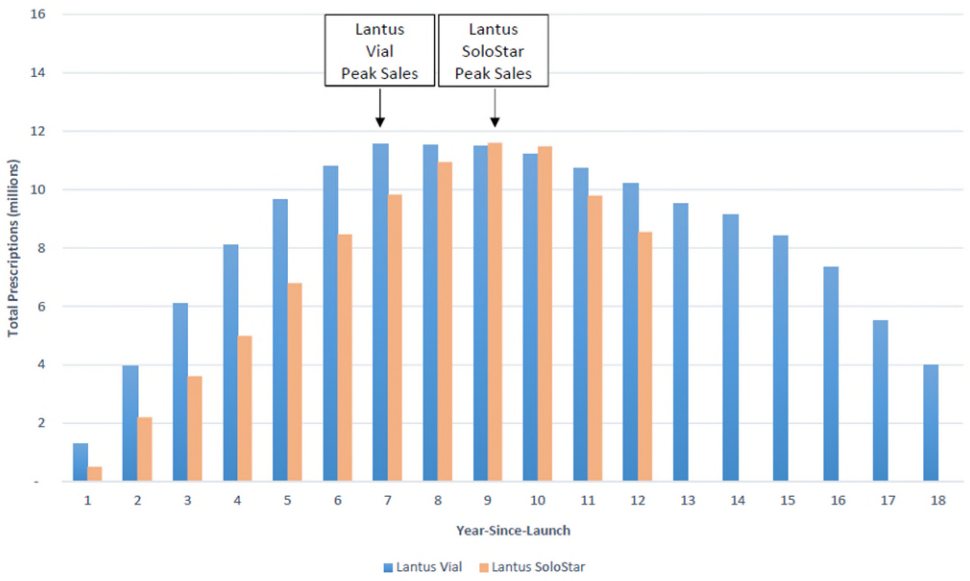


Neither the FlexTouch nor the KwikPen practice the challenged claims. EX1055, 86:20-87:6, 88:14-19, 103:18-104:6, 104:14-105:3-5. This economic evidence confirms Lantus SoloStar's commercial performance does not reflect demand for the SoloStar pen or for the challenged claims. EX1048, ¶35. That Lantus SoloStar's commercial performance is tied to the active ingredient covered by several blocking patents supports finding a lack of nexus to the alleged secondary considerations. EX1048, ¶¶30-35, 61-65.

Sanofi contends that SoloSTAR replaced OptiClik because the claimed invention was superior. As explained above, however, SoloSTAR did not enhance Lantus sales, and Dr. Grabowski's testimony misrepresents the market and the data.

EX1048, ¶¶20, 25-27, 40-41. Attachments B-8, B-9 demonstrate that Sanofi merely shifted Lantus vial prescriptions to Lantus SoloStar prescriptions:

Attachment B-8
Chart of Lantus Vial and Lantus SoloStar Total Prescriptions by Year-Since-Launch



Attachment B-9
Chart of Lantus Product Total Prescriptions by Year

Sanofi's own documents confirm Sanofi pushed Lantus consumers to use SoloSTAR instead of OptiClik, not any market preference for the claimed invention. EX1048, ¶¶46-47; EX2145.008 ("conversion strategy"), EX2145.0099 (OptiClik samples discontinued), EX2145.0099 ("limit competition between portfolio entities"), EX2145.010. Sanofi switched patients from OptiClik to SoloStar "in support of its business considerations." EX1055, 125:16-127:6. Sanofi's business decision to convert Lantus customers to SoloStar does not establish nexus, it undermines it.

Sanofi argues unclaimed properties provide nexus between SoloStar and the claims. But as Mr. Leinsing testifies, the challenged claims are not essential for these unclaimed properties. EX1095, ¶156. Furthermore, these unclaimed properties do not drive Lantus SoloStar performance. EX1048, ¶¶52-56; *see also* EX1048, ¶¶25, 27-30.

Sanofi argues industry praise and recognition support nexus, but these documents are either made or written by Sanofi affiliates, do not praise the pen as being "inventive," or do not attribute praise to the properties Sanofi relies upon. There is no connection between the alleged "awards and praise" and the claims-at-issue. EX1048, ¶¶57-60. Because of lack of nexus, none of the alleged secondary considerations can be attributed to the challenged claims.

A. No Long-Felt, Unmet Need For the Claimed Invention

Sanofi concedes that existing pens were used successfully to administer insulin analogs before SoloStar, but argues they were difficult to use because of a "relatively high injection force," that Lantus SoloStar "revolutionized the injection pen market, in large part because [it] was easy to use," and that patients preferred SoloStar for its low injection force. POR 49-51. Although Sanofi's OptiClik was a uniquely bad pen, Sanofi's replacement, SoloStar, was not an unusually good pen. EX1048, ¶¶43. 49. Indeed, other available pens were easy to use and "largely fungible" with SoloStar from the perspective of the patient and the prescriber. EX1048, ¶¶27, 29, 32-44, 52.

As Dr. Biggs testifies, "there was no long-felt unmet need for another insulin pen." EX1048, ¶39. In more than 30 years of practice, Dr. Goland never heard from a patient wishing they had a pen with low injection force, never saw using a syringe prevent a patient from taking Lantus, and never prescribed an insulin solely based on

its pen. EX1056, 52:6-9, 71:4-16. In contrast to Sanofi-sponsored injection force studies, (EX2143.010; EX2144.010; EX2100.006; EX2126.004; EX2116.009; EX2123.007; EX1048, ¶58), other studies found SoloStar did not have a lower injection force. *See, e.g.*, EX214.015 (versus FlexPen and Lillypen), EX2145.020-021 (NovoPen 4; Innlet).

Contrary to Sanofi's arguments, other insulin pens were already considered easy to use both generally and for patients with special challenges like age or dexterity issues. EX1048, ¶¶45-47, 52; EX1046.0057, .0062-.0063. Sanofi's studies confirm that both SoloStar and FlexPen were "very easy to use." EX2145.026; EX1048, ¶55; EX2143.001, EX2143.010, EX2143.070; EX2126.001. Sanofi's studies concluded both the SoloStar and FlexPen were suitable in both elderly and younger patients and those with visual and dexterity impairments, and "were associated with ***comparable usability***." EX2126.003 (emphasis added); EX1048, ¶56; EX2143.005, EX2143.009. SoloStar was a "best-performing pen device ***in a statistical tie with FlexPen***." EX2146.009; *see also id.* at .0037, .0039, .0075; EX1048, ¶52. SoloStar may have addressed Sanofi's business needs, but not any unmet patient needs. EX1048, ¶53.

Sanofi incorrectly contends that "injection force was a primary concern." POR 50. As Dr. Biggs explains, "injection force was never the reason patients were unwilling or unable to inject themselves," and patients who could not self-inject "would not have been aided by the marginal differences in injection force between

FDA-approved injector pens." EX1048, ¶¶29-30; *see also* EX1048, ¶53 (discussing EX2146.037-040). The ease-of-use evidence discussed above confirms any alleged difference in injection force was not material and there was no unmet need.

Sanofi cites post-SoloStar, Sanofi-funded, -authored, or -edited publications that do not demonstrate industry recognition of an unmet need. EX2128.009; EX2123.007; EX2185 (PR Newswire distribution of Sanofi press release). It also cites an article placed in the "Lifestyle" section of the "Philippine Daily Inquirer" under the url of "showbizandstyle" alongside stories like "Mesmerized by Harry Connick's blue eyes." EX2184.001; *see also* EX2184.003 ("Buy Content"). Moreover, statements in the article Sanofi misattributed to Sjoberg Kho appear to be from Sanofi's press release. *Compare* POR 51 (citing EX2184.0001) *with* EX2185.001 ("self-injection can be a barrier"). These exhibits do not constitute "industry recognition"; they are Sanofi marketing.

B. No Industry Praise for the Claimed Invention

None of the cited documents establish industry praise for the claimed invention. For example, Sanofi relies on a "case study of SoloSTAR" submitted to the DBA, implying the DBA awards recognized SoloStar's "inventiveness." POR 52 (citing EX2121.003). But this "case study" was written, funded, and sponsored by Sanofi

(with SoloStar designer DCA). EX1048, ¶¶57-58; EX1075. It is self-praise, not industry praise. EX1055, 79:6-81:19.

Sanofi relies on an Architecture and Design award as "recognition of [SoloStar's] inventiveness." POR 52-53 (citing EX2201). The document Sanofi cites does not attribute the award to "inventiveness." Nor does the statement that SoloSTAR "represents a design for social good". POR 53. Neither the document nor the statement praises what is claimed or the features (*e.g.*, low injection force) Sanofi argues uniquely flow from what is claimed. EX1048, ¶¶57-59.

Sanofi argues that Sanofi and DCA were finalists for the Prix Galien USA 2009 Award but again fails to demonstrate this is evidence that SoloStar was "inventive," much less that the claims were inventive. EX1048, ¶60. Sanofi's proffered evidence fails to establish that industry praise supports the challenged claims.

C. No Commercial Success of the Claimed Invention

Sanofi argues that Lantus SoloSTAR enjoyed fast and long-sustained growth in terms of overall levels and shares of dollar sales, new prescriptions, total prescriptions, as well as profitability and formulary placement. POR 53-54 (citing EX2109, ¶12). But Dr. Grabowski never evaluated profitability. EX1048, ¶¶23-24. Furthermore, Sanofi provides no benchmarks for evaluating success, applies a faulty "pens only"

market definition, and formulary status does not separately demonstrate commercial success. EX1048, ¶¶17-22, 25-28.

For example, Dr. Grabowski relies on a misleading 8,000% growth rate for SoloStar when, as Dr. McDuff points out, the failed OptiClik pen similarly enjoyed an 8,000% growth rate in its first three years. EX1048, ¶20. Similarly, Dr. Grabowski argues Lantus SoloStar's commercial success is supported by the "strong performance" of Apida SoloStar, Toujeo SoloStar, and Admelog SoloStar, even though peak annual sales of Apidra SoloStar and Admelog SoloStar fall below the sales of Lantus OptiClik that he describes as "deficient." EX1048, ¶¶70-71. Sanofi also inappropriately excluded insulin injectable products from its market share analyses to inflate Lantus SoloStar's marketshare 2-3 times. EX1048, ¶¶25-27. Sanofi's commercial success arguments thus improperly take Lantus SoloStar's commercial performance out of context.

Sanofi argues that Lantus SoloStar sales and prescriptions remained strong despite the entry of several competing long-acting insulin pen products beginning in 2015. POR 54. However, introduction of competing Basaglar and Tresiba long-acting insulin products completely changed the trajectory of both the Lantus and Toujeo SoloStar products without practicing the claims-at-issue. EX1048, ¶¶30-35, 64; EX1055, 96:13-20. Dr. Grabowski himself previously explained that generic entry of a biologic is expected to have less and a slower impact on the sales of the existing

biologic than it would have for a small molecule because of biologics' increased manufacturing costs. EX1055, 143:10-144:10. Dr. Goland confirmed that existing diabetes patients are particularly reluctant to switch to a different insulin product. EX1056, 71:17-22. The trajectory change of Lantus and Toujeo SoloStar product performance upon introduction of competing long-acting insulins provides strong evidence that SoloStar itself is not a commercial success.

Lantus SoloStar enjoyed the benefit of a Lantus franchise that predated the Levemir franchise by five years and the foundation of earlier Lantus pen (OptiClik). EX2186.002. Lantus OptiClik had twice as many prescriptions in 2007 as Levemir FlexPen. EX2198. Lantus SoloStar overtook Levemir FlexPen not because of any unique SoloStar attributes, but because of what it shared in common with OptiClik: Sanofi selected it as the exclusive Lantus pen in the United States. EX1048, ¶¶20-22, 30-35.

Sanofi's alleged secondary considerations do not diminish the strong obviousness case.

VIII. Conclusion

The challenged claims should be held unpatentable and cancelled.

Respectfully submitted,

Date: 18 September 2019

/Richard Torczon/
Richard Torczon, Reg. No. 34,448

CERTIFICATION UNDER 37 CFR §42.24(d)

I certify the word count for this reply totals 5,510, which is less than the 5,600 words allowed under 37 CFR §42.24(a)(i).

Respectfully submitted,

Date: 18 September 2019

/Richard Torczon/
Richard Torczon, Reg. No. 34,448

CERTIFICATE OF SERVICE

I certify that this reply was served today on the Patent Owner at the email correspondence address of the Patent Owner as follows:

Elizabeth Stotland Weiswasser	**elizabeth.weiswasser@weil.com**
Anish R. Desai	**anish.desai@weil.com**
Sundip K. Kundu	**sundip.kundu@weil.com**
Kathryn M. Kantha	**kathryn.kantha@weil.com**
William S. Ansley	**sutton.ansley@weil.com**
Matthew D. Sieger	**matthew.sieger@weil.com**
Adrian C. Percer	**adrian.percer@weil.com**
Brian C. Chang	**brian.chang@weil.com**
WEIL, GOTSHAL & MANGES LLP	**Sanofi.IPR.Service@weil.com**
John S. Goetz, Joshua A. Griswold, Matthew S. Colvin, Kenneth W. Darby and W. Karl Renner	**PTABInbound@fr.com**

Respectfully submitted,

Date: 18 September 2019

/Richard Torczon/
Richard Torczon, Reg. No. 34,448