UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN (consolidated with 15-cv-62081-CIV-COHN)

AMGEN INC. and AMGEN MANUFACTURING LIMITED,

Plaintiffs,

vs.

APOTEX INC. and APOTEX CORP.,

Defendants.

DEFENDANTS APOTEX INC. AND APOTEX CORP.'S
MOTION UNDER FED. R. CIV. P. 52(c)

Defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex") hereby submit this Motion for Judgment on Partial Findings pursuant to Fed. R. Civ. P. 52(c).

TABLE OF AUTHORITIES

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I. INTRODUCTION

Defendants/Counterclaim Plaintiffs Apotex Inc. and Apotex Corp. (collectively, "Apotex") move for judgment of non-infringement of all asserted claims of U.S. Patent No. 8,952,138 ("the '138 patent") pursuant to Federal Rule of Civil Procedure 52(c). Now that Plaintiffs/Counterclaim Defendants Amgen Inc. and Amgen Manufacturing Limited (collectively "Amgen") has been heard on all issues relating to Apotex's alleged infringement of the '138 patent, Amgen has not met its burden to prove that Apotex's protein refolding process uses "a refold mixture" having "a high protein concentration, where a high protein concentration is at or above about 1g/L protein."[1] Specifically, Amgen's evidence for Apotex's alleged literal infringement of this claim limitation—that Apotex's inclusion bodies are mainly protein and that Apotex's pre-litigation communications to Amgen stated that the inclusion bodies are G-CSF—is insufficient for Amgen to meet its burden. In view of Amgen's lack of evidence, judgment for Apotex of non-infringement of all asserted claims of the '138 patent is appropriate.

II. RELEVANT LAW FOR ENTRY OF A JUDGMENT OF NON-INFRINGEMENT IN FAVOR OF APOTEX

After a party has been fully heard with respect to its case-in-chief, a Court may grant a motion under Rule 52(c) at any time. *See Drew Estate Holding Co., LLC v. Fantasia Dist., Inc*., No. 11-21900-CIV, 2014 WL 1319328, at *3 (S.D. Fla. Apr. 1, 2014) (citing *EBC, Inc. v. Clark Bldg. Sys., Inc*., 618 F.3d 253, 272 (3d Cir. 2010) (internal quotation marks omitted)); *see also Granite State Ins. Co. v. Smart Modular Techs., Inc*., 76 F.3d 1023, 1031 (9th Cir. 1996) (Rule 52(c) "authorizes the court to enter judgment at any time that it can appropriately make a dispositive finding of fact on the evidence.").

"To show literal infringement of a patent, a patentee must supply sufficient evidence to prove that the accused product or process meets every element or limitation of a claim." *Rohm and Haas Co. v. Brotech Corp*., 127 F.3d 1089, 1092 (Fed. Cir. 1997) (quoting *Lemelson v. United*

[1] This Motion addresses Amgen's failure to meet its burden of proof concerning a single limitation of claim 1 of the '138 patent. Apotex maintains that its pegylated filgrastim product is materially changed, and that Amgen has not met its burden of proof concerning the "redox component," "refold buffer," and "redox buffer strength" limitations of claim 1, but will only focus on the 1 g/L limitation in this Motion. Apotex explicitly reserves its rights to dispute Amgen's similar failures to meet its burden of proof concerning Apotex's alleged infringement of any other limitations of the asserted claims of the '138 patent.

States, 752 F.2d 1538, 1551 (Fed. Cir. 1985)). "If the patentee fails to meet that burden, the patentee loses regardless of whether the accused comes forward with any evidence to the contrary." *See Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1327 (Fed. Cir. 2008).

In the context of analyzing infringement of a proposed drug product under 35 U.S.C. § 271(e)(2), the question is grounded in traditional patent law principles. *See Abbott Labs. v. TorPharm, Inc*., 300 F.3d 1367, 1373 (Fed. Cir. 2002). The relevant inquiry is whether the specifications set forth in an applicant's FDA regulatory filings define a drug product that falls within the scope of an issued patent. *See id*. Further, the relevant inquiry is dominated by the specifications set forth in an applicant's FDA regulatory filings since the applicant is bound by strict statutory provisions to sell only those products that comport with the description of the drug product provided in the FDA regulatory filings. *Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1401, 1408 (Fed. Cir. 2014). If the specifications set forth in an application to market a drug speak directly to the issue of infringement, then that resolves the infringement inquiry. *See Sunovion Pharm., Inc. v. Teva Pharm. USA, Inc.*, 731 F.3d 1271, 1279-80 (Fed. Cir. 2013) (finding infringement under § 271(e)(2) where a drug product's specification clearly described a product that met the limitations of the asserted claims).

Where a proposed drug product's specification does not directly address the question of infringement, then it is proper to expand the infringement inquiry to consider evidence beyond the application submitted to the FDA, such as testing of actual drug product samples. *See Ferring*, 764 F.3d at 1409. Thus, under Section 271(e)(2), "the relevant inquiry is whether the patentee has proven by a preponderance of the evidence that the alleged infringer will likely market an infringing product," and that burden is never shifted to the alleged infringer. *See Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1568 (Fed. Cir. 1997) (finding no infringement because the drug product's specification alone did not resolve the question of infringement, and examination of actual data from manufactured batches showed that what was likely to be manufactured did not infringe).

Finally, a finding of infringement under 35 U.S.C. § 271(g) is necessarily premised upon a finding that an accused process infringes an asserted claim. *See id*. at 1571 (finding no abuse of discretion in dismissing an infringement claim under 35 U.S.C. 271(g) where the plaintiff failed to prove that the defendant was using a process claimed in an essential patent).

III. AMGEN HAS NOT MET ITS BURDEN TO PROVE INFRINGEMENT OF THE ASSERTED CLAIMS OF THE '138 PATENT

Amgen has not met its burden to prove infringement of the asserted claims of the '138 patent because Amgen has not proffered evidence sufficient to show that Apotex's protein refolding process uses a "refold mixture" having "a high protein concentration, where high protein concentration is at or above about 1 g/L protein." Further, Amgen has only alleged that Apotex literally infringes this claim limitation, and did not allege infringement of this limitation under the doctrine of equivalents. (*See* Ex. A, Trial Tr. Day 1 (7/11/2016) at 214:9 – 216:7 (Willson).)

Apotex is statutorily bound by the content of its regulatory documents. (*See* Ex. C, Trial Tr. Day 3 (7/13/2016) at 96:8 – 97:6 (Dowd).)[2] Thus, it is these documents that control the infringement inquiry. *See Ferring*, 764 F.3d at 1408; *see also Glaxo*, 110 F.3d at 1565. Judgment for Apotex under Rule 52(c) is appropriate because Apotex's applications to market its Filgrastim and pegylated Filgrastim drug products do not specify an infringing process. What is more, examination of Apotex's batch records show that when Apotex's refolding process is practiced according to specifications set forth in Apotex's abbreviated Biologics License Application ("aBLA"), there is in fact no literal infringement of the '138 patent.

A. Apotex's Pre-Litigation Statements Under 42 U.S.C. § 262(*l*)(3)(B) Are Not Probative of Infringement

Amgen pointed to Apotex's pre-litigation statements made pursuant to 42 U.S.C. § 262(*l*)(3)(B) to contend that Apotex asserted that the concentration of its Filgrastim drug substance "in the refill buffer [*sic*] as 0.9 to 1.4 grams per liter." (Ex. A, Trial Tr. Day 1 (7/11/2016) at 215:10 – 216:7 (Willson)) (discussing JTX112 and JTX113).) However, these documents are not probative of the infringement inquiry because they are not a part of Apotex's aBLAs, but were instead merely communications from Apotex's lawyers to Amgen's lawyers. *See Ferring*, 764 F.3d at 1409 (finding that the infringement evaluation is concerned only with the final product for which the applicant sought FDA approval to market); (Ex. A, Trial Tr. Day 1 (7/11/2016) at 215:18 – 216:3 (Willson); Ex. C, Trial Tr. Day 3 (7/13/2016) at 79:15-21 (Dowd)) (discussing JTX112).) Therefore, Apotex's pre-litigation communications to Amgen have no bearing on the specifications set forth in Apotex's aBLAs.

[2] Amgen called Dr. Dowd as an adverse witness in its case-in-chief. Only testimony from Dr. Dowd's cross-examination by Amgen is cited in this Motion.

In cases such as this, the Federal Circuit has held that the "[patent] statute requires an infringement inquiry focused on what is likely to be sold following FDA approval." *Glaxo*, 110 F.3d at 1568. Amgen proffered no evidence that Apotex's communications to Amgen under 42 U.S.C. § 262(*l*)(3)(B) were part of Apotex's aBLAs, or ever submitted to FDA. (*See* Ex. A, Trial Tr. Day 1 (7/11/2016) at 215:10 – 216:7 (Willson); Ex. C, Trial Tr. Day 3 (7/13/2016) at 79:15 – 82:23 (Dowd).) Because it is a drug applicant's regulatory documents that are submitted to FDA—here, Apotex's aBLAs for Filgrastim and pegylated Filgrastim—that control the operation of Apotex's protein refolding process, any statements made outside of those regulatory filings are simply not relevant to the infringement inquiry. *Glaxo*, 110 F.3d at 1565 ("Glaxo must prove by a preponderance of the evidence that the product sold by Novopharm pursuant to the approved ANDA will at least more probably than not read on the patent." (internal quotations omitted).)

B. Evidence Relied Upon by Amgen Is Not Probative of Infringement

Amgen also pointed to Apotex's aBLAs for the proposed Filgrastim and pegylated Filgrastim products as requiring an amount of inclusion bodies per volume of refolding buffer that resulted in a "refold mixture" having "a high protein concentration where high protein concentration is at or above about 1 gram per liter protein." (*See* Ex. A, Trial Tr. Day 1 (7/11/2016) at 214:9 – 215:9 (Willson)) (discussing JTX-014 and JTX025).) Specifically, Amgen's expert Dr. Richard Willson testified that he relied upon the specifications set forth in Apotex's aBLAs, "which set[] an operating range of 0.9 to 1.4 grams per liter for the inclusion body concentration as setting Apotex's protein concentration in the refold mixture." (Ex. B, Trial Tr. Day 2 (7/12/2016) at 71:21 – 72:4 (Willson).) Dr. Willson also testified that "to get to that protein concentration of 0.9 to 1.4 grams per liter . . . [he] took the total weight of the [Apotex] inclusion bodies after they had been washed four times" and "divided it by 160." (*See* Ex. B, Trial Tr. Day 2 (7/12/2016) at 72:5 – 73:16 (Willson).) However, Dr. Willson admitted that he "didn't take into account the water in any calculation between 0.9 and 1.4 grams per liter." (Ex. B, Trial Tr. Day 2 (7/12/2016) at 77:17 – 78:2 (Willson).)

Judgment of no literal infringement is appropriate where a regulatory specification does not reveal whether the allegedly infringing element is actually present as required by the asserted claim. *See Sunovion*, 731 F.3d at 1279-80 ("In *Glaxo* [110 F.3d at 1569] we likewise upheld a judgment of no literal infringement because the ANDA application specified only that the

generic product would have one crystalline form with certain purity, but did not reveal whether a different crystalline form claimed by the asserted patents would be present at all."). Similarly here, Apotex's aBLA specifications merely require an amount of inclusion bodies to be used as an input in Apotex's protein refolding process, but does not specify the amount of protein present in those inclusion bodies. (Ex. C, Trial Tr. Day 3 (7/13/2016) at 83:3-19 (Dowd)) (discussing JTX25).) Further, Apotex's aBLAs require washing of the inclusion bodies prior to being weighed. (Ex. A, Trial Tr. Day 1 (7/11/2016) at 27:15-19 (Willson); Ex. C, Trial Tr. Day 3 (7/13/2016) at 73:9 – 74:4 (Dowd).) Judgment of no literal infringement is therefore appropriate because the portions of Apotex's aBLAs that Amgen cited as evidence of infringement do not reveal what amount of protein is present in the refold mixture.[3]

IV. APOTEX'S BATCH RECORDS SHOW THAT THE DRUG PRODUCTS LIKELY TO BE APPROVED ARE MANUFACTURED BY A NON-INFRINGING PROCESS

Where a drug applicant's regulatory filings do not reveal that a product that is likely to enter the market would infringe the asserted claims of a patent, it is proper to expand the infringement inquiry to consider evidence beyond the application submitted to the FDA, such as testing of actual drug product samples. *See, e.g., Glaxo*, 110 F.3d at 1570 (In conducting this infringement analysis, the district court properly considered the ANDA itself, the materials the defendant submitted to the FDA, and other pertinent evidence provided by the parties.); *see also Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1382, 1387-1388 (Fed. Cir. 2014) (holding that in instances where the ANDA specification alone cannot resolve the question of infringement, the correct analysis is to look at actual data from samples in the manufacturing process as the Court instructed in *Glaxo*).

It was therefore Amgen's burden to proffer evidence that in its operation Apotex's refolding process would, in fact, infringe the asserted claims. However, in his infringement analysis, Amgen's expert, Dr. Willson, was aware of, but did not consider the water that is present in Apotex's inclusion bodies, as reflected in Apotex's batch records. (*See* Ex. B, Trial Tr. Day 2 (7/12/2016) at 76:11 – 78:2 (Willson).) Nor did Amgen's expert conduct any

[3] Apotex expressly reserves its right to assert that other portions of its aBLAs specify an upper limit on the total protein concentration in the refold mixture. *See, e.g.*, DTX-89. However, these documents were not relied upon by Amgen in its case-in-chief, and thereofre are not the focus of this Motion.

independent measurement of what is present in Apotex's inclusion bodies. (Ex. B, Trial Tr. Day 2 (7/12/2016) at 73:17-19 (Willson).)

Apotex actually measures the protein content of its inclusion bodies and records this information in its batch records. (Ex. B, Trial Tr. Day 2 (7/12/2016) at 78:12-17 (Willson).) By that measurement, Apotex reports both the amount of wet inclusion bodies that are used to begin Apotex's protein refolding process, as well as the total protein amount present in those inclusion bodies. (Ex. B, Trial Tr. Day 2 (7/12/2016) at 79:7-22 (Willson).) On cross examination, Apotex's Director of Product Development, Dr. Dowd, confirmed that Apotex's washed inclusion bodies are approximately two-thirds water. (Ex. C, Trial Tr. Day 3 (7/13/2016) at 75:2-6 (Dowd).) Specifically, Dr. Dowd established that "out of 172 grams of inclusion bodies, only 66.8 grams of that were protein . . . ." (Ex. C, Trial Tr. Day 3 (7/13/2016) at 87:3 – 6 (Dowd).)

Apotex is therefore entitled to an entry of judgment that its protein refolding process, as defined by its aBLAs for Filgrastim and pegylated Filgrastim does not infringe any asserted claim of the '138 patent under § 271(e)(2). Further, because a finding of infringement under 35 U.S.C. § 271(g) is necessarily premised upon a finding that an accused process infringes an asserted claim, Apotex is similarly entitled to an entry of judgment that its protein refolding process does not infringe any asserted claim of the '138 patent under § 271(g). *See Glaxo*, 110 F.3d at 1571 (finding no abuse of discretion in dismissing an infringement claim under 35 U.S.C. 271(g) where plaintiff failed to prove that defendant was using a process claimed in the '133 process patent).

V. CONCLUSION

Based on the foregoing, the Court should find that the accused process described in Apotex's aBLAs do not infringe the asserted claims of the '138 patent. Based on this, the Court should find that importation, offer to sell, sale, and/or use of Apotex's Filgrastim and pegylated Filgrastim within the United States would not infringe any asserted claim of the '138 patent.

Date: July 18, 2016

Respectfully submitted

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on July 18, 2016, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to counsel and that a true and correct copy was served via electronic mail on all counsel of parties of record.

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EXHIBIT A

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN

AMGEN INC., and AMGEN MANUFACTURING LIMITED,

Plaintiffs,

-v-

APOTEX INC., and APOTEX CORPORATION,

Defendants.

Fort Lauderdale, Florida
July 11, 2016
8:54 a.m.

TRANSCRIPT OF BENCH TRIAL PROCEEDINGS

BEFORE THE HONORABLE JAMES I. COHN

U.S. DISTRICT JUDGE

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Claim 1 is probably representative of the disputes that the Court will be called upon to decide.

So we have broken up the claim here into seven pieces. Four of those, we believe, there will be no dispute; that they are satisfied in the Apotex process, and so those are marked with the green checks.

What I would like to do now is just run through the other parts where we think there is a dispute. And I'll preview what we think the evidence will be on those.

So the first one, as Your Honor may recall from the claim construction side of the case, is a protein present in a volume at a concentration of 2 grams per liter or greater. And here, Your Honor, what we're going to see, I think, is that the Apotex process does that.

So we have on the left-hand side here that is part of the series of steps in the Apotex process, and importantly for this element, when they have that inclusion body that they have extracted from the bacteria, one of the things they do is wash it a series of times.

First of all, there is this buffer wash. Buffer is a -- is some chemical components. And then next, there are three successive water washes. And, Your Honor, we will hear evidence that this is a very thorough and extensive washing process. And that's significant because the end result is a very highly-washed inclusion body from which all of the things

bodies, by the specified 7.2 liters of solubilization buffer to get the 30 grams per liter. And those are the numbers which are to be compared with 2 grams per liter in the claim language.

Q. And so what is your opinion as to whether or not the present in the volume at a concentration of 2 grams per liter are greater is satisfied with respect to protein concentration?

A. It's my opinion that claim element is satisfied.

Q. I would like to talk about one last claim element, perhaps if the Court will permit, before we end for the day, and that's the claim element to form a refold mixture.

What's your understanding of what this claim element requires based on the Court's claim construction?

A. Yes. Refold mixture has been constructed as a mixture form from contacting, one, the volume in which the concentration of protein is 2.0 grams per liter or greater, which is the element we just talked about a moment ago, with, two, the refold buffer.

The refold mixture has a high protein concentration where high protein concentration is at or above about 1 gram per liter protein.

So that's the constructed claim language.

Q. Is that claim met in Apotex's processes?

A. Yes. In my opinion, that claim element is met.

Q. Why is that?

A. The evidence is, again, from the BLA documents JTX14 and JTX25, which talks about the operating parameter. And the highlighted first yellow line is inclusion body amount per liter of refolding buffer, the total volume being 160 liters, which we'll talk about later, but inclusion body amount per liter of refolding buffer operating range 0.9 to 1.4 grams per liter and set point 1.1 grams per liter.

Q. Where did this table come from?

A. These are from the Apotex BLA documents JTX14 and JTX25.

Q. Is there other evidence that Apotex's protein concentration in its refold mixture is at or above 1 gram per liter?

A. Yes. Yes. On the next slide -- there's been some correspondence between Apotex and Amgen in which -- and these are different exhibits, JTX113 and 112.

Would you like me to confirm those in the binder?

Q. If you wish. It would be Tabs 52 and 53 --

A. Thank you.

Q. -- of your second binder. It would be Page 16 of JTX112 and Page 22 of JTX113.

A. Oh, thank you. Yes. I was miscombining those elements.

Yes, okay. Perhaps I won't do both, but I have confirmed the JTX112.

And so these are communications from Apotex to Amgen in which Apotex asserts the concentration of its filgrastim drug substance. So that's not inclusion bodies. That's not

total protein. That's actually the filgrastim drug substance itself, pure G-CSF, in the refill buffer as 0.9 to 1.4 grams per liter.

And then the pegfilgrastim process, which is identical, has the similar number. The concentration of its filgrastim critical intermediate, which is the same molecule, in the refill buffer is 0.9 to 1.4 grams per liter.

Q. Just to wrap up this element, what is your opinion as to whether or not the Court's definition of refold mixture is met in Apotex's processes?

A. It is my opinion that the Court's definition of refold mixture is met in each of these processes.

MS. WU: Your Honor, if this is a good time to stop, we can pick up tomorrow.

THE COURT: We will recess for the evening. We'll reconvene at 9:00 a.m. tomorrow morning.

Folks, even though I get here a little bit before 9:00, you don't have to be here until 9:00 o'clock. So just because I'm here, I will wait on you. I can assure both sides I will wait on you until 9:00 o'clock.

So you all have a nice evening, and we'll see you tomorrow morning.

MR. GROOMBRIDGE: Thank you.

MS. WU: Thank you, Your Honor.

(Recess at 5:02 p.m., until 9:00 a.m., July 12, 2016.)

EXHIBIT B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN

AMGEN INC., and AMGEN MANUFACTURING LIMITED,

Plaintiffs,

-v-

APOTEX INC., and APOTEX CORPORATION,

Defendants.

Fort Lauderdale, Florida
July 12, 2016
8:52 a.m.

TRANSCRIPT OF BENCH TRIAL PROCEEDINGS

BEFORE THE HONORABLE JAMES I. COHN

U.S. DISTRICT JUDGE

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limited fashion after all of the column steps, et cetera, that are in. In there, the protein in question would be a higher fraction filgrastim at the beginning, but even there it won't are be perfectly pure.

Q. In your opening expert report, where you gave your infringement opinions, you said that Apotex was isolating the G-CSF from the refolding step; isn't that correct?

A. That's true.

Q. Now, under the Court's claim construction, a protein concentration of about 1 gram per liter or greater is required in the refold mixture; isn't that correct?

A. That's correct.

Q. And when you analyzed the protein concentration in Apotex's refold mixture, you specifically looked at the concentration of inclusion bodies, correct?

A. That's correct.

Q. And in your opinion, Apotex's concentration of inclusion bodies in the refold mixture is the same as the protein concentration; isn't that correct?

A. Certainly very close, yes.

Q. Mr. Mortonson, if you could pull up JTX14, which is -- call-out 13. And we'll go to Page 45, which is blown up here, and this is Table S.2.2-26.

Now, Dr. Willson, you cite the specification given here, which sets an operating range of 0.9 to 1.4 grams per

liter for the inclusion body concentration as setting Apotex's protein concentration in the refold mixture; isn't that correct?

A. That's correct.

Q. And to get that protein concentration of 0.9 to 1.4 grams per liter, you took the total weight of the inclusion bodies present at the outset of Apotex's downstream process; isn't that correct?

A. I want to be very clear that the downstream process in this sort of usual term of art would include the cell lysis and certainly all of the washing. And so let us just agree to say that I took the weight of the inclusion bodies after they had been washed four times.

Q. But you took the total weight of the inclusion bodies present after, you know, Apotex's downstream process; isn't that correct?

A. Again, downstream process doesn't fit accurately into what I think you're trying to communicate in the way that people use downstream process.

So let's just agree to say I took the total weight of Apotex's inclusion bodies after washing.

Q. And that value was 144 grams to 266 -- sorry. Let me backup.

That value was 144 grams to 216 grams of frozen inclusion bodies; is that correct?

A. That number is not on my screen, but that sounds right by my memory. I'll take your word for it, frankly.
Q. And you divided this 144 grams to 216 grams by the volume of Apotex's refold buffer, which is 160 liters; isn't that correct?
A. I'm not quite sure where you're going. The .9 to 1.4 grams per liter come from the Apotex document.
Q. I agree. So you took the 144 grams and you divided it by 160; isn't that correct?
A. I believe I did do that calculation, and I'm pretty sure you have the numbers. They're not in front of me, and my memory is not perfect here, but that sounds like it would be about .9. And I believe I did do that calculation, yes.
Q. And 216 grams divided by 160 would be 1.4 grams per liter; isn't that correct?
A. That's certainly about right, yes.
Q. You didn't take an independent measurement of the inclusion bodies from Apotex process; isn't that correct?
A. Experimentally, no, I did not.
Q. Now, Mr. Mortonson, I would like to stay in JTX14 and go to call-out 14, which is Page 46.
And if we go to Table S.2.2-27, we see here, Dr. Willson, that it lists a concentration of filgrastim in the solubilized inclusion bodies; isn't that correct?
A. I'm sorry. Which line are we talking about, the second

inclusion bodies in the refolding buffer, which is 1.1 gram per liter; isn't that correct?

A. Yes. The 1.08 approximately .1, yes, I see that, yes.

Q. And that would be the 172 grams that we looked at earlier divided by 160 liters; isn't that correct?

A. That sounds right to me, yes.

Q. And that's within the range that was specified at 0.9 to 1.4 grams per liter that we discussed earlier; isn't that correct?

A. That's correct.

Q. And it says here at 5.4, Step 5.4, that the weight of the inclusion bodies is the total wet weight of the inclusion bodies; isn't that correct?

A. It does say that, yes.

Q. And, Dr. Willson, you didn't account for the weight of the water in the inclusion bodies; isn't that correct?

A. I'm sorry. In what context? We have stated protein concentrations from Apotex, which are not subject to a water compensation. So in what context are you referring to?

Q. So if we look at here when Apotex reports the inclusion body concentration being within the range of 0.9 to 1.4 in the batch record, do you see where I'm at?

A. Uh-huh. Yes.

Q. And when they report that inclusion body concentration, which we said is 1.1 grams per liter; that's correct?

A. Correct.
Q. They're reporting it as a total wet weight of inclusion bodies taken in gram per liter of 160 liters of refolding buffer; isn't that correct?
A. Yes, that's correct.
Q. So when I asked you earlier when you looked at the 0.9 to 1.4 grams per liter of inclusion bodies, you didn't take into account the amount of water within that weight; is that correct?
A. Are you talking about -- I mean, 0.9 to 1.4 has occurred three or four times in the general consideration of this case, including being specified by Apotex to Amgen and to the FDA as protein amounts, specifically as G-CSF amounts.

But there's also the calculation you just walked me through and certainly, in that case, I did not take into account the water, that's true.
Q. But you did not take into account the amount of water that would be within that 0.9 to 1.4 grams per liter; isn't that correct?
A. In the calculation you just walked me through, that's correct.
Q. You didn't take into account the water in any calculation between 0.9 and 1.4 grams per liter; is that correct?
A. I think that's true. I'll note that there are places where Apotex talks about water, and I was a bit worried about it.

And there are places where there's a great deal of water and places where there is less water, but you're correct, I think.

Q. Dr. Willson -- or I'm sorry. Mr. Mortonson, if we go to call-out 17. And if we can go to Page 118.

A. That's in the same document?

Q. Yes, in the same document.

A. Yes.

Q. And that would be DTX81.

And we have Steps 5.20, 5.21 and 5.22. Do you see where I'm at?

A. Yes, uh-huh.

Q. Now, Dr. Willson, you'll agree with me that after the inclusion bodies are dissolved, which is shown here in Line 5.20 in Apotex's batch record, that Apotex then measures the total protein concentration in the solubilized inclusion bodies shown in Line 5.22; isn't that correct?

A. Yes, that's correct.

Q. And that's done by measuring the optical density at 280 nanometers; isn't that correct?

A. That's correct.

Q. And it says here that that value is recorded in Section 7, so let's take a look at that.

So, Mr. Mortonson, if you could pull up call-out 18. And that's Page 120. And if we go to Section 7.

We see here, Dr. Willson, that you agree with me that

Section 7 reports a protein concentration in the solubilization buffer; isn't that correct?

A. It reports the -- oh, yes, I see that, yes.

Q. It reports the protein concentration in the solubilization buffer; isn't that correct?

A. Yes, that's correct.

Q. And if we go to No. 8 here, where it says, "yield" in the Apotex batch record, you'll agree with me, Dr. Willson, that Apotex reports the total protein amount in the solubilized inclusion bodies as being 66.8 grams; isn't that correct?

A. I'm sorry. The first entry, of course, is a three line description. I am a trying to understand what it says here.

So concentration filgrastim -- Part 14 times solubilized inclusion body of --

Yes, I think I understand that. Uh-huh.

Q. You agree, Dr. Willson, that Apotex reports the total protein amount in the solubilized inclusion bodies as being 66.8 grams; is that correct?

A. Yes.

Q. And we saw earlier that the inclusion body amount was 172 grams; isn't that correct?

A. Yes, I think that's right.

MR. COBLENTZ: I pass the witness, Your Honor.

THE COURT: All right. Redirect. Ms. Wu?

MS. WU: Thank you, Your Honor.

EXHIBIT C

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN

AMGEN INC., and AMGEN MANUFACTURING LIMITED,

Plaintiffs,

-v-

APOTEX INC., and APOTEX CORPORATION,

Defendants.

Fort Lauderdale, Florida
July 13, 2016
9:00 a.m.

TRANSCRIPT OF BENCH TRIAL PROCEEDINGS - SEALED PORTION

BEFORE THE HONORABLE JAMES I. COHN

U.S. DISTRICT JUDGE

Appearances:

For the Plaintiff:
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questioned during the direct examination, correct?
A. I was.
Q. Now, this is a document recording what Intas had done back in 2004, correct?
A. It is.
Q. Now, let's turn in this to the page numbered 14. Do you have that?
A. I do.
Q. And this part of the document deals with the so-called downstream process, correct?
A. It does.
Q. And that is the part of the process in which the refolding step happens, correct?
A. Yes.
Q. And by the way, where we have this, the Intas people write "Initial process acquired from technology source."
Do you see that?
A. I do, yes.
Q. Do you know where they got it from?
A. Yes. It was from an Italian group. I believe the acronym is ICGEB. And so in the late 1990s, they would have developed this process and transferred it to Intas.
Q. And, sir, the process that is described here with respect to refolding is different from what Apotex currently uses is it not?

A. So the refolding step -- yeah, it's certainly smaller scale.
Q. The refolding redox components are used in different amounts, correct?
A. Oh, I haven't -- I would have to look at it more closely. I assume that you're referring to the table there. I'd have to do some calculations to double-check.
Q. Do you see amounts given for cysteine and cystine given there?
A. I do.
Q. And you testified on your direct examination that that portion of the process hadn't changed, right, from Process I through Process IX?
A. Yes.
Q. But, in fact, this is very different from what is done in Process IX; is that not true?
A. I don't have the full details here. But this is a very short description, so I don't.
Q. Sir, do you not know whether the concentrations of cysteine and cystine in this process, as it stood in 2004, were very different from the one you currently use?
A. That's a good question. I don't know, because I'm used to mass and grams per liter and these are expressed in millimolar. I'm sorry. I can't speak to whether it's the same or different.

Q. If I were to suggest to you that in your current process, you use an amount of reductant that is seven times lower and an amount of oxidant that is eight times higher, would you have any way of knowing whether that's correct?
A. I wouldn't, no.
Q. Now, let's turn on -- let's turn, actually, back. Let's go to the Page No. 11 in this document, please. Let me know when you have that.
A. Yes.
Q. And you see there's a section headed "Visual Observation" at the top of the page?
A. Yes.
Q. And that's about the inclusion body pellet that is obtained after centrifugation, correct?
A. Yes.
Q. And it says, "The IB pellet is creamy white in color and hard-packed."
Isn't that what it actually looks like?
A. Again, I was through a window into the operational area, and I have not physically felt the pack or the pellet in order to know if it was hard-packed or a paste.
Q. You have know direct personal knowledge about the hard packing of the pellet?
A. No. I haven't physically handled the pellet. They were doing GNP operations. I'm not trained to be an operator in the

Q. In fact, rather than saying that, they repeated the same statement that Apotex now claims to be a mistake, correct?
A. I'm sorry. I missed that question.
Q. Let's try it a different way.
Could you turn, please, to the next tab in the book and you should find JTX 113 there.
A. Yes.
Q. Do you have that?
A. Yes, I see it. Sorry.
Q. This is another letter about two and a half months after the one we were just looking at, correct?
A. Okay. Yes, it seems to be. Yes.
Q. And if we turn in this one to Page 22, and we look again in the paragraph that is just above the footnotes, we see the same statement with respect to how much filgrastim protein is in the refold buffer, correct?
A. Yes. I see that.
Q. And, again, it's stated to be 0.9 to 1.4 grams per liter, correct?
A. Yes. And it seems to be that the start of the sentence is around the 2.0 grams per liter. So, again, presumably the same logic was applying at that time.
Q. Now, sir, let's look at what the FDA documents, the documents your company submitted to the FDA say about this, please.

A. Okay.
Q. And let's turn, please, to the next tab. And you should find there JTX25.
Do you have that?
A. Yes, I do.
Q. And this is one of the documents that you looked at on your direct examination, correct?
A. I did.
Q. So let's look -- let's begin with Page 39 of the document, please.
A. Yes. I'm here.
Q. And you see there that the last paragraph of the page is talking about the inclusion bodies and how much of them are used?
A. Yes.
Q. And, again, it tells us that it's 0.9 to 1.4 grams per liter when they go into the refolding buffer, correct?
A. Yes.
Q. And here, by the way, it says that four of those centrifugation bottles are always used, correct?
A. Yes.
Q. And is that true for Process IX?
A. That's as far as my recollection, yes.
Q. So it is always four bottles?
A. Yes. We have managed to uniform, make that uniform.

Q. Now, if we turn over the page, we see -- let's just have a moment to get there. Look at the third paragraph there. Let me know when you've got there.
A. Yes.
Q. And that deals in part with the so-called OD280 technique --
A. Yes.
Q. -- about which you testified?
A. Yes.
Q. And it says that the total protein concentration is calculated by dividing the OD280 result by 0.86 liters per mole percentage centimeter and in parentheses it says, (extinction coefficient).
Do you see that?
A. Yes.
Q. You understand what that means?
A. I understand what that means, yes.
Q. So extinction coefficient is the technical name for what that number of 0.86 liters per mole per centimeter means, correct?
A. Yes.
Q. And that number is a number that is unique to filgrastim or G-CSF as a protein, correct?
A. There might be other proteins. Certainly, there's a wide panel of proteins for which 0.86 might apply. But G-CSF

certainly is the one of interest here.
Q. Each protein has its own extinction coefficient, correct?
A. Yes.
Q. Some of them are higher than 0.86, correct?
A. Yes.
Q. And some of them are lower than 0.86?
A. Yes.
Q. What you've done in the way you run the test is assume that every protein in the mixture has an extinction coefficient that is exactly the same as filgrastim, correct?
A. That is true.
Q. All right. And you also are not taking account here of whatever other things might be in the mixture that would affect the OD280 value?
A. That is true.
Q. And, in fact, on your direct examination, you told us that one of the reasons why that number of 100.2 grams in the batch sheet was wrong was because cystine and cysteine have been carried through as contaminants and they throw it off, correct?
A. That is true.
Q. And that's a perfect example of the way in which a small of amount of contaminant can dramatically influence the OD280 value; fair?
A. Yeah. There's a fair bit of loss of cysteine and cystine added to the refolding mixture, but it's a fair statement.

Q. But in that situation, you testified the true value is about 68 grams of protein, but the value you get in the test is 100 because of contaminants, right?
A. Yes.
Q. So that tells us that contaminates can have a profound effect on the accuracy of the information you get using an OD280 technique?
A. That is true.
Q. Now, sir, in the refold mixture, the proteins that go into that, they come with contaminants that have been carried through from the fermentation step?
A. Yes. They would if they've managed to pass the washes, the water washes initially, and then been solubilized and hasn't been filtered out, yes, they would be there.
Q. And that could include DNA from the bacteria, correct?
A. It could.
Q. And a small amount of DNA would have a profound effect on the OD280 reading, would it not?
A. I don't know what the definition of small amount is.
Q. 5 percent.
A. Well, 5 percent, by weight, that's a substantial amount of protein -- of DNA. Sorry. But it is -- yeah, it certainly -- that's a lot of DNA.
Q. So if the inclusion bodies were 90 percent protein and 5 percent DNA, the value you would get in the OD280 technique

Q. Now, sir, let's turn to Page 2 of Exhibit 81.
A. Yes.
Q. And you testified about this. This is where you say out of the 172 grams of inclusion bodies, only 66.8 grams of that were protein, correct?
A. Yes.
Q. And in the form here in the middle, it says, Total Filgrastim In Input." Do you see that?
A. I do.
Q. And you said in your direct examination that, well, it was really the lion's share of it was filgrastim, correct?
A. Yes.
Q. But that phrase isn't correct, even according to your calculations here, is it? It's not total filgrastim, it's total protein?
A. It's total protein, but the in-process stream is termed filgrastim because it's the lion's share of the product is at that stage.
Q. Now, the -- and there's no way in this batch record that has an entry saying how much of the inclusion bodies was water, right?
A. No. It wasn't calculated, no.
Q. In fact, there's nowhere in any of the documents that we've seen where it says in writing that the inclusion bodies are 64 or 65 percent water; fair?

means, in essence, the active ingredient, right?
A. Yes. In this case, it's the drug substance of the PEGylated Apo-filgrastim, yes.
Q. Let's establish our terminology because the Court has heard a number of these things.
So when we're dealing with the FDA, drug substance is a term that would be applied to an active ingredient, correct?
A. Yes. This is the bulk before it gets filled.
Q. And drug product is the terminology the FDA would use to refer to the finished product?
A. Yes.
Q. And there's also a term "critical intermediate." You're familiar with that, correct?
A. Yes.
Q. And critical intermediate means it's intermediate in the sense that something else is going to happen to it in order to create the drug substance?
A. Yes. The PEGylated process this is -- the filgrastim drug substance is the same as the filgrastim critical intermediate for the PEGylation process.
Q. And here in this slide, one of the things that's addressed is the chemical process that is used to attach the PEG to the filgrastim, right?
A. Yes.
Q. And it says, "N-terminal PEGylation process developed based

on the reaction published by Amgen." And then in parentheses, (Molineux 2004.) Do you see that?

A. Yes.

Q. N-terminal PEGylation means I'm taking a PEG, and I'm attaching it to the N-terminal of the protein, right?

A. Yes.

Q. And that is done purposefully and deliberately in the Apotex process, right?

A. Yes.

Q. And Molineux that's referenced there is a publication by an Amgen scientist, correct?

A. I believe so, yeah.

Q. Could you turn, please, to the next tab in the book?

A. Yes.

Q. Now, can you identify or confirm for us that what we find there, JTX066, is indeed the 2004 Molineux publication?

A. I believe so. There were several Molineux presentations or publications in that time frame, but I believe so.

Q. Can you confirm that this is a publication by Dr. Molineux?

A. I can.

Q. And it is published in 2004?

A. It is.

Q. And do you see in the abstract in the second paragraph about two-thirds of the way through, it says, "Pegfilgrastim retains the same biological activity as filgrastim and binds to

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN (consolidated with 15-cv-62081-CIV-COHN)

AMGEN INC. and AMGEN MANUFACTURING LIMITED,

Plaintiffs,

vs.

APOTEX INC. and APOTEX CORP.,

Defendants.

[PROPOSED] ORDER ON DEFENDANTS APOTEX INC. AND APOTEX CORP.'S MOTION FOR JUDGMENT ON PARTIAL FINDINGS PURSUANT TO FED. R. CIV. P. 52(C)

THIS CAUSE has come before the Court upon Defendants Apotex Inc. and Apotex Corp.'s Motion for Judgment on Partial Findings pursuant to Fed. R. Civ. P. 52(c) ("Apotex's Rule 52(c) Motion"). Upon reviewing Apotex's Rule 52(c) Motion and being otherwise fully advised in the premises, it is

ORDERED and ADJUDGED that Apotex's Rule 52(c) Motion is hereby **GRANTED**.

DONE AND ORDERED at Chambers, Fort Lauderdale, Florida, this __ day of July, 2016.

_____
JAMES I. COHN
United States District Judge

Copies furnished to all counsel of record