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May 27, 2026

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RE: ***Shareholder Representative Services, LLC v. Alexion Pharmaceuticals, Inc.,***
C.A. No. 2020-1069-MTZ

Dear Counsel:

I write to resolve your clients' claims regarding problems with drug materials Alexion acquired when it acquired Syntimmune.[1] This letter is fairly characterized as inside baseball. After trial, and with assistance from a court-appointed expert, I

[1] Readers seeking more background, defined terms, and citation formats can refer to *S'holder Representative Servs. LLC v. Alexion Pharms., Inc.*, 2024 WL 4052343 (Del. Ch. Sept. 5, 2024) [hereinafter "*Alexion I*"]. This letter assumes familiarity with that opinion.

Citations in the form "Sharpnack Rep." refer to the Expert Report of Robert Sharpnack, available at D.I. 414. Citations in the form "DB Exp. __" refer to Defendant and Counterclaim Plaintiff Alexion Pharmaceuticals, Inc.'s Brief Regarding the Conclusions of the D.R.E. 706 Expert Robert Sharpnack, available at D.I. 425. Citations in the form "PB Exp. __" refer to Plaintiff and Counterclaim Defendant's Brief Regarding the Opinions and Testimony of Court-Appointed D.R.E. 706 Expert Robert Sharpnack, available at D.I. 426. Citations in the form "PB Exp. Ex. __" refer to the exhibits to the Transmittal Affidavit of Michael A. Barlow in Support of Plaintiff and Counterclaim Defendant's Brief Regarding the Opinions and Testimony of Court-Appointed D.R.E. 706 Expert Robert Sharpnack, available at D.I. 426. Citations in the form "Sharpnack Dep." refer to the Deposition of Bob Sharpnack available at D.I. 426 Ex. 1.

have concluded that Alexion proved by the preponderance of the evidence that Syntimmune breached its representation about the manufacture of those drug materials, and that Alexion is entitled to approximately $11 million in indemnification.

Before the Merger, Syntimmune was attempting to develop a monoclonal antibody into a clinical drug. That work requires drug substance, meaning the active ingredient intended to provide a therapeutic effect, and drug product, meaning the final product in dosage form as in a tablet, capsule, or solution.[2] Drug substance is a necessary component of drug product.

When Alexion bought Syntimmune, Alexion also bought Syntimmune's drug product and drug substance on hand and in its manufacturing pipeline.[3] Syntimmune

[2] 21 C.F.R. § 314.3(b). The FDA defines a "[d]rug product" as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients." *Id*. And it defines "[d]rug substance" as "an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body." *Id*; *see* 21 C.F.R. § 210.3(b)(4) (defining "[d]rug product as "a finished dosage form, for example, tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients. The term also includes a finished dosage form that does not contain an active ingredient but is intended to be used as a placebo.").

[3] *S'holder Representative Servs., LLC v. Alexion Pharms., Inc.*, 2025 WL 1089166, at *5 (Del. Ch. Apr. 11, 2025) [hereinafter "*Alexion II*"] ("Alexion bought all of Syntimmune's drug supply with the goal of rapid development through clinical trials. Alexion bought a promise that the supply would be compliant.").

represented in Section 4.13 of the Merger Agreement that its "Product Candidates" were and would continue to be manufactured "in compliance in all material respects" with applicable federal law and regulations relating to current good manufacturing practices ("cGMP").[4]

Alexion claims drug product lots AJ8794A, AK3858, AF6404A and AG3356A (each a "DP Lot," and together the "DP Lots"), and drug substance lots CMC-L-0125 and CMC-M-0009 (each a "DS Lot," and together the "DS Lots," and with the DP Lots the "Acquired Lots"), were not manufactured in compliance with cGMP.[5] At closing, Alexion knew DP Lot AJ8794A was contaminated with a particulate and could not be used.[6] Shortly after closing, Alexion learned DS Lots CMC-L-0125 and CMCM-0009 were under investigation due to ongoing issues.[7] Alexion also learned DP Lot AK3858, which was intended to resupply clinical trials,[8] was contaminated with protein particles. That spurred investigations by

[4] Merger Agr. § 4.13(a).

[5] *Alexion II*, 2025 WL 1089166, at *1, n.42.

[6] JX 722 at 3–4; JX 668 at 1–3, 5; JX 1191.

[7] JX 784 at 11; JX 2846 at 2 ("Batch was not released by time of acquisition due to open QC investigation for spiked DNA recovery failure . . . potential presence of polyallylamine in DS"); JX 804 at 4, 13; JX 668 at 3 (noting CMC-L-0125 and CMCM-0009 "pending final release").

[8] JX 804 at 13, 16; JX 843 at 3, 10; Ledwith Tr. 1030–31.

Alexion and its manufacturers.[9]

In early 2019, Alexion learned of adverse events and infusion-related reactions ("IRRs") in a clinical trial dosed with DP Lot AG7907A.[10] That trial was paused; then all of Alexion's clinical studies were paused pending an investigation into the manufacture of the Acquired Lots.[11] In March, Alexion's investigation revealed DP Lots AF6404 and AG7907 were unusable.[12] Alexion's investigation found the DS Lots slated for release, and the DS Lots that produced the drug product already in clinical use, were adulterated.[13] The study with the IRRs was terminated.[14]

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[9] JX 804 at 5; JX 817; JX 2846; JX 890; JX 1040; Ledwith Tr. 1030–31.

[10] JX 1164 at 3, 78–80 (describing the four reported IRRs from clinical trial subjects in study SYNT001-104); JX 923 at 64 (noting the IRRs reported in trials SYNT001-104, SYNT001-103, and SYNT001-102).

[11] JX 983 at 5–16 (noting trials SYNT001-104 and SYNT001-103 were already "closed out" and "GMT recommends to terminate Study 102 (WAIHA) as well"); JX 996 at 2; JX 1164 at 75.

[12] JX 911 at 2 (noting DP Lots AF6404 and AG7907 "will not be used anymore" given recent infusion related reactions); JX 959 at 1 (noting "all studies were paused in 15 Feb [20]19 . . . AF6404 & AG7907 will be reconciled from the clinic"); JX 945 ("Because of the high HCP (host cell protein) contamination of the one DP lot we thought could potentially be re-released for use in Cohort 2 WAIHA, we will not be able to proceed with dosing more patients in the Ph 1b/2a trial."); JX 996 at 1.

[13] Ledwith Tr. 1038–40; *see* JX 996 at 16 ("HCP testing has demonstrated that the Cygnus 2nd generation kit used for release is not sensitive enough to detect HCP levels present in OS product.").

[14] JX 945 at 1; JX 959 at 3; JX 1164 at 75 ("Due to the occurrence of the IRRs, this study was paused as a precautionary measure and a manufacturing investigation was initiated.

Alexion claims Syntimmune failed to manufacture the Acquired Lots in accordance with cGMP standards in breach of Section 4.13(a).[15] Alexion seeks indemnification under the Merger Agreement for the losses it incurred investigating, remediating, and remanufacturing the Acquired Lots.[16] SRS seeks a declaratory judgment that it is not liable for indemnification.[17]

Those claims went to trial. Alexion and SRS disagree on the applicable regulations or guidance, and on whether the Acquired Lots fell short. Their experts diverged along party lines. The Court appointed an independent expert to assist in bridging that divide.[18]

This letter first resolves some gating issues on the interpretation of Section 4.13(a) and the weight to give the court-appointed expert's opinion. Then it provides two capsule post-trial opinions explaining why the DP Lots and the DS Lots breached Section 4.13(a). Then it applies the Merger Agreement's indemnification

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The study was subsequently terminated. Although there was no conclusive clinical or safety link to the IRRs, the investigation identified higher levels of HCP and a leachate (polyallylamine) in the clinical study material.").

[15] Counterclaims ¶¶ 109–19; *see* JX 1202.

[16] JX 1202; Merger Agr. §§ 8.1(a), 8.3(d); *see* Counterclaims ¶¶ 37–38, 113–14; *see also* Alxn Op. Br. at 39–43; JX2502 [hereinafter "Marshall Rep."] at ¶¶ 125–33, App. B.

[17] D.I. 155 ¶¶ 279–83.

[18] D.I. 410 [hereinafter "Expert Order"] ¶¶ 1–2(a).

provisions, and concludes Alexion is entitled to indemnification for costs incurred replacing the Acquired Lots, but not for half the purchase price as Alexion contends.

A. Gating Issues

1. Section 4.13

Syntimmune promised in Section 4.13(a) that the Acquired Lots:

> are being, and at all times have been, developed, tested, labelled, manufactured, stored, imported, exported and distributed, as applicable, in compliance in all material respects with the FDCA and applicable implementing regulations issued by the FDA, the EMA and any other applicable Governmental Entities, including, as applicable, those requirements relating to the FDA's current good manufacturing practices, good laboratory practices, good clinical practices, investigational use, pre-market approval and applications to market a new pharmaceutical product, except as disclosed on Section 4.13(a) of the Disclosure Schedule.[19]

Section 4.13(a) mandates the Acquired Lots be manufactured "in compliance in all material respects" with "applicable" "requirements relating to" cGMP.[20] The Merger Agreement does not define "in all material respects" or identify the "applicable" "requirements."

The meaning of those terms is a question of law.[21] Neither party contends

[19] Merger Agreement § 4.13(a).

[20] *Id*.

[21] I therefore decline SRS's suggestion to hold an additional evidentiary hearing. PB Exp. 51–57; Sharpnack Dep. at 14 (testifying the phrase "in all material respects" is not an FDA term of art).

Section 4.13(a) is ambiguous. Delaware's well-established principles of contract interpretation govern.[22] "In construing a contract, our goal is to give effect to the intent of the parties."[23] "The court's task is to fulfill the parties' shared expectations at the time they contracted."[24] "Delaware adheres to the 'objective' theory of contracts, *i.e*. a contract's construction should be that which would be understood by an objective, reasonable third party."[25] "When interpreting a contract, the Court will give priority to the parties' intentions as reflected in the four corners of the agreement."[26] "Delaware courts read the agreement as a whole and enforce the plain meaning of clear and unambiguous language."[27] "If a contract is unambiguous, extrinsic evidence may not be used to interpret the intent of the parties, to vary the

[22] *Weinberg v. Waystar, Inc.*, 294 A.3d 1039, 1043 (Del. 2023).

[23] *Id.* at 1044 (citing *Salamone v. Gorman*, 106 A.3d 354, 368 (Del. 2014)).

[24] *Centene Corp. v. Accellion, Inc.*, 2022 WL 898206, at *5 (Del. Ch. Mar. 28, 2022) (quoting *Leaf Invenergy Co. v. Invenergy Renewables LLC*, 210 A.3d 688, 696 (Del. 2019) (internal quotation marks omitted)).

[25] *Osborn ex rel. Osborn v. Kemp*, 991 A.2d 1153, 1159 (Del. 2010) (quoting *NBC Universal v. Paxson Commc'ns*, 2005 WL 1038997, at *5 (Del. Ch. Apr. 29, 2005)).

[26] *GMG Cap. Invs., LLC v. Athenian Venture P'rs I, L.P.*, 36 A.3d 776, 779 (Del. 2012).

[27] *Manti Hldgs., LLC v. Authentix Acq. Co., Inc.*, 261 A.3d 1199, 1208 (Del. 2021).

terms of the contract or to create an ambiguity."[28]

a. "In All Material Respects"

The phrase "in all material respects" is familiar to the Court, particularly in the context of a merger agreement. In *Akorn, Inc. v. Fresenius Kabi AG*, the Court surveyed treatises and case law and determined "in all material respects" is a qualifier that seeks to "limit the operation of the [representation] to issues that are significant in the context of the parties' contract, even if the breaches are not severe enough to excuse a counterparty's performance under a common law analysis."[29] The Delaware Supreme Court embraced that approach, holding the phrase "in all material respects" in a merger agreement "seeks to exclude small, *de minimis*, and nitpicky issues that should not derail an acquisition."[30] The Court has consistently interpreted the qualifier "in all material respects" to be "less onerous"

[28] *Eagle Indus., Inc. v. DeVilbiss Health Care, Inc.*, 702 A.2d 1228, 1232 (Del. 1997).

[29] 2018 WL 4719347, at *86 nn.782–86 (Del. Ch. Oct. 1, 2018), *aff'd*, 198 A.3d 724 (Del. 2018) (TABLE).

[30] *AB Stable VIII LLC v. MAPS Hotels & Resorts One LLC*, 268 A.3d 198, 216 (Del. 2021) (citing *Akorn*, 2018 WL 4719347, at *86).

for the party asserting breach than the common law material breach standard.[31]

b. "Applicable . . . Requirements"

Section 4.13 represents "compliance in all material respects with the FDCA and applicable implementing regulations issued by the FDA . . . , including, as applicable, those requirements relating to the FDA's current good manufacturing practices."[32] Those requirements are rooted in the Federal Food, Drug, and Cosmetic Act of 1938 (the "FDCA"). The FDCA's guiding principle is to avoid adulteration of drugs and drug components by cGMP-compliant manufacturing.[33]

As empowered by the FDCA, the FDA promulgated regulations governing

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[31] *Dermatology Assocs. of San Antonio v. Oliver St. Dermatology Mgmt. LLC*, 2020 WL 4581674, at *26 (Del. Ch. Aug. 10, 2020) (explaining "in all material respects" excludes those "small, *de minimis*, and nitpicky issues that should not derail an acquisition"); *Snow Phipps Grp., LLC v. Kcake Acq., Inc.*, 2021 WL 1714202, at *38 (Del. Ch. Apr. 30, 2021) (same); *AB Stable VIII LLC v. Maps Hotels & Resorts One LLC*, 2020 WL 7024929, at *73 (Del. Ch. Nov. 30, 2020) (same), *aff'd*, 268 A.3d 198 (Del. 2021); *Channel Medsystems, Inc. v. Bos. Sci. Corp.*, 2019 WL 6896462, at *17 (Del. Ch. Dec. 18, 2019) (applying the *Akorn* standard); *In re Anthem-Cigna Merger Litig.*, 2020 WL 5106556, at *134 n.426 (Del. Ch. Aug. 31, 2020) (distinguishing "material breach" from "in all material respects"), *aff'd sub nom. Cigna Corp. v. Anthem, Inc.*, 251 A.3d 1015 (Del. 2021) (TABLE); *Williams Cos., Inc. v. Energy Transfer LP*, 2021 WL 6136723, at *25 (Del. Ch. Dec. 29, 2021), *aff'd sub nom. Energy Transfer, LP v. Williams Cos., Inc.*, 346 A.3d 1089 (Del. 2023).

[32] Merger Agreement § 4.13(a).

[33] 21 U.S.C. § 351(j); *id.* § 351(a)(2)(B) (providing a drug is adulterated if "the methods used in, or the facilities or controls used for, its manufacture . . . do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter").

drug products.[34] Those regulations, in C.F.R. Parts 210 and 211, have the force of law for drug product.[35]

Those regulations also guide drug substance manufacture.[36] The FDA announced, "[T]hese cGMP are not applied to the manufacture of bulk drug components," but noted "there are numerous instances where good manufacturing practices for [drug substances] would parallel the requirements set forth in Part 211."[37] The FDA stated it "will utilize the standards of Part 211 as guidelines during

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[34] 21 U.S.C. § 371(a); *see* 21 C.F.R. § 10.40.

[35] Current Good Manufacturing Practice in Manufacture, Processing, Packing or Holding, 43 Fed. Reg. 45076 (Sept. 29, 1978); 21 C.F.R. § 210.1(a) ("The regulations set forth in this part and in parts 211, 213, 225, and 226 of this chapter contain the minimum current good manufacturing practice for . . . the manufacture, processing, packing, or holding of a drug to assure that such drug meets the requirements of the act as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess."); i*d*. § 210.1(b) ("The failure to comply with any regulation set forth in this part and in parts 211, 213, 225, and 226 of this chapter . . . shall render such drug to be adulterated under section 501(a)(2)(B) of the act and such drug, as well as the person who is responsible for the failure to comply, shall be subject to regulatory action."); *id*. §§ 211.1 *et seq*.

[36] 43 Fed. Reg. at 45026; *see* U.S. Food & Drug Admin., *Compliance Program: Chapter 56 – Drug Quality Assurance Active Pharmaceutical Ingredient Process Inspection,* at 4 (Aug. 1, 2025) [hereinafter "FDA Ch. 56"]; *see also Wright-Gottshall v. New Jersey*, 2024 WL 1826421, at *1 n.2 (3d Cir. Apr. 26, 2024) (noting it is appropriate to "take judicial notice of information that is publicly available on government websites" (internal quotation mark and citation omitted)), *cert. denied*, 145 S. Ct. 438, 220 L. Ed. 2d 187 (2024).

[37] 43 Fed. Reg. 45026; *accord*, Dennis Tosh, FDA Enforcement Manual § 1631 Scope and Application of cGMP Requirements (Jan. 2023) [hereinafter "FDA Enforcement Manual §1631"]; *see* FDA Ch. 56 at 4 ("No distinction is made between an API and a drug product in the FD&C Act, and if either fail to comply with CGMP requirements, they will be in violation of the FD&C Act.").

inspections of manufacturers of bulk drug components . . . ."[38] To determine whether drug substances are adulterated, "the FDA makes an assessment of what manufacturing practices are 'current' and 'good' for these ingredients."[39]

For drug substance, the FDA issues interpretive guidance documents, which are not legally binding.[40] The FDA's guidance documents "describe the agency's interpretation of or policy on a regulatory issue."[41] One may "use an approach other than the one set forth in a guidance document," but a different approach must still

[38] 43 Fed. Reg. 45014, 45026; *id*. at 45027 ("[T]he cGMP regulations set forth in part 211 apply only to establishments engaged in the preparation of a drug product.").

[39] FDA Enforcement Manual § 1631.

[40] 21 C.F.R. § 10.115(b)(1); *id*. § 10.115(d)(1) ("Guidance documents do not establish legally enforceable rights or responsibilities. They do not legally bind the public or FDA."); *see* 21 U.S.C. § 371(h)(1)(A) ("The Secretary shall develop guidance documents with public participation and ensure that information identifying the existence of such documents and the documents themselves are made available to the public both in written form and, as feasible, through electronic means. Such documents shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the Food and Drug Administration."); *id*. § 371(h)(1)(C)(i); *see also* 43 Fed. Reg. 45027.

The FDA recently explained that recommendations for regulatory action on drug substance should use the guidance as a guideline, then explain how the deficiencies affect the drug substance quality and cite the underlying FDCA statute—not guidance or regulations. FDA Ch. 56 at 33.

[41] 21 C.F.R. § 10.115(b)(1).

"comply with the relevant statutes and regulations."[42]

The parties dispute what regulations are applicable to the DP Lots, and what guidance is applicable to the DS Lots. I will resolve those disputes in the context of the appropriate lots. They present legal issues on which expert opinions are not helpful or appropriate.[43]

2. Sharpnack's Report

After hearing divergent trial testimony from the parties' technical experts, the Court selected Robert Sharpnack to serve as a court-appointed expert under Delaware Rule of Evidence 706 to assist in resolving the cGMP claims.[44] The Court directed Sharpnack to submit a report addressing the following:

> Whether the Syntimmune drug product lots and drug substance lots Alexion has identified were manufactured in compliance in all material respects with the FDCA and applicable implementing regulations issued by the FDA, the EMA and any other applicable Governmental Entities, including, as applicable, those requirements relating to the

[42] *Id*. §§ 10.115(d)(1)–(3).

[43] *Itek Corp. v. Chicago Aerial Indus., Inc*., 274 A.2d 141, 143 (Del. 1971) ("[I]t is exclusively within the province of the trial judge to determine issues of domestic law."); *United Rentals, Inc. v. RAM Hldgs., Inc.*, 2007 WL 4465520, *1 (Del. Ch. Dec. 13, 2007) ("It is within the exclusive province of this Court to determine such issues of domestic law. I, in interpreting the disputed contractual provisions at issue in this case, need not-indeed, *may not*-look beyond the well-established precedent of the Delaware courts.").

[44] Expert Order ¶¶ 1–2. This letter assumes familiarity with the surprisingly extensive procedural history of his appointment. D.I. 381; D.I. 389; D.I. 390; D.I. 394; *S'holder Representative Servs., LLC v. Alexion Pharms., Inc.*, 2025 WL 289505 (Del. Ch. Jan. 24, 2025); *Alexion II*, 2025 WL 1089166, at *5; D.I. 402.

FDA's current good manufacturing practices.[45]

On June 30, 2025, Sharpnack's report (the "Report") was provided to the parties and the Court.[46] The Report opines on the cGMP requirements applicable to the DS and DP Lots, and applies the cGMP requirements to the facts.[47] It concludes Syntimmune's DS and DP manufacturers made "several unapproved changes to the manufacturing process" in contravention of cGMP standards requiring change control and oversight.[48]

The parties deposed Sharpnack and briefed the Report's conclusions.[49] SRS argued it is unreliable and should be excluded.[50] SRS contends Sharpnack lacks expertise with monoclonal antibody products; is unaware of the applicable regulatory framework; employed a flawed methodology; walked back certain conclusions at his deposition; and failed to provide an explanation of materiality in

[45] Expert Order ¶ 2(a).

[46] D.I. 414.

[47] *See generally* Sharpnack Rep.

[48] *Id*. ¶¶ 60–72, 74–79, 82.

[49] Sharpnack Dep.; PB Exp.; DB Exp.; D.I. 427; D.I. 430; D.I. 433; D.I. 455; *see* Charles A. Wright & Arthur R. Miller, *Federal Practice & Procedure* § 6305 (2d ed.) [hereinafter "Wright & Miller"] (noting formal depositions of court-appointed experts are relatively infrequent).

[50] PB Exp. 11–16.

the context of cGMP noncompliance.[51]

Rule 706 permits the Court to appoint an expert of its choosing, so long as that expert is qualified under Rule 702.[52] Under Rule 702, an expert's specialized knowledge must be helpful to the trier of fact; the testimony must be based on sufficient facts or data; the testimony must be the product of reliable principles and methods; and the expert must have reliably applied those principles and methods to the facts of the case.[53] When an expert's "factual basis, data, principles, methods, or their application" are challenged, Rule 702 requires the court to decide if the expert's testimony "has a reliable basis in the knowledge and experience of [the relevant] discipline."[54] "[A]lthough it is critical in a jury trial for a court to exercise its gatekeeper function in advance of allowing an expert to testify, the importance of addressing issues raised under *Daubert* and Rule 702 before an expert testifies is

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[51] *See id*. at 10–50.

[52] D.R.E. 706(a); *see* Wright & Miller § 6304.

[53] D.R.E. 702.

[54] *M.G. Bancorporation, Inc. v. Le Beau*, 737 A.2d 513, 523 (Del. 1999) (*quoting Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 149 (1999)); *see Goodridge v. Hyster Co.*, 845 A.2d 498, 503 (Del. 2004) ("A witness may testify as an expert when qualified as an expert and the trial judge determines that the witness has scientific, technical or other specialized knowledge that will assist the finder of fact in understanding evidence or in determining a fact at issue."); *Cede & Co. v. Technicolor, Inc.*, 758 A.2d 485, 498 (Del. 2000) ("Delaware Rules of Evidence 702 and 703 requires a trial judge to act as a 'gatekeeper' and to screen scientific, technical or specialized opinion evidence in order to exclude from consideration such evidence as it finds to be unreliable as a matter of law.").

more attenuated in a bench trial."[55] In a bench trial, the issue is more of weight than admissibility.[56]

Sharpnack has fifty-three years of helpful cGMP compliance experience.[57] He worked at the FDA from 1972 to 2004, including 18 years as a member of FDA's Foreign Inspection Cadre, inspecting APIs at manufacturing sites outside the United States.[58] He also served as an FDA Drug Expert, one of five FDA employees tasked with training FDA investigators on pharmaceutical inspection requirements and standards.[59] Since departing the FDA, Sharpnack spent 22 years as a cGMP

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[55] *Beard Rsch., Inc. v. Kates*, 2009 WL 7409282, at *6 (Del. Ch. Mar. 31, 2009); *accord, Alcoa, Inc. v. Alcan Rolled Prod. Ravenswood LLC*, 2020 WL 433856, at *3 (D. Del. Jan. 28, 2020) ("The main purpose of *Daubert* exclusion is to protect juries from being swayed by dubious scientific testimony. . . . [t]hat interest is not implicated where the judge is the decision maker. The [] court's 'gatekeeping function' under *Daubert* ensures that expert evidence 'submitted to the jury' is sufficiently relevant and reliable, but '[t]here is less need for the gatekeeper to keep the gate when the gatekeeper is keeping the gate only for himself.'" (quoting *United States v. Brown*, 415 F.3d 1257, 1269 (11th Cir. 2005))).

[56] *BCD Assocs., LLC v. Crown Bank*, 2022 WL 1316234, at *5 (Del. Super. Ct. May 2, 2022) ("Expert testimony should receive whatever weight and credit the Court thinks appropriate, given all the other evidence in the case."), *aff'd,* 292 A.3d 759 (Del. 2023); *Strategic Inv. Opps. LLC v. Lee Enters., Inc.*, 2022 WL 453607, at *12 n.131 (Del. Ch. Feb. 14, 2022) (declining to exclude report under Rule 702 but instead giving "the [expert] report the weight deemed appropriate").

[57] Sharpnack Rep. ¶¶ 10–32.

[58] *Id*. ¶¶ 10–13.

[59] *Id*. ¶¶ 19–20. Sharpnack was also one of five FDA reviewers deployed to represent the FDA on the newly formed International Society of Pharmaceutical Engineers Baseline Guide on Commissioning and Qualification. *Id*. ¶ 21. Sharpnack's excellence has been recognized. In 1998, he received the "International Hammer Award" from then-Vice

consultant, drafting process validation protocols and presenting remediation plans to the FDA.[60]

Sharpnack's experience in cGMP-compliant manufacturing is helpful even without significant experience with monoclonal antibodies.[61] I need assistance in identifying manufacturing problems in deviation from federal regulations and guidance; I do not see that the problems here are specific to monoclonal antibodies. SRS also claims Sharpnack lacks familiarity with the applicable regulatory framework.[62] But that is a legal issue on which I did not consider Sharpnack's

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President Al Gore and then-Prime Minister Tony Blair for his efforts combatting international API counterfeiting. *Id*. ¶ 30.

[60] *Id*. ¶¶ 23–27.

[61] Sharpnack Dep. at 82–83; *see Withrow v. Spears*, 967 F. Supp. 2d 982, 992 (D. Del. 2013) ("The basis of this specialized knowledge may be 'practical experience as well as academic training and credentials.' At a minimum, however, 'a proffered expert witness must . . . possess skill or knowledge greater than the average layman.'" (quoting *Elcock v. Kmart Corp.*, 233 F.3d 734, 741 (3d Cir. 2000))).

[62] PB Exp. 41–42 (citing Sharpnack Dep. at 94). SRS contends when "presented with an FDA document establishing the Phase I clinical trial exemption to 21 C.F.R. Part 211, Sharpnack admitted he 'never saw [the 2008] amendment to Part 211 and acknowledged that awareness of this exemption 'could' 'change some of [his] opinions in this case.'" *Id*. 41 (quoting Sharpnack Dep. at 94). But Sharpnack was shown a book excerpt authored by a consulting firm, not "an FDA document." Sharpnack Dep. at 93. The excerpt provided: "For approved products, the requirements for in-process and final release testing are further defined in 21 CFR 210 and 21 CFR 211. Recently, FDA acknowledged that during the development of a new drug, full compliance with the regulations in 21 CFR 210 and 21 CFR 211 is not required until late in the development process and, in July, 2008, issued an amendment to 21 CFR 210 specifying that 21 CFR 211 no longer applies to Phase 1 investigational drugs." PB Exp. Ex. 21 (BioProcess Tech. Consultants, Inc., *The Development of Therapeutic Monoclonal Antibody Products: A Comprehensive Guide to*

opinion.[63]

SRS also argues Sharpnack's methodology is flawed. "The *foci* of a *Daubert* analysis are the 'principles and methodology' used in formulating an expert's testimony, not on the expert's resultant conclusions."[64] The Court must determine whether the "expert's opinion [is] based upon proper factual foundation and sound methodology."[65] The "proper factual foundation" criterion requires the expert's opinion to be based on "facts" and not "suppositions."[66]

SRS claims Sharpnack uncritically adopted certain conclusions reached by

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CMC/Activities from Clone to Clinic, 64 (Howard L. Levine & Gunter Jagschies) (2017)). The excerpt differs from 21 C.F.R. § 210.2(c) in that it appears to provide a blanket exemption from the requirements imposed by Part 211, while the codified amendment provides that "this exemption does not apply to an investigational drug for use in a phase 1 study once the investigational drug has been made available for use by or for the sponsor in a phase 2 or phase 3 study . . . ." 21 C.F.R. § 210.2(c).

More importantly, Sharpnack demonstrated his familiarity with Part 211's regulatory scheme. Sharpnack Dep. at 45, 57–58, 90–91 (demonstrating his knowledge of Part 211 exemptions). He explained that because the DP Lots were intended for Phase 2, Patheon was subject to Part 211. Sharpnack Dep. at 18–20, 24, 28–32.

[63] *See infra*, Sections B2 and C2.

[64] *Bowen v. E.I. DuPont de Nemours & Co.*, 906 A.2d 787, 794 (Del. 2006) (quoting *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 595 (1993)); *see Tumlinson v. Advanced Micro Devices, Inc.*, 81 A.3d 1264, 1269 (Del. 2013).

[65] *Perry v. Berkley*, 996 A.2d 1262, 1267 (Del. 2010).

[66] *Id.* at 1269 (quoting 4 *Weinstein's Federal Evidence* § 792.95[2][b] (2d ed. 2009)).

Alexion's expert Paul Marshall without examining the underlying records.[67] Specifically, SRS emphasizes Sharpnack concluded a Syntimmune manufacturer failed a system suitability test by wholly relying on Marshall, without independently assessing any of the underlying data.[68] But Sharpnack could not independently verify the suitability test results because that manufacturer failed to perform one.[69]

Finally, SRS attacks Sharpnack's methodology on the basis he failed to consider certain key documents.[70] An assessment of whether the expert's opinion is based upon information reasonably relied upon by experts in the field "does not

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[67] PB Exp. 28–40; *see* Sharpnack Rep. ¶ 76 ("Mr. Marshall notes that the HCP assay used by AGC failed its SST and under-reported actual HCP contamination by 3-8-fold, which would render the product far out of specification for human use. . . . Although I did not receive the laboratory records to verify where the SST failed, if Mr. Marshall's statements are accurate, no reliance should have been placed on the HCP Assay results.").

[68] PB Exp. 3, 28–30, 32–36.

[69] JX 1025 at 3; Marshall Tr. 1893–96 (addressing JX 1025 and explaining why the record demonstrates a suitability test was never performed). In May 2019, Syntimmune's co-founder Laurence Blumberg asked Syntimmune's cGMP consultant, Susan Dana Jones, for the suitability test results, and she responded, "AGC had proposed quite early in the program that we do the assessment of how much coverage the generic kit provided for our process but we chose to not make that investment early on." JX 1025 at 3. Blumberg asked Jones her thoughts on the threshold, and Jones answered, "Endotoxin and DNA are fine . . . HCP is the question mark because of course you can become immune to one of the HCP and that increases over time. That's why FDA and others are so concerned about characterizing all HCP and detecting it." *Id*. at 2. Blumberg responded, "we need to speak . . ." and followed up with "I don't want to put this in writing." *Id*. at 1. On cross, Marshall was not challenged on his conclusions based on JX 1025. Marshall Tr. 1905–26; *see also* Dep. Dana-Jones, Susan at 238–43.

[70] PB Exp. 30–32 (citing JX 2625, JX 284, JX 979; PB Exp. Ex. 18).

pertain to information which the expert has not relied on."[71] And Sharpnack's opinion was reliably informed by adequate knowledge of the relevant manufacturer's process.[72] He opined that once the manufacturer learned of a particular protein-loading inconsistency, it should have investigated the issue because "variation[s] . . . in the loading ranges would raise a flag" that should be addressed.[73]

In my view, nothing about Sharpnack's experience or methodology detracts from the weight his Report deserves. There is certainly no reason to exclude it. From there, SRS simply disagrees with how Sharpnack applied his knowledge of

[71] *Norman v. All About Women, P.A.*, 193 A.3d 726, 731 (Del. 2018).

[72] *E.g.*, Sharpnack Rep. ¶¶ 80–84 (describing Patheon's manufacture process and concluding "Patheon failed to properly evaluate the differences between Suite #1 and Suite #2 and the impact the manufacturing differences may have had on product quality, in violation of cGMP requirements, per 21 CFR §§ 211.100 and 211.63."); Sharpnack Dep. at 52 (explaining AGC's use of the Cygnus 2 Kit violated cGMP requirements because "for all chromatographic assays you do a system suitability first. . . . It didn't pass yet they continued to use the instrument to analyze the product.").

[73] Sharpnack Dep. at 124–31 ("Q. What was the basis of your statement that AGC did not have adequate control over protein loading? A. Because it wasn't addressed."). SRS claims "Sharpnack was compelled to adopt Boyle's conclusions" regarding AGC's protein loading ranges. PB Exp. 36. Not so. When confronted with the data from Boyle's report and asked if he agreed with it, Sharpnack explained, "I don't know if I can make that statement" and added he was "looking for ranges during the manufacturing process" and that the data he received did not resolve his questions. Sharpnack Dep. at 136–38.

cGMP compliance to these facts.

B. The DS Lots

1. Background

AGC Biologics ("AGC") manufactured the DS Lots for Syntimmune's Phase I and Phase II clinical trials.[74] In the governing Development and Manufacturing Services Agreement, AGC agreed that where the "Stage of the Services defines the performance of that Stage to be in accordance with cGMP standards, then [AGC] shall comply with the applicable cGMP criteria" and represented each cGMP Batch would meet the cGMP standards required by the work order.[75]

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[74] JX 202 at 4 ("The objective of [Project Change Order No. 48] is to add additional work to manufacture and release [] one 2000L batch for Phase I/II in March/April 2018."); JX 203 at 1 ("The objective [of Project Change Order No. 49] is to add additional work to manufacture and release one 2000L batches for phase I/II in Q4 2018."); JX 97 at 2 (noting Project Change Order No. 53 subject to cGMP manufacturing standards); JX 172 at 1, 6.

[75] JX 95 at 13 ("Where applicable [AGC] will comply with the requirements stipulated in the International Conference on Harmonisation guidelines on quality."); *see* JX 111 at 4 ("[AGC] is responsible for ensuring that the quality requirements for DS . . . is developed, manufactured, stored, and released in accordance with current Good Manufacturing Practice (cGMP) and quality requirements as defined in applicable EU, US and international guidance's and regulations, referenced in Section 6."). Section 6 of the Quality Agreement then defined the "[a]pplicable US Guidance's and Regulations include . . . CFR parts 210, 211, 312 Subpart D, 600, 601 [and] US FDA Guidance for Industry: cGMP for Phase 1 Investigational Drugs." *Id*. at 15. The cGMP work orders differed from prior work orders where certain engineering or pilot batches would be manufactured "under non-GMP conditions . . . to identify issues with the process, product, and/or batch records prior to executing a GMP run." JX 101 (ordering a "100L Pilot Batch" and providing the object of the amendment "is to generate non-GMP pilot materials"); *but see* JX 172 at 6 (noting "[t]he objective of [Stages 46 and 47] is to execute one manufacturing run under

AGC's DS Lots had too much host cell protein ("HCP") and DNA in them.[76] DS Lots CMC-L-0125 and CMC-M-0009 were contaminated to the point of being unusable.[77]

AGC concluded "with a high degree of likelihood" the contamination was caused by changing the filter and not washing the new filter according to the vendor's instructions.[78] AGC used two smaller Sartobind Filters in manufacturing previous lots, but changed to one STIC Jumbo Filter for the DS Lots.[79] AGC failed to adjust its filtration settings when it introduced the STIC Jumbo Filter, prolonging the DS Lots' exposure to the filter membrane, which caused a particular compound that inhibits DNA recovery to leach into the DS Lots.[80] AGC did not wash the STIC Jumbo filter membrane according to the vendor's instructions, which increased the

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cGMP conditions. . . . Bulk Substance generated by the process will be used to support Phase II clinical trials.").

[76] JX 1044 at 13; JX 866 at 2–3.

[77] JX 933 at 3, 9, 14, 16, 19; JX 1044 at 1.

[78] JX 1044 at 13.

[79] *Id*. at 5 ("For batch CMC-L-0125, CMC-M-0009 and CMC-M-0010, the STIC filter used were the Jumbo version with a membrane volume of 2.5 L and an area of 9.1m², compared to previous batches using 2 parallel filters with a total membrane volume of 1.1L and an area of 4m²."); Marshall Tr. 1855–56.

[80] JX 866 at 2–3 ("It was found that when the filter was introduced . . . the required CIP volume, flow rate and time . . . was not transferred from the Development to Master Production Instructions. The mode of operation was copied from then on to other Master Production Instructions and Master Production Records.").

leaching of that compound.[81] And when AGC introduced the Jumbo STIC Filter, it "effectively did a cut and paste on the operating conditions" using flow and wash setting for the original filter.[82] When AGC "shift[ed] from 2x STIC 2m² to a 9.1 L Jumbo filter for batch CMC-L-0125, the flow rate was not adjusted to retain the same flux during filtration."[83] AGC's Master Production Instructions ("MPI") and Master Production Records ("MPR") ignored the difference between the two smaller filters and one STIC Jumbo Filter.[84] The failure to adjust the flow and wash settings doubled the filtration time, prolonging the DS Lots' exposure, which caused more

[81] JX 1044 at 4, 5, 9, 12, 13 ("A contributing root cause was that the membranes were not washed in accordance with the vendor recommendation (100 MV) after the CIP."); JX 270 at 16 ("[T]he fact that all batches up to and including CMC-M-0010 were operated without adequate flushing of the STIC membrane per vendor instructions and specifically batch CMC-K-0068 also having a loss of control in the use of a larger STIC membrane area during production makes all batches manufactured in this manner suspect."); JX 866 at 2–3.

[82] Marshall Tr. 1871; *see* JX 866 at 2–3; JX 1044 at 4, 5, 9, 12, 13.

[83] JX 1040 at 5.

[84] *Compare* JX 283 at 15 (noting MPR Revision 2 was effective April 30, 2018, when the DS Lots were manufactured) *with* JX 2629 at 19 (providing the MPR was not revised to update the filter and wash setting until Revision 4, which became effective on May 15, 2019). The DS Lots were manufactured in April 2018. JX 277. MPR Revision 2 was operative when AGC manufactured the DS Lots. JX 283 at 15. Following the investigations into AGC's manufacturing processing the MPR was updated to mandate the STIC Jumbo Filter's use would be in accordance with their instructions. JX 866 at 3 ("8571 Downstream processing CMC16087 was updated to revision 03 27NOV2018 to ensure STIC Membranes were used as required.").

leaching into the DS Lots.[85] AGC acknowledged this error and updated its MPI and MPR.[86]

Alexion found another problem at AGC. AGC's protein loading range varied greatly from 123 g/m² up to 1110 g/m².[87] The inconsistent protein loading ranges contributed to excessive levels of foreign HCP.[88]

AGC measured HCP with an assay called the "Cygnus 2 Kit."[89] AGC neglected to evaluate the Cygnus 2 Kit's potential impact on drug substance purity.[90] The Cygnus 2 Kit instructions require that its suitability "must be determined and qualified experimentally by each laboratory" prior to use.[91] But AGC failed to properly qualify the Cygnus 2 Kit, as the testing it performed failed to confirm the

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[85] JX 1044 at 4, 5, 9, 12, 13; JX 866 at 2–3 (describing the "root cause" of the leaching into the DS Lots as the failure to update the MPR and the MPI to account for the attributes of the STIC Jumbo Filter); *see* Gupta Tr. 2039 ("[The] Jumbo STIC Filter, as you've already heard has not been washed appropriately and AGC admitted that."); Sharpnack Rep. ¶ 71.

[86] JX 958 at 1–5.

[87] JX 949 at 1–2, Table A1 ("Avg STIC AEX loading").

[88] JX 270 at 10 ("Analysis of DP AF6404A (and parent DS lot CMC-K-0002) contained an average of 835 ng/mg HCP, which is > 8x above specification limit (per CMC00747) as <100 ng/mg protein.").

[89] *Id*. at 16 ("HCP testing has demonstrated that the Cygnus 2nd generation kit used for release is not sensitive enough to detect HCP levels present in DS product."); *see* JX 211 (providing vendor's instructions on determining the suitability of the Cygnus 2 Kit).

[90] JX 270; Marshall Tr. 1888–92; JX 2240 at 3, 78–80.

[91] JX 211 at 2.

Cygnus 2 Kit's HCP coverage capacity.[92] AGC used the Cygnus 2 Kit anyway, and that kit failed to detect the excessive HCP in the DS Lots.[93]

Alexion launched its own investigation into AGC's manufacturing process after the reported IRRs.[94] Alexion's investigation revealed the Cygnus 2 Kit was "not sensitive enough to detect HCP levels present in the DS [Lots]."[95] Alexion "recognized that the [Cygnus 2] kit may underrepresent CHO HCP by potentially an order of magnitude compared to the 3rd generation kit and the true magnitude of the difference can only be determined experimentally."[96] Alexion determined the Cygnus 3rd generation kits would be utilized going forward "to evaluate HCP levels

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[92] JX 2240 at 77–78 ("Capacity for clearance of HCP cannot be documented as the load is below LOQ."); JX 128 at 15–16 (noting certain samples were reported as < LOQ); JX 2602 at 17 ("Dilutional linearity was not assessed as buffer spiked samples were below LOQ."). SRS's expert Boyle asserted AGC qualified Cygnus 2 Kit's HCP coverage by "perform[ing] a spike recovery study and determine[ing] the dilutional linearity." Boyle Tr. 1997. But, on cross-examination Boyle was forced to concede the dilutional linearity figure does nothing to determine the HCP coverage of the Cygnus 2 Kit. *Id*. 2017–18; *see* JX 2577 at 6 ("[S]imply determining the appropriate dilution factor does nothing to verify an HCP assay or its suitability for use with a particular sample. Nearly every analytical assay, including HCP assays, require appropriate dilution, and determining that dilution factor does not verify an assay's specificity, accuracy, or precision, which should have been done by AGC.").

[93] JX 270 at 16; *see* JX 2240 at 78.

[94] JX 270; Ledwith Tr. 1030–40.

[95] JX 270 at 16.

[96] *Id*. at 6.

for all upcoming DS batches."[97]

2. The Applicable Regulations

The DS Lots' compliance with the FDCA's cGMP mandate are informed by particular nonbinding FDA guidance documents, including "ICH Q7," "ICH Q7 Q&A," and "ICH Q8."[98] The FDA published the relevant ICH Q7 guidance in

[97] *Id*. at 13.

[98] The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use ("ICH") is an international nonprofit association that brings together regulatory authorities, including the FDA, and industry to harmonize scientific and technical aspects of drug registration. *International Regulatory Harmonization*, https://www.fda.gov/drugs/cder-international-program/international-regulatory-harmonization (last visited May 24, 2026) (noting the FDA "has participated in ICH as a Founding Member since 1990 and implements all ICH Guidelines as FDA Guidance); *see* JX 2541 [hereinafter "Elder Rep."] ¶ 33; Sharpnack Rep. ¶ 49. The FDA has adopted and published several official guidances from that organization: *ICH: Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients Guidance for Industry* ("ICH Q7"); *Guidance for Industry: cGMP for Phase 1 Investigational Drugs* ("Phase 1 Guidance"); *Guidance for Industry: Q8* ("ICH Q8"); and *Guidance for Industry: Validation of Analytical Procedures* ("ICH Q2"). In April 2018, the FDA published an official companion guidance to ICH Q7 titled *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, Questions and Answers, Guidance for Industry* ("ICH Q7 Q&A"). Elder Rep. ¶ 34; *see e.g.*, Sharpnack Rep. ¶¶ 44, 68; JX 2497 [hereinafter "Gupta Rep."] ¶¶ 67–68; JX 2539 [hereinafter "Gupta RR."] ¶ 20; Marshall Rep. ¶81 n.73; JX 2538 [hereinafter "Boyle Rep."] ¶ 23.

The experts were unanimous that ICH Q7 informs the cGMP requirements applicable to evaluating AGC's compliance. S*ee* Elder Rep. ¶¶ 27, 33–42, 48; JX 2544 [hereinafter "Marshall RR."] ¶ 7; Sharpnack Rep. ¶¶ 38, 40, 44, 49; Gupta Rep. ¶¶ 36, 41, 51; *see* FDA Ch. 56 at 5 ("ICH Q7 represents FDA's current thinking on CGMP for APIs. Thus, API and related manufacturing and testing facilities that follow this guidance will generally be considered in compliance with the statutory CGMP requirement. However, alternative approaches may be used if such approaches satisfy the requirements of section

2016.[99] ICH Q7 provides GMP guidance for APIs used in clinical trials.[100] The FDA's intention behind ICH Q7 is "to help ensure that all APIs meet the standards for quality and purity they purport or are represented to possess."[101]

The parties dispute which sections of ICH Q7 inform the DS Lots. Alexion asserts ICH Q7 is applicable in its entirety.[102] Alexion contends AGC's manufacturing process of the DS Lots failed to satisfy the cGMP standards in Sections 5, 8, 12, 13, and 19.[103] SRS claims the DS Lots were a "new" API used in a clinical trial governed exclusively by ICH Q7 Section 19,[104] and that Section 19's

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501(a)(2)(B) of the FD&C Act and ensure that the API meets its purported purity, identity, and quality characteristics.").

[99] *See generally* ICH Q7; *id*. § 1.1 ("This guidance revises and replaces the guidance Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients. This revision changes the ICH codification from Q7A to Q7.").

[100] *Id*. §§ 1.1–1.3.

[101] Guidance on Good Manufacturing Practice for Active Pharmaceutical Ingredients, 66 Fed. Reg. 49028 (September 25, 2001).

[102] ALXN Op. Br. 21–22, 29, 30–31, 34; DB Exp. 10, 11, 15–16 (identifying ICH Q7 Section 5, 13, and 19 as providing the cGMP standards governing the DS Lots).

Alexion also claims "[t]o the extent SRS argues that only §19 of ICH Q7 is applicable here, each of these batches failed to comply with numerous provisions of § 19." ALXN Op. Br. at 29 n.111.

[103] DB Exp. 10, 15; ALXN Op. Br. 29–31 (asserting AGC's manufacturing process violated ICH Q7 Sections 5.10, 5.11, 5.12, 5.22, 13.10, 13.13, 13.15, 19.11, and 19.30).

[104] SRS Ans. Br. 59; ICH Q7 § 19.10 ("Not all the controls in the previous sections of this guidance are appropriate for the manufacture of a new API for investigational use during its development. Section XIX (19) provides specific guidance unique to these circumstances.").

specific guidance supplants every other section of ICH Q7.[105] SRS argues Section 19.10, which provides that "[n]ot all the controls in the previous sections of this guidance are appropriate for the manufacture of a new API for investigational use during its development,"[106] exempts the manufacture of APIs intended for use in clinical trials from the other ICH Q7 "controls."[107] And SRS asserts Section 19.7 "is specific to changes for clinical trial material" and supplants the more general oversight described in Section 13.10.[108] SRS contends AGC complied with Section 19.7 because AGC "adequately recorded" its use of the STIC Jumbo Filter.[109]

In the first instance, SRS does not gain much from limiting ICH Q7 to Section 19. Section 19.11 provides "manufacturers should ensure that APIs are manufactured in suitable facilities using appropriate production and control

[105] SRS Op. Br. 88; PB Exp. 20–21, 25; Gupta Tr. 2040–42; Gupta RR. ¶¶ 66-67.

[106] ICH Q7 § 19.10.

[107] SRS Op. Br. 88–89 (citing Gupta Tr. 204–44); SRS Ans. Br 58–67; PB Exp. 21; *see* Gupta Tr. 2040–45; Gupta RR. ¶¶ 66-67.

[108] PB Exp. 25–27; SRS Ans. Br. 58–62; Gupta Tr. 2042–43; *compare* ICH Q7 § 13.10 ("A formal change control system should be established to evaluate all changes that could affect the production and control of the intermediate or API."); *with id.* § 19.70 ("Changes are expected during development, as knowledge is gained and the production is scaled up. Every change in the production, specifications, or test procedures should be adequately recorded."); see also *id.* § 19.11.

[109] PB Exp. 25–27; SRS Ans. Br. 58, 61.

procedures to ensure the quality of the API."[110] FDA guidance documents, including ICH Q7, provide that "the term *should* identifies recommendations that, when followed, will ensure compliance with CGMPs."[111] The FDA recognizes alternative approaches may be implemented only "if such approach satisfies the requirements of the applicable statutes."[112] In addition, Section 19.30 requires manufacturers to "ensure that equipment is calibrated, clean, and suitable for its intended use."[113]

And SRS's attempt to evade the entirety of ICH Q7 fails on the merits. SRS relies on the opinion of its expert, Patricia Gupta, that Section 19 governs APIs used in clinical trials while the remaining sections "are commercial manufacturing requirements for validated processes, which apply to Phase 3 and FDA-approved products."[114] Gupta contends "developmental batches and batches to be used in

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[110] ICH Q7 § 19.11.

[111] *Id*. § 1.1 (emphasis added); *see* FDA Ch. 56 ("ICH Q7 represents FDA's current thinking on CGMP for APIs. . . . manufacturing and testing facilities that follow this guidance will generally be considered in compliance with the statutory CGMP requirement. However, alternative approaches may be used if such approaches satisfy the requirements of section 501(a)(2)(B) of the FD&C Act and ensure that the API meets its purported purity, identity, and quality characteristics.").

[112] ICH Q7 § 1.1; 21 C.F.R. § 10.115(d)(2).

[113] ICH Q7 § 19.30.

[114] SRS Ans. Br. 59; PB Exp. 21, 25 (citing Gupta Rep. ¶¶ 58–60, 65–68). SRS contends "ICH Q7 §§ 5.10, 5.11, 5.12, 5.22, 13.10, 13.13, and 13.15 are commercial manufacturing requirements for validated processes, which apply to Phase 3 and FDA-approved products." SRS Ans. Br 59 (citing ICH § 19.10; Gupta RR. ¶¶ 15–17, 24–26, 37–38; Gupta Tr. 2040–41).

clinical trials" are exempt from ICH "Q7's general requirements" and cGMP requirements informing "commercial batches of finished drug production."[115] She claims drug substances must meet ICH Q7 "commercial" cGMP requirements only" upon the completion of "process validation."[116] She characterizes the DS Lots as "scale-up" or "development batches" because AGC had not previously manufactured a 2000L batch and the DS Lots were intended for use in clinical trials.[117]

The record does not support characterizing the DS Lots as "scale-up" or "development" batches. The DS Lots were intended for dosing human subjects in Phase 1/2 clinical trials,[118] and were specifically ordered to be manufactured under cGMP standards.[119]

From there, it follows that ICH Q7 did not exempt those clinical DS Lots from

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[115] Gupta Rep. ¶¶ 69–70 (citing ICH §§ 1–17.2, 18.1–18.53).

[116] *Id*. ¶ 70.

[117] *Id*. ¶¶ 41, 62–65, 67–72, 88, 112–115, 119, 131, 133–134, 136.

[118] JX 202 at 4 ("The objective of [Project Change Order No. 48] is to add additional work to manufacture and release [] one 2000L batch for Phase I/II in March/April 2018); JX 203 at 1 (The objective is to add additional work to manufacture and release one 2000L batches for phase I/II in Q4 2018."); JX 172 at 1, 6; JX 949 at 6; JX 382.02; *see also* JX 97 at 2.

[119] *Compare* JX 101 at 6 (ordering a 100L "Pilot batch" and noting "[t]he objective of this Stage is to generate non-GMP pilot material") *with* JX 202 (ordering "one 2000L batch for phase I/II" and specifying the batch preparation subject to "cGMP manufacturing" standards).

any cGMP requirements.[120] The guidance on which Gupta relies, called the "New Drug Guidance," states that "[w]hen drug development reaches the stage where the drug products are produced for clinical trials in humans or animals, then compliance with the cGMP regulations is required."[121] As a contrast, the New Drug Guidance exempts preclinical work: "cGMP regulations do not apply for the preparation of new drug substance or drug products during such *initial preclinical experimentation*."[122]

The New Drug Guidance also refutes Gupta's opinion that the DS Lots were

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[120] Marshall RR. ¶¶ 13–14, n.9 (noting ICH Q7 mentions term "scale-up" only in the context of scale-up reports when describing proper documenting systems and additionally noting the term the fails to appear in 21 C.F.R. §§ 210 or 211.); Elder Rep. ¶¶ 44–45, 52, n.31, n.32; *see* U.S. Food and Drug Administration, Center for Drug Evaluation and Research, *Guideline on the Preparation of Investigational New Drug Products (Human and Animal)* (1991) [hereinafter "New Drug Product Guidance"] ("The cGMP regulations do not apply for the preparation of new drug substance or drug products during [] *initial preclinical experimentation*." (emphasis added)).

[121] New Drug Guidance at 2; *see* Gupta Rep. ¶ 41 (citing New Drug Guidance; Phase 1 Guidance; ICH Q8; *Guidance for Industry: INDs for Phase 2 and Phase 3 Studies – Chemistry, Manufacturing, and Controls* Information ("Phase 2 and 3 Guidance"); U.S. Food and Drug Administration, *Compliance Program Guidance Manual 7346.832*, Chapter 46–New Drug Evaluation (2022)).

[122] New Drug Guidance at 2*; but see* Gupta Rep. ¶¶ 41, 58 ("the Q7 regulations, practices, and regulatory expectations ***applicable to drug substances used in batches manufactured for commercial use or clinical trials*** differ from those articulated in 21 CFR Parts 210 and 211 ***which apply to commercial manufacturing of finished drug products (tablets, capsules or injectables, etc.) only***." (emphasis in original)).

The New Drug Guidance informs the cGMP requirements for drugs covered by an investigational new drug application ("INDA"). New Drug Guidance at 1–3. Syntimmune

exempt for cGMP requirements regarding production and process controls.[123] It recognizes certain control procedures for the manufacture of an investigational drug may undergo "considerable refinement," but "[i]t is essential that all changes from initial procedures be fully document[ed] and be based on well-founded scientific data."[124] The FDA's Phase 1 Guidance is in accord, noting that compliance with cGMP requirements necessitates manufacturers to use "methods, facilities, and manufacturing controls to ensure that the phase 1 investigational drug meets appropriate standards of safety, identity, strength, quality, and purity."[125]

And finally, no aspect of ICH Q7 limits its applicability or distinguishes the

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submitted its INDA on July 1, 2016 and the DS Lots were subject to FDA's INDA reporting regime. JX 149; JX 151.

[123] Gupta Rep. ¶¶ 61–62 ("FDA . . . recognize[s] that pharmaceutical companies developing new products and processes must have more flexibility in making process changes (especially after product or process failures) in these small experimental batches *without* the same degree of GMP documentation and process validation required for commercial products that are specified in 21 CFR Part 211." (citing ICH Q8)). Gupta's report does not identify any section of ICH Q8 to support that proposition but instead relies on a "see generally" citation. *Id.* ¶ 62. But ICH Q8, like ICH Q7, requires the manufacturing process to be controlled. ICH Q8 § 2.3 ("The manufacturing process development program or process improvement program should identify any critical process parameters that should be monitored or controlled (e.g., granulation end point) to ensure that the product is of the desired quality.").

[124] New Drug Guidance at 4.

[125] Phase 1 Guidance § 5.

relevance of any section based on the drug's "commercial" status.[126] To the contrary, ICH Q7's scope of applicability covers "the manufacture of APIs for use in human drug (medicinal) products."[127] ICH Q7 further states its applicability covers the manufacture of APIs "up to the point immediately prior to the APIs being rendered sterile."[128] ICH Q7's own limiting principle turns on sterilization—not commercial use.[129]

The companion piece to ICH Q7, called ICH Q7 Q&A, makes clear ICH Q7 applies to the DS Lots in its entirety.[130] It provides that when a "mixture is classified

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[126] ICH Q7 defines the term "manufacturing" as "include[ing] all operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage and distribution of APIs and the related controls." ICH Q7 § 1.1. ICH Q7 further provides "[w]ithin the world community, materials may vary as to their legal classification as an API. When a material is classified as an API in the region or country in which it is manufactured or used in a drug product, it should be manufactured according to this guidance." *Id*. § 1.2. ICH Q7 notes terms "API" and "drug substance" are intended to have the same meaning and can be used interchangeably. *Id*. at Glossary ("Active Pharmaceutical Ingredient (API) (or Drug Substance): Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.").

[127] *Id*. § 1.3.

[128] *Id*. ICH Q7 explicitly notes it informs the cGMP requirements during the isolation and purification step of the manufacturing process. *Id*. at Table 1.

[129] *Id*. § 1.3; *see id*. at Table 1.

[130] ICH Q7 Q&A §§ 1.2, 2.2, 5.4 ("ICH Q7, paragraphs 5.23 and 8.50 set forth the expectations that equipment be cleaned at appropriate intervals (e.g., time or number of

in the regulatory filing as an API . . . ICH Q7 should be applied to the manufacturing of the mixture."[131] It further explains "[t]he ICH Q7 document should be read in its entirety regardless of the nature of the manufacturing activities being conducted to fully understand the linkages between certain sections and successfully implement appropriate good manufacturing practices [ ] at all stages of the [APIs] supply chain, including distribution."[132]

I conclude ICH Q7 is applicable in its entirety. AGC's manufacturing rubs up against ICH Q7 Section 13.[133] Section 13.10 mandates "[a] formal change control system [ ] be established to evaluate all changes that could affect the production and control of the intermediate or API."[134] Section 13.13 requires "[t]he potential impact of the proposed change on the quality of the intermediate or API should be

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batches) to prevent build-up and carryover of contaminants so that they do not adversely alter the quality of the API."). Gupta acknowledged "jumbo STIC filter . . . had not been washed appropriately, and AGC . . . did not take into account this additional PAA that was in the jumbo STIC filter," and "the flow rate was also miscalculated when they calculated the wash aspect." Gupta Tr. 2039; *but see* Gupta Tr. 2040–42 (claiming Section 5 is inapplicable because it is supplanted by Section 19.3).

[131] ICH Q7 Q&A § 1.2; *see* JX 335.08 at 1, 4 (Amendment 4.0 to Protocol SYNT001-103 and stating the amendment is for a "Phase 1b/2" clinical trial); JX 763.02 at 1 (Amendment 5.0 to Protocol SYNT001-102 for WAIHA stating the amendment is for "Phase 1b/2" clinical).

[132] ICH Q7 Q&A § I.

[133] ICH Q7 §§ 13.10, 13.11, 13.13, 13.14, 13.15.

[134] *Id*. § 13.10.

evaluated."[135] Similarly, Section 5 addresses oversight of the equipment used in the manufacturing process. And Section 5.11 provides that "[e]quipment should be constructed so that surfaces that contact raw materials, intermediates, or APIs do not alter the quality of the intermediates and APIs beyond the official or other established specifications."[136]

3. The Experts

At trial, Alexion's experts Paul Marshall and David Elder concluded AGC's manufacturing process revealed multiple cGMP violations grounded in ICH Q7's oversight requirements.[137] They both found AGC's failure to follow a "formal change control system" and failure to ensure the use of the Jumbo Filter would not

[135] *Id*. § 13.13.

[136] *Id*. § 5.11.

[137] Elder Rep. ¶¶ 80–87 (finding AGC violated ICH Q7 Section 5 in its adoption of the STIC Jumbo filter); Marshall Rep. ¶¶ 70–3 (finding AGC's failure to make the necessary adjustments to the manufacturing process in its introduction of STIC Jumbo filter violated ICH Q7 §§ 5.10, 5.20, 5.22); Marshall RR. ¶¶ 30, 34, 36 (concluding AGC violated ICH Q7 §§ 13.10, 13.13, 13.15); Marshall Tr. 1872–76 (explaining AGC violated ICH Section 19 in failing to evaluate the impact the introduction of the STIC Jumbo Filter could have on the DS Lots); Elder Tr. 1955–62 (concluding AGC violated ICH Q7 Sections 5.10, 5.11, 5.12, 5.22, 13.13, 19.11, 19.30 and 19.70 in its implementation of the STIC Jumbo Filter); *see* ICH Q7 § 1.1 (stating its objective is to "provide guidance regarding good manufacturing practice (GMP) for the manufacturing of active pharmaceutical ingredients (APIs)" and to "ensure that APIs meet the quality and purity characteristics that they purport, or are represented, to possess."). Elder was not asked to address either the protein loading issue or the Cygnus 2 kit. Elder Tr. 1949.

alter the quality of the DS Lots to be a cGMP violation.[138] Marshal and Elder agreed the DS Lots "were not manufactured in compliance with the cGMP requirements of the FDCA and are therefore adulterated."[139] Marshall also determined AGC's failure to assess the potential impact from its inconsistent protein loading range and failure to verify the Cygnus 2 Kit constituted cGMP violations.[140]

SRS's experts, Gupta and Dr. Denis Boyle, concluded AGC's process was cGMP compliant.[141] Gupta found the introduction of the STIC Jumbo Filter complied with cGMP requirements because AGC had a procedure in place to wash the filter, documented changes that arose like the leakage, rejected the DS Lots for being contaminated, and investigated the root cause of the contamination.[142] As for

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[138] Elder Rep. ¶¶ 80–87; Marshall Rep. ¶¶ 67–77.

[139] Elder Rep. ¶ 80; Marshall RR. ¶ 35 (describing the "change in control procedures at AGC" failed to evaluate the potential impact of the introduction of the STIC Jumbo Filter constituting "a failure of cGMP, which is designed to prevent haphazard, disorganized, and unsystematic changes in manufacturing procedures that can impact product quality and purity").

[140] Marshall Rep. ¶¶ 25, 80–94; Marshall Tr. 1881–1900.

[141] Gupta Rep. ¶¶ 35, 79–94, 116–29, 137; Boyle Rep. ¶¶ 31–34, 51–113. Boyle was not qualified as a cGMP expert. Boyle Tr. 1992 ("I'm not a GMP compliance expert, but I am very well aware of the GMPs as they apply to the space in which I work."); *id*. Tr. 2010 (confirming on cross-examination that Boyle is not opining as a cGMP compliance expert).

[142] Gupta Rep. ¶¶ 79–90, 116–29; Gupta Tr. 2031. Gupta concluded there was no "GMP process gap" because AGC complied with its MPI and MPR. Gupta Rep. ¶¶ 84–86, 128 (citing JX 2629); Gupta RR. ¶¶ 62–64, 82. But Gupta relies on MPR Revision 5 to support her claim, which only became effective on August 16, 2019. JX 2629 at 19; *see* Gupta Rep. ¶¶ 128, n.138 (citing JX 2629). AGC revised its MPR to specify the STIC Jumbo

AGC's failure to adjust the flow and wash settings to the STIC Jumbo Filter's vendor settings, Gupta opined that was not a cGMP deviation because AGC followed the standard wash settings it "defined several years earlier" and had been using without incident or product impact for years.[143] Again relying on her characterization of the DS Lots as "scale-up" batches, Gupta concluded "AGC's usage of the improper washing procedure is not considered a GMP deviation."[144] Gupta further opined AGC could "only" be found to violate cGMP requirements "[i]f AGC had NOT performed a thorough investigation or had released the [DS Lots]."[145]

Boyle, who is not a cGMP compliance expert, opined neither AGC's use of the Cygnus 2 Kit nor the protein loading ranges violated cGMP standards.[146] As for

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Filter must be washed according to the vendor's instruction only after it was determined the DS Lots were unusable. JX 958; JX 1285 at 2 (noting the downstream processing MPI was updated "to ensure STIC Membranes [are] used as required."). The operative MPR when the DS Lots were manufactured included wash and filter settings that deviated from the vendor's instructions, and were only revised following AGC's manufacture of the DS Lots. JX 2629 at 19 (noting the MPR was updated on May 15, 2019 to conform with "CMC16085 rev05"); JX 958 at 2 (revising CMC 16085 to change the max load and wash setting for the STIC Jumbo Filter).

[143] Gupta Rep. ¶¶ 88, 90, 123.

[144] *Id.* ¶ 88. Gupta's Expert Report also identified Alexion's settlement agreement with AGC as supporting her conclusion because the settlement noted the DS Lots were "executed to protocol." *Id.* ¶ 89 (quoting JX 1243 at 2).

[145] *Id.* ¶ 90.

[146] Boyle Tr. 1992, 2010 (confirming he is not a cGMP compliance expert); Boyle Rep. ¶¶ 28–30; Boyle Tr. 1992–94 (concluding the "Cygnus 2 assay was an appropriate choice" and "the protein loading ranges were appropriately established").

the Cygnus 2 Kit, Boyle concluded "AGC performed the verification of the Cygnus 2 [Kit], as indicated in the kit's instructions, and found that the sample must be appropriately diluted in order to deliver valid test results."[147] On cross-examination, Boyle was forced to concede the "verification" he relied upon addressed the dilution linearity range, which does nothing to determine the assay's HCP coverage.[148] Nevertheless, Boyle concluded cGMP did not require an independent assessment of an off-the-shelf assay like the Cygnus 2 Kit for use in Phase 1 and Phase 2 studies.[149] As for protein loading, Boyle found that "[w]hile protein loading did vary from batch to batch, it is incorrect to conclude that this variation was problematic" because "Syntimmune correctly defined protein loading ranges in GMP batch records and controlled protein loading within those ranges."[150]

Sharpnack explained that AGC's failure to evaluate its introduction of the STIC Jumbo Filter "is a significant issue" and demonstrates "a very poor display of

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[147] Boyle Rep. ¶ 92 (citing to JX 2602 at 16); JX 2602 at 16 ("Dilutional linearity was not assessed as buffer spiked samples were below LOQ."). Boyle Tr. 2017–18 (confirming JX 2602 at 16 is the document he relied upon for the conclusion the Cygnus 2 Kit was verified); JX 538 at 29 (concluding "[i]valid assay" because "*e. coli* recovery can be detected.").

[148] Boyle Tr. 2017–18 (describing the tests reflected in Section 7.5 of JX 2602).

[149] Boyle Rep. ¶ 92.

[150] *Id*. ¶ 64.

the quality oversight at AGC."[151]

4. Analysis

AGC's failure to ensure the STIC Jumbo Filter was suitable for its intended use materially deviated from the guidance provided by multiple sections of ICH Q7. AGC fell short of Section 19.11 in failing to ensure the DS API was manufactured according to appropriate production and control procedures.[152] And it fell short of Sections 13.10 and 13.13 in failing to establish a formal control system to evaluate the filter switch, and to evaluate the potential impact of that change.[153] AGC's failures constitute cGMP violations.[154]

Section 4.13(a) promised "compliance in all material respects."[155] The determination of whether a party breached a representation to comply "in all material

[151] Sharpnack Rep. ¶ 71; Sharpnack Dep. at 42.

[152] ICH Q7 § 19.11.

[153] *Id*. §§ 13.10, 13.13.

[154] 21 U.S.C. § 351(a)(2)(B) ("A drug or device shall be deemed to be adulterated . . . (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess. . . .").

[155] Merger Agr. § 4.13(a).

respects" turns on the effect the purported noncompliance had on the company.[156] "Put differently, the materiality standard at issue asks whether the business deviation significantly alters the buyer's belief as to the business attributes of the company it is purchasing."[157] The question is whether AGC's noncompliant manufacturing process "would have been viewed by the reasonable investor as having significantly altered the 'total mix' of information."[158] " It strives to limit the operation of [Section 4.13(a)] to issues that are significant in the context of the parties' contract, even if the breaches are not severe enough to excuse a counterparty's performance under a common law analysis."[159]

The usability of the drug substance Alexion bought from Syntimmune was significant. Alexion sought value from quick development and winning the race to the market, so Alexion needed drug product that was compliant and usable.[160] "Time

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[156] *Akorn*, 2018 WL 4719347, at *65; *Dermatology Assocs.*, 2020 WL 4581674, at *26–29; *Channel Medsystems*, 2019 WL 6896462, at *17; *see also Anthem-Cigna*, 2020 WL 5106556, at *134 n.426 (distinguishing common law "material breach" standard from "in all material respects" standard).

[157] *Snow Phipps Grp., LLC*, 2021 WL 1714202, at *30–*35, *38.

[158] *Akorn*, 2018 WL 4719347, at *86.

[159] *Id.*

[160] Sarin Tr. 950–53, 975–76; Ledwith Tr. 1030–34, 1039–41; Alford Tr. 1172–73, 1863, 1876, 1904.

was of the essence" for Alexion to begin clinical trials.[161] That significance is baked into the Merger Agreement. The parties agreed Section 4.13 was a "Fundamental Representation," and was singled out as being in effect for four years.[162] And the Merger Agreement's indemnification regime exempts the Fundamental Representations from the $2,000,000 "Threshold" applicable to all other indemnification claims based on the Agreement's representations and warranties.[163]

AGC's cGMP violations resulted in the DS Lots being rendered completely unusable, including the DS Lots that produced the DP already in clinical use.[164] Alexion concluded "[a]ll clinical DP [Lot] Batches in circulation are not suitable for human use," requiring the nonroutine disposal of the released DP Lots.[165] Without drug product, Alexion could not perform clinical trials. Alexion's trials were paused, then terminated.[166] Alexion fell behind its competitors in performing

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[161] Sarin Tr. 975–76.

[162] Merger Agr. § 1.1 (defining "Fundamental Representations" to mean "the representations or warranties contained in Section 4.1 (Organization, Standing and Power), Section 4.2 (Authorization), Section 4.3 (Capitalization), Section 4.13 (Regulatory), Section 4.14 (Intellectual Property) and Section 4.18 (Brokers)."); *id.* § 8.5 (addressing Sections 4.13 and 4.14).

[163] *Id.* §§ 8.4(a)–(e).

[164] JX 1044 at 1; JX 866 at 2–3.

[165] JX 977 at 17.

[166] JX 923 at 39, 42–43 (noting study 104 and 102 were paused due to the reported IRRs pending the outcome of an investigation into AGC's manufacturing process); JX 1164 at

trials.[167] Alexion's inability to use the DS Lots in clinical trials caused a year-long delay.[168]

These are not "small, *de minimis*, [or] nitpicky issues"[169]—Alexion had purchased a time-sensitive pathway to developing a molecule into a medication, and that pathway was clogged. Alexion has proven the DS Lots breached Section 4.13(a).

C. The DP Lots

1. Background

On March 29, 2018, Syntimmune contracted with Patheon Manufacturing

78–80 (noting the first reported IRRs occurred in mid-January 2019 and the study was terminated in March 2019); JX 1508.05 at 4 ("The top two candidate root causes identified were the potential leachate (Poly-allylamine, PAA) from the STIC membrane step (after it was determined the DS CMO did not follow manufacturer's instructions for operation) and the use of the less sensitive Cygnus 2nd generation HCP kit for residual HCP determination."); JX 996 at 2; Ledwith Tr. 1032–35.

[167] Ledwith Tr. 1032–41; JX 945 at 1 ("Because of the high HCP (host cell protein) contamination of the one DP lot we thought could potentially be rereleased for use in Cohort 2 WAIHA, we will not be able to proceed with dosing more patients in the Ph 1b/2a trial. On the other hand, the clinical investigation suggests that the culprit in the observed infusion reactions is likely contamination by PAA (polyalyamine) that leached from the last chromatography step. These two contamination issues (HCP and PAA) will be addressed in the new DS campaigns starting now, but we will not have DP available until Dec (for Ph 2 grade) or March 2020 for P3 start."); *id*. at 2–3 (explaining the DS Lots "will need to be recalled" due to the leached particulate).

[168] JX 965; JX 933; JX 932; JX 930; JX 927.02; JX 845 at 4–6; JX 835; *see* JX 833.

[169] *AB Stable VIII LLC*, 268 A.3d at 216 (citing *Akorn*, 2018 WL 4719347, at *85).

Services LLC ("Patheon") to manufacture the DP Lots for a Phase 2 clinical study.[170] Patheon agreed to comply with cGMP standards and to strictly adhere to "the applicable guidances and regulations" including 21 C.F.R. Parts 210, 211, 312 Subpart D, and FDA's Phase 1 Guidance.[171]

Patheon's investigation after the IRRs revealed all samples tested had visible particulates.[172] An independent lab analyzed eight vials of DP Lot AJ8794A and found each vial had bubbles,[173] and each sample had "a moderate to heavy load of amorphous particulate residue"[174] determined to be "protein with silicone."[175]

Patheon and Alexion conducted a joint root cause analysis and focused on the fact that manufacturing moved from one Patheon suite to another ("Suite 1" to "Suite

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[170] JX 312.03 at 4 ("Syntimmune has requested Patheon to provide a proposal for the manufacture of clinical supply of aseptically filled SYNT001 Sterile Liquid Vials (the 'Product') for a Phase II study. Client has stated the clinical trial will be conducted in the USA, thus, all formulation components and finished product must meet the regulatory requirements of USP/EP. Patheon intends to execute the sterile manufacture on PDS Suite 2 in Patheon's Steriles North facility."); JX 220 at 3–4.

[171] JX 138 at 9, 33.

[172] JX 1338 at 1.

[173] JX 827 at 2.

[174] *Id*. at 4; *see also* JX 2854 ("Particle IDs for lot AK3858 pending. Most likely root cause identified to be a result of excess pump speed during fill which creates particulation from the fill tubing & shear to the molecule.").

[175] JX 827 at 3; *see also* JX 2854 ("Particle IDs from lot AJ8794A determined to be silicone oil & proteinaceous matter.").

2"), with different methods and equipment.[176] Syntimmune's contract with Patheon had authorized the use of Suite 2. [177] DP Lots AJ8794A and AK3858 were the first lots filled in Suite 2: all previous Syntimmune lots had been filled in Suite 1.[178] The two suites had different equipment: Suite 1 used a Watson-Marlow Flexion filler at 16 vials/min, with a batch size of approximately 500 L and filler pump speed of 200-300 revolutions per minute ("RPM"); Suite 2 used a high-speed Bosch filler at 80 vials/min, with a 2000 L batch size and faster filler pump speed of 500 RPM.[179]

Patheon created its Change Control Report for moving filling to Suite 2, which noted a required stability study, and that Suite 2 needed to be validated.[180] There is no evidence Patheon evaluated the potential impact the switch to Suite 2 could have on the drug products; the inference is that it did not do so before the move.[181] Patheon decided to perform that investigation only after particulates were

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[176] JX 1338 at 7; JX 2605 (noting the differences between Patheon's Suite 1 and Suite 2 and identifying five "key potential root cause[s]").

[177] JX 312.03 at 4; JX 275 at 1.

[178] JX 830.04 at 2–3; JX 799; JX 800 at 8 (suspending all work orders on Suite 2).

[179] JX 799 (highlighting the differences between Suite 1 and Suite 2).

[180] JX 275 at 1, 4.

[181] Marshall Tr. 1861–62; Elder Tr. 1954–55; Sharpnack Rep. ¶ 82 ("Patheon's failure to implement a change control when switching from Suite #1 to Suite #2, combined with the unresolved protein loading range issue as well as the changed filtration system without a change control, resulted in the drug product batches not being in compliance with cGMP requirements, per 21 CFR §§ 211.100 and 211.63.").

discovered.[182]

Patheon never identified any one specific root cause.[183] Patheon ordered the destruction of DP Lots AK3858B and AJ8794A "impacted" by their production at Suite 2.[184]

2. The Applicable Regulations

The FDA promulgated relevant cGMP requirements in the Code of Federal Regulations, at 21 C.F.R. parts 210 and 211.[185] Parts 210 and 211 "contain the minimum current good manufacturing practice . . . to assure that such drug meets the requirements of the act as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess."[186] Section 210.1(b) states the failure to comply "with any regulation" in Part 210 or

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[182] JX 1338 at 7 (noting the joint root cause analysis "determined that a potential root cause could be attributed to a change in Suites and equipment."); JX 799 (highlighting the differences between Suite 1 and Suite 2).

[183] JX 1338 at 8 ("A Root cause Analysis was performed. During the RCA no assignable root cause for this particulate issue was identified. A possible root cause could be contributed to change in production from PDS Suite 1 to PDS Suite 2 (Refer to File Attachment 1: Suite Comparison)."). That "File Attachment 1" is JX 2605. *Compare* JX 2605 (titled "Suite Comparison DIR 514770) *with* JX 1338 at 2–3 (describing "DIR 514770" investigation).

[184] JX 1338 at 7.

[185] 21 C.F.R. § 210.1(a); *see United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1324 (D.C. Cir. 2014) ("The FDA has established the specific elements of current good manufacturing practice at 21 C.F.R. parts 210–211.").

[186] 21 C.F.R. § 210.1(a).

211 "shall render such drugs to be adulterated," and that the party responsible for failing to comply shall be "subject to regulatory action."[187] The cGMP requirements announced in Parts 210 and 211 "apply to all aspects of drug manufacture, including packaging and labeling operations, drug testing and quality control operations."[188]

The parties disagree whether Part 211's regulations for finished drug products apply to the DP Lots. Alexion contends they are governed by Part 211; SRS contends they are exempt.[189] Section 210.2(c) exempts some introductory work from Part 211. Its exemption reads as follows:

> *An investigational drug for use in a phase 1 study*, as described in § 312.21(a) of this chapter, subject to the statutory requirements set forth in 21 U.S.C. 351(a)(2)(B). The production of such drug is exempt from compliance with the regulations in part 211 of this chapter. *However, this exemption does not apply to an investigational drug for use in a phase 1 study once the investigational drug has been made available for use by or for the sponsor in a phase 2 or phase 3 study*, as described in § 312.21(b) and (c) of this chapter, or the drug has been lawfully marketed. If the investigational drug has been made available in a phase 2 or phase 3 study or the drug has been lawfully marketed, the drug for use in the phase 1 study must comply with part 211.[190]

SRS contends "Part 211 applies to finished pharmaceuticals products only," so the

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[187] *Id*. § 210.1(b).

[188] FDA Enforcement Manual § 1631; *see* 21 C.F.R. § 210.1(a).

[189] *See* PB Exp. 38–40; DB Exp. 4–9; SRS Op. Br. 88; ALXN Op. Br. 21–22.

[190] 21 CFR §210.2(c) (emphasis added).

DP Lots were exempt as "scale-up" batches intended for use in clinical trials.[191] SRS argues DP Lot AK3858 is exempt because it was intended for stability testing only,[192] and because it was manufactured in May 2018 before any Phase 2 dosing began.[193] Alexion contends Part 211 kicks in once a drug product is manufactured with the intention it will be used, or is used, in a Phase 2 or 3 clinical trial, and points to FDA's Phase 1 Guidance applying cGMP to investigational drugs used in Phase 1 trials.[194]

The statute's meaning is plain. By its text, an investigational drug to be used in a Phase 1 study is exempt from Part 211's cGMP requirements, and that exemption applies unless and until the drug "has been made available for use by or for the sponsor in a Phase 2 or Phase 3 study."[195] The Phase 1 Guidance is in accord:

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[191] PB Exp. 19 (citing Gupta Rep. ¶ 58); Gupta Rep. ¶ 112 ("[T]he Patheon drug product lot was a scale-up batch similarly subject to the requirements applicable to scale-up/clinical production as opposed to commercial manufacturing.").

[192] SRS Ans. Br. 53 n.4; Gupta Tr. 2034–35.

[193] SRS Ans. Br. 53–54.

[194] DB Exp. 3–5; Elder Rep. ¶¶ 43–95, 109 n.130 (citing to Phase 1 Guidance); Phase 1 Guidance § III ("[I]f an investigational drug has already been manufactured by an IND sponsor for use during phase 2 or phase 3 clinical trials or has been lawfully marketed, manufacture of such a drug must comply (21 CFR 211.1) with 21 CFR part 211 for the drug to be used in any subsequent phase 1 clinical trials, irrespective of the trial size or duration of dosing."); Marshall RR. ¶¶ 12–43.

[195] 21 C.F.R. § 210.2(c).

"if an investigational drug has already been manufactured by an IND sponsor for use during phase 2 or phase 3 clinical trials . . . such a drug must comply with 21 C.F.R. Part 211 for the drug to be used in any subsequent phase 1 clinical trials, irrespective of the trial size or duration of dosing."[196] Investigational drug products manufactured for Phase 2 and Phase 3 clinical trials "must comply with the appropriate sections of 21 C.F.R. Part 211 for the drug to be used in any subsequent phase 1 clinical trial, irrespective of the trial size or duration of dosing."[197] The FDA has explained this exemption makes sense because the "FDA oversees drugs for use in Phase 1 trials through its existing IND authority" which authorizes it to place a clinical study on hold or terminate the study for inadequate controls.[198] And that

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[196] Phase 1 Guidance § III (citing 21 C.F.R. 210.2(c)).

[197] *Id.* § III n.7; Marshall Tr. 1942–46, 1987–88; *see* Phase 1 Guidance § III ("This guidance does not apply to the following phase 1 investigational products . . . manufactured for phase 2 and phase 3 clinical trials."); *see* 21 C.F.R. § 312.21(b) ("Phase 2 includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug.").

[198] Current Good Manufacturing Practice Regulation and Investigational New Drugs, 71 Fed. Reg. 2458, 2494–95 (June 1, 2006) (describing drugs subject to IND application are subject to the requirements of 21 C.F.R. § 312.23(a)(7)); 21 C.F.R. § 312.23(a)(7) ("[T]he the emphasis in an initial Phase 1 submission should generally be placed on the identification and control of the raw materials and the new drug substance."); *see* 21 C.F.R. §§ 312.44(a)–(b)(iii) ("This section describes the procedures under which FDA may terminate an IND. . . . A termination action may be based on deficiencies in the IND or in the conduct of an investigation under an IND. . . . [including if] The methods, facilities, and controls used for the manufacturing, processing, and packing of the investigational

"even if exempted from the requirements of parts 210 and 211, investigational drugs remain subject to the statutory requirement that deems a drug adulterated" if the manufacturing process 'do[es] not conform to or [is] not operated or administered in conformity with current good manufacturing practices . . . .'"[199]

The preponderance of the evidence shows DP Lots AJ8794A and AK3858 were manufactured for use in Phase 2 studies, such that they are not exempt from Part 211. The clinical study protocol amendments establish those DP Lots were manufactured for use in "Phase 1b/2" studies.[200] Phase 1b/2 studies are a hybrid of Phase 1 and Phase 2 studies: "they seek to establish proof of concept in patients while testing the safety of dosing through a MAD protocol."[201] The manufacturing directives to AGC and Patheon decisively show DP Lots AJ8794A and AK3858

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drug are inadequate to establish and maintain appropriate standards of identity, strength, quality, and purity as needed for subject safety.").

[199] 73 Fed. Reg. 40454 (quoting 21 U.S.C. § 351(a)(2)(B)).

[200] JX 335.08 at 1, 4 (Amendment 4.0 to Protocol SYNT001-103 and stating the amendment is for a "Phase 1b/2" clinical trial); JX 763.02 at 1 (Amendment 5.0 to Protocol SYNT001-102 for WAIHA stating the amendment is for "Phase 1b/2" clinical); JX 1163.04 at 1 (Amendment 5.0 to Protocol SYNT001-103 for WAIHA stating the amendment is for "Phase 1b/2" clinical); JX 183 at 1(explaining the protocol amendments "related to the release of additional drug substance (DS) batches and an additional drug product (DP) lot for use in planned clinical trials."); JX 205 at 15 ("Specifications for SYNT001 DS . . . used to release the 500L cGMP batches that have been used or are intended for human clinical trials."); *see* Elder Rep. ¶¶ 31–32; Elder Tr. 1943–46, 1976, 1984.

[201] *Alexion I* at *9; *see* JX 1229 at 29.

were manufactured with the intention to be used in a Phase 2 study.[202] Syntimmune contracted with Patheon specifically for DP Lots AJ8794A and AK3858 to be manufactured "for a Phase 2 study."[203] Syntimmune's agreements with Patheon mandating compliance with cGMP requirements identify Part 211 as an applicable regulation.[204]

SRS makes two arguments to the contrary. First, its expert opined that DP Lot AK3858A is exempt from Part 211 because it was intended for stability testing,

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[202] JX 172 at 6 ("Bulk Drug Substance generated by the process will be used to support Phase II clinical trials"); JX 202 at 4 ("Bulk Drug Substance generated by the process will be used to support Phase I/II clinical trials."); JX 203 at 3 (directing AGC to prepare "for cGMP manufacturing of one 2000L" batch); JX 97 at 2 ("Bulk Drug Substance generated by the process will be used to support Phase I/II clinical trials."); *see* JX 275 at 2 (Patheon change control report regarding DP Lots for "Phase II to Suite 2 … Syntimmune has requested Patheon to manufacture of [sic] clinical supply … for a Phase II study"); JX 183 at 4 (noting the DS Lots "were ear-marked for both Phase 1 re-supply and initial Phase 3 IV supply, and now should be considered not suitable for clinical use."); JX 878 at 4 (same); *see also* JX 872 at 1 (same).

[203] JX 312.03 at 4 ("Syntimmune has requested Patheon to manufacture of clinical supply of aseptically filled SYNT001 Sterile Liquid Vials [] for a Phase II study."); *id*. at 6 (noting the objective of the agreement is "[t]o provide Client with one batch of 10,000 units of [clinical trial material] active for use in Phase II clinical trials."). Patheon further agreed the scope of the project included compliance with "cGMP conditions & QA review." *Id*. at 7.

[204] JX 138 at 9 ("Patheon will ensure that Product(s) are manufactured and tested in strict compliance with the applicable guidances and regulation listed in Appendix F."); *id*. at App. F (listing 21 C.F.R. Parts 210 and 211 and ICH Q7 among applicable guidances and regulations).

not a Phase 2 clinical trial.[205] But DP Lot AK3858A doses that remained after stability testing were intended for clinical trials; they were diverted by the determination that Lot was unusable.[206]

Second, SRS argues Section 210.2(c)'s exemption applies to DP Lots AJ8794A and AK3858 because they were not made available to Syntimmune until fall of 2018, and at that time no Phase 2 study was underway.[207] SRS has not offered any support for a regulatory scheme under which a manufacturer could produce a stockpile of drug product intended for Phase 2, but evade Phase 2 cGMP requirements until dosing began.[208] SRS's argument is contradicted by the FDA's commentary accompanying Section 210.2(c):

> This direct final rule adds § 210.2(c) to make clear that production of *an investigational drug for use in a Phase 1 study conducted under an IND*, when the drug has not yet been, or is *not being, manufactured for use in Phase 2* or 3 studies or for an already approved use, *is not subject*

[205] Gupta Rep. ¶ 58; Gupta Tr. 2034–35.

[206] JX 784 at 82 ("limited leftover for clinical inventory"); JX 819 at 17; Ledwith Tr. 1030–31.

[207] SRS Ans. Br. 57–8; Gupta Tr. 2046; *see* JX 2632 at 2 ("Lot was only filled for stability; forward processed by Syntimmune - remaining DS was inventory at time of deal close."); Ledwith Tr. 1030–31; *see* also JX 804 at 5 (noting 2053 vials of DP Lot AK3858 are currently available and that "pending release" the "[l]imited leftover [is] for clinical inventory").

[208] *See* Elder Tr. 1944–45, 1987–88.

> *to the requirements in part 211*.[209]

DP Lots AJ8794A and AK3858 were manufactured "for use" in a Phase 2 study.[210] Therefore, the cGMP requirements in Part 211 are applicable.

Part 211, Subpart F (Production and Process Controls) requires written procedures for production and process control.[211] It requires changes to such written procedures to be reviewed and approved.[212] Section 211.63 requires that "[e]quipment used in the manufacture, processing, packing, or holding of a drug product shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance."[213] Part 211, Subpart J (Records and Reports) requires master batch records that include complete manufacturing and control instructions[214] and batch production records that include complete information relating to the production and control of the

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[209] Current Good Manufacturing Practice Regulation and Investigational New Drugs, 71 Fed. Reg. 2458 (June 1, 2006).

[210] *E.g.*, JX 335.08 at 1, 4; JX 763.02 at 1; JX 1028 at 2; JX 312.03 at 4; JX 275 at 2.

[211] 21 C.F.R. § 211.100.

[212] *Id*.

[213] *Id*. § 211.63.

[214] *Id*. § 211.186.

batch.[215]

Patheon would have been held to the same standard even if the DP Lots were exempt from Part 211. Even investigational and exempt drug substances and drug products are subject to FDCA Section 351(a)(2)(B), which requires all drugs to be manufactured in accordance with cGMP requirements.[216] And an exempt investigational drug product is evaluated as if it were a drug substance—by guidance looking to Part 211.[217] The Sterile Products Guidance speaks directly to Patheon's

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[215] *Id*. § 211.188.

[216] 21 U.S.C. § 351(a)(2)(B); FDA Ch. 56 at 4–5; 73 Fed. Reg. 40453–54 (quoting 21 U.S.C. § 351(a)(2)(B)).

[217] *Compare* Phase 1 Guidance § D ("The manufacturer should establish acceptance criteria for specified attributes on each material. . . . attributes and acceptance criteria selected for assessment should be based on scientific knowledge and experience for use in the specific phase 1 investigational drug.") *with* 21 C.F.R § 211.63 ("Equipment used in the manufacture, processing, packing, or holding of a drug product shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.") *with* 21 C.F.R § 211.100 ("There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart. These written procedures, including any changes, shall be drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit."); *with Guidance for Industry: Sterile Drug Products produced by Aseptic Processing—cGMP* [hereinafter "Sterile Products Guidance"] § II ("Any manual or mechanical manipulation of the sterilized drug, components, containers, or closures prior to or during aseptic assembly poses the risk of contamination and thus necessitates careful control."); *with Guidance for Industry: Quality Systems Approach to Pharmaceutical cGMP Regulations* [hereinafter "Pharmaceutical cGMP Guidance"] § III.A ("Every pharmaceutical product has established identity, strength, purity, and other quality characteristics designed to ensure the required levels of safety and effectiveness. For the purposes of this guidance

manufacture of the DP Lots and mandates compliance with Part 211, including requirements governing oversight and change of control during the manufacturing process.[218] The Pharmaceutical cGMP Guidance "applies to manufacturers of drug products" like Patheon.[219] Pharmaceutical cGMP Guidance requires that "[c]hanges to an established process must be controlled and documented to ensure that desired attributes for the finished product will be met (§ 211.100(a))" and when a change is implemented "its effect should be determined by monitoring and evaluating those specific elements that may be affected based on an understanding of the process."[220] And ICH Q7 Section 19.11 provides that once a drug product is intended for clinical

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document, the phrase achieving quality means achieving these characteristics for a product.").

[218] Sterile Products Guidance at 6 ("This guidance pertains to current good manufacturing practice (CGMP) regulations (21 CFR parts 210 and 211) when manufacturing sterile drug and biological products using aseptic processing."). Patheon's Change Control Report stated that "Syntimmune has requested Patheon to manufacture [] clinical supply of aseptically filled SYNT001 Sterile Liquid Vials" and that the "manufacturing process consists of thawing, pooling, aseptic filtering and then aseptically filling." JX 275 at 2. The Sterile Products Guidance mandates that "21 CFR 211.63, 211.65, and 211.67 address, respectively, 'Equipment design, size, and location,' 'Equipment construction,' and 'Equipment cleaning and maintenance' [and] 21 CFR 211.100(a) states, in part, that '[t]here shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart.'" Sterile Products Guidance at 24.

[219] Pharmaceutical cGMP Guidance at 6.

[220] *Id*. at 23.

trials, "manufacturers should ensure that APIs are manufactured in suitable facilities using appropriate production and control procedures to ensure the quality of the API."[221] Whether supplied by Part 211 or one of the guidances, the potential impact of moving from Suite 1 to Suite 2 needed to be evaluated.

3. The Experts

Alexion's experts opined Patheon's filling process failed to comply with cGMP standards because Patheon failed to evaluate the potential impact on the drug product from moving to Suite 2.[222] Alexion's experts and Sharpnack concluded Patheon's change control documentation to be "completely inadequate" because Patheon "failed to properly evaluate the differences between Suite 1 and Suite 2 and the impacts that these differences may have on product quality, before transferring production from Suite 1 to Suite 2."[223]

SRS's expert Gupta started from the premise that Part 211 applies only "to

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[221] ICH Q7 § 19.11.

[222] Marshall RR. ¶¶ 44–52 (concluding Patheon violated the cGMP requirements set forth in 21 C.F.R. §§ 211.100, 211.63, 211.188); Elder Rep. ¶¶ 96–112 (concluding Patheon violated the cGMP requirements set forth in 21 C.F.R. §§ 211.100, 211.186, 211.188).

[223] Marshall Tr. at 1861–1862; Marshall Rep. ¶ 105; Elder Rep. ¶ 106 ("There is no information contained within this Change Control Report that demonstrates that the differences between the [Suite] 1 and [Suite] 2 [] were identified and evaluated prior to implementation of this change. . . . which is a violation of cGMP and 21 C.F.R § 211.100."); Sharpnack Rep. ¶ 84 ("Patheon failed to properly evaluate the differences between Suite #1 and Suite #2 and the impact the manufacturing differences may have had

commercial batches, not to the development or 'scale-up' batches being manufactured by Patheon in this case."[224] As explained, I disagree. I give no weight to Gupta's opinion that Patheon satisfied cGMP requirements.

4. Analysis

Patheon's switch to Suite 2 failed to comply with Part 211.100 by failing to evaluate what further testing might be necessary to ensure drug product quality.[225] Section 211.100 mandates the implementation of "process control designed to assure that the drug products have the identity, strength, quality, and purity they purport" and that "[a]ny deviation from the written procedures shall be recorded and justified."[226] By failing to undertake an evaluation of the differences until after the discovery of the particulate, Patheon failed to ensure the DP Lots' quality and purity

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on product quality, in violation of cGMP requirements, per 21 CFR §§ 211.100 and 211.63.").

[224] Gupta Rep. ¶¶ 131–37. Gupta opined she saw "no evidence" Patheon failed to comply with change control requirements and further noted that based on "my experience from prior inspections at Patheon . . . [it] most certainly documented the change from Suite 1 to Suite 2." *Id*. ¶ 132.

[225] 21 CFR §§ 211.100(b) ("Written production and process control procedures shall be followed in the execution of the various production and process control functions. . . . Any deviation from the written procedures shall be recorded and justified."). Patheon's root cause analysis reveals the significant difference between Suite 1 and Suite 2 was not evaluated under after visible particles appeared in the DP Lots. JX 800; *see* Marshall Report ¶¶ 101–04.

[226] 21 CFR §§ 211.100(a)–(b).

would not be impacted by Suite 2.

Section 211.63 mandates that equipment used in the manufacturing process for a drug product "shall be of appropriate design, adequate size, and suitably located" for its intended use.[227] Patheon used Suite 2 to fill over 8,900 vials of drug product to be used in a Phase 2 study.[228] Patheon failed to evaluate whether Suite 2 was suitable to produce the drug product.[229] The subsequent root cause analysis "determined that a potential root cause could be attributed to a change in Suites and Equipment."[230] Patheon's use of Suite 2 without evaluating its suitability for the production of drug product for a Phase 2 Study constitutes a failure to comply with Section 211.63's cGMP requirements.[231]

Patheon's cGMP violations were material.[232] The differences between Suite 1 and Suite 2 were significant, yet Patheon failed to evaluate those differences until

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[227] *Id*. § 211.63.

[228] JX 804 at 13; JX 799; Marshall Tr. 1852–57.

[229] JX 800; *see* Marshall Rep. ¶¶ 97–106.

[230] JX 800 at 8; JX 799.

[231] 21 CFR § 211.63 ("Equipment used in the manufacture, processing, packing, or holding of a drug product shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.").

[232] *Akorn*, 2018 WL 4719347, at *85.

three months after processing the DP Lots.[233] They resulted in the required destruction of over 8,900 vials of drug product.[234] Patheon's lack of oversight in switching to Suite 2 derailed Alexion's planned clinical trial schedule and frustrated the very purpose of Section 4.13(a).[235] Patheon's cGMP deviations constitute a material failure of cGMP, and therefore a breach of Section 4.13(a).

D. Indemnification

Alexion and Syntimmune agreed to a specific regime governing indemnification for breached representations. Section 8.2 of the Merger Agreement provides for indemnification against "Losses . . . arising out of or resulting from . . . any breach of any covenant" in the Merger Agreement.[236] The Merger Agreement defines "Losses" as "costs and expenses, including reasonable attorneys' fees and expenses" resulting from "any breach of any representation or warranty of [Syntimmune] contained in Article IV[.]"[237] Section 8.3 sets forth specific

[233] JX 1338 at 2–3; *see* JX 799 (highlighting the differences between Suite 1 and Suite 2).

[234] JX 1338 at 8 ("Customer signature on the investigation authorizes rejection and destruction of the batches AJ8794A and AK3858B impacted by this deviation per site processes.").

[235] JX 816 at 15–25 (describing the delay on planned clinical studies).

[236] Merger Agr. § 8.2.

[237] *Id*. §§ 8.1–8.1(a). Alexion does not seek attorneys' fees. DB Exp. 17 n.69.

requirements on a party submitting a direct claim for indemnification.[238]

On November 1, 2019, Alexion submitted notice of its direct claim for indemnification under Section 8.1(a).[239] The basis for Alexion's direct claim was the "impurities in the Company's supplies of drug substance" which rendered "th[e] drug product unusable."[240] Alexion's notice claimed the impurities with the drug substance and drug product resulted from a breach of Section 4.13(a).[241] The notice asserted Syntimmune breached Section 4.13(a) in the manufacture of DS Lots CMS-L-0125, CMC-L-009, and CMC-L-0079.[242] The notice stated the amount of its direct claim was for "the replacement batches of drug substance and drug product" which Alexion valued at the time of $6,983,361.08.[243] In addition to the replacement costs, Alexion noted it "suffered additional Losses" in the form of substantial delays

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[238] These include specific notice requirements. Merger Agr. § 8.3(d). While SRS claims the DP and DS issues Alexion complains of were disclosed before closing, SRS does not claim Alexion's notice failed to comply with Section 8.3's requirements. SRS Op. Br. 89–90.

[239] JX 1202.

[240] *Id*. at 1.

[241] *Id*. ("[T]he Impurity and Stability Issues resulted from the failure of the Product Candidates to be (and at all times to have been) manufactured in compliance in all material respects with the FDA's good manufacturing practices ('GMP') in effect at the time of the Closing.").

[242] *Id*. at 1–2. DS Lot CMC-L-0079 became DP Lot AJ8794A. *Alexion II*, 2025 WL 1089166, at *3 n.34.

[243] JX 1202 at 2.

to its planned clinical studies.[244]

I take on the replacement costs first. Alexion seeks $13,368,796.33 for the direct costs and expenses it incurred to manufacture replacement DS and DP, and personnel costs to investigate and remediate Syntimmune's cGMP failures.[245] To replace DS Lots CMC-L-0125 and CMC-M-0009, Alexion had to manufacture two replacement drug substance lots at 2000L scale and at the 50mg/mL concentration.[246] Alexion manufactured CMC-N-0040 to replace DS Lot CMC-L-0125, at a cost of $2,590,669.60.[247] Alexion manufactured CMC-N-0041 to replace DS Lot CMC-M-0009, at a cost of $2,490,997.53.[248] As for DP Lots, Alexion manufactured drug substance lot CMC-N-0039 to replace DP Lot AJ8794, at a cost

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[244] *Id*.

[245] DB Exp. 18–21; ALXN Op. Br. 37–44. While Alexion claims its actual costs were more than $16.6 million, the amount claimed subtracts out a settlement between Alexion and AGC. *See* JX1242; DB Exp. 18 n. 70. Alexion also sought indemnification in the amount of $2,540,958.38 for the costs incurred to replace DS Lot CMC-M-0010. DB Exp. 18; Marshall Rep. ¶ 131. But the Court ruled "CMC-M-0010 was not intended for human use," and therefore is not included under Section 4.13(a)'s representations. *Alexion*, 2025 WL 1089166, at *1 n. 6.

[246] Marshall Rep. ¶ 128. DS Lot CMC-L-0125 was filled into 2,053 5mL vials of finished drug product at Patheon, but Alexion does not seek to recover "an additional allocation for filling replacement drug product vials to replace this 15L stability drug product fill." *Id*. ¶ 128 n. 157; *see* JX 804 at 5.

[247] JX 1754.02 at ALXN1830; Marshall Rep. ¶ 128 n.159; *see* JX 1027; JX 1593.03; JX 1081; JX 1148; JX 1031; JX 1257.04; JX 1184.

[248] Marshall Rep. ¶ 128 n.162; *see* JX 1027; JX 1128; JX 1201; JX 1697; JX 4002; JX 1247.

of $2,821,208.[249] DP Lot AK3858 was filled from DS Lot CMC-L-0125, which was replaced with CMC-N-0040.[250] To replace DP Lots AF6404A and AG3356A, Alexion manufactured CMC-N-0018, which was filled into drug product lot 028G19A, at a cost of $3,212,681.20.[251]

SRS's argument against indemnification of those costs is limited to restricting the lots. SRS argues Alexion is limited to seeking indemnification for the replacement costs of the three specific DS Lots identified in Alexion's Counterclaim: CMC-N-0039, CMC-N-0040, and CMC-N-0041.[252] The Court previously ruled that DP Lots AK3858, AF6404A, and AG3356A were tried by consent.[253] So the fact that they were not identified in the Counterclaim is no reason to exclude them from indemnification.[254] Alexion is entitled to $11,115,556.33 in

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[249] JX 1754.02 at ALXN1830; Marshall Rep. ¶ 129 n.165; *see* JX 948; JX 1147; JX 1250; JX 940; JX 1183; JX 4003 at 17.

[250] *Alexion II*, 2025 WL 1089166, at *3 n.35.

[251] JX 1754.02 at ALXN1830; Marshall Rep. ¶ 130 n.169; *see* JX 948; JX 1249.07; JX 1249.06; JX 1249.05; JX 1249.04; JX 1249.04; JX 1249.04; JX 1249.03; JX 1132.03; JX 4003 at 17.

[252] SRS Ans. Br. 50–1; Counterclaim ¶ 113. To be clear, SRS's argument is based on the Counterclaim, not Alexion's initial indemnification notice.

[253] *Alexion II*, 2025 WL 1089166, at *3 n.42.

[254] *Id.*; *see Zutrau v. Jansing*, 2014 WL 6901461, at *3 (Del. Ch. Dec. 8, 2014), *aff'd*, 123 A.3d 938 (Del. 2015) (noting Rule 15(b) is "intended to correct the theory of an existing claim and not to assert new or different claims" (internal quotation omitted)).

costs to manufacture replacement drug substance and drug product lots due to Syntimmune's breach of Section 4.13(a).[255]

Alexion also seeks indemnification to cover the personnel cost for twelve employees it claims investigated and remediated Syntimmune's cGMP failures.[256] Alexion relies on its expert Yogesh Bahl's analysis to substantiate that request.[257] But the Court struck Bahl's report from the record as untimely and precluded Bahl from testifying.[258] Alexion fails to provide any other evidence of personnel costs. Alexion is not entitled to indemnification of those costs.

Finally, Alexion seeks to recover "benefit-of-the-bargain damages" based on the amount that would put Alexion in the position it would have been in if Syntimmune's representation in Section 4.13(a) had been true.[259] Alexion claims if

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[255] Merger Agr. § 4.13(a).

[256] ALXN Op. Br. 38 n.157 (citing JX2551); JX 2551 (Bahl CRE Rebuttal Report).

[257] ALXN Op. Br. 38; DB Exp. 18–20; DB Exp. 20 n.77 ("In addition, but-for the Court's order excluding such testimony [ ], Alexion would have offered the expert testimony of Yogesh Bahl quantifying the damages, including diminution in value damages, that Alexion suffered as a result of Syntimmune's breaches of §4.13."). Alexion seeks $300,000 per FTE associated with its remediation and replacement efforts and argues Marshall's report provides evidence of this expenditure (ALXN Op. Br. 38–39), but Marshall's report fails to calculate an FTE cost. Marshall Rep. ¶ 126 (noting he spoke with two Syntimmune employees and concluding "it is my opinion that utilizing 7 FTEs for an investigation and mitigation effort of this scale is typical and reasonable").

[258] D.I. 272.

[259] ALXN Op. Br. 39–44.

it had known clinical trials would be delayed by a year, it would have sought "a very different deal with a very different up-front and earnout" structure.[260] Alexion seeks the contractual maximum of half the purchase price, which Alexion calculates in briefing at $374,854,080.[261]

As SRS points out, this figure is wholly unsupported by any evidence. Under Delaware law, the standard remedy for breach of contract is based upon the parties' ex ante reasonable expectations.[262] "Expectation damages are calculated as the amount of money that would put the non-breaching party in the same position that the party would have been in had the breach never occurred."[263] The Supreme Court has explained "expectation damages must be proven with reasonable certainty, and 'no recovery can be had for loss of profits which are determined to be uncertain, contingent, conjectural, or speculative.'"[264] While the law does not "require

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[260] *Id*. (quoting Sarin Tr. 980).

[261] Merger Agr. § 8.4(a); ALXN Op. Br. 43; DB Exp. 21 (calculating half the purchase price).

[262] *Siga Techs., Inc. v. PharmAthene, Inc.*, 132 A.3d 1108, 1130–31 (Del. 2015); *E.I. DuPont de Nemours & Co. v. Pressman*, 679 A.2d 436, 445 (Del. 1996) (observing that "damages for breach of contract have been limited to the non–breaching parties' expectation interest").

[263] *Cobalt Operating, LLC v. James Crystal Enters*., 2007 WL 2142926, at *29 (Del. Ch. July 20, 2007), aff'd, 945 A.2d 594 (Del. 2008).

[264] *Siga Techs., Inc.*, 132 A.3d at 1131 (quoting *SIGA Techs., Inc. v. PharmAthene, Inc*., 67 A.3d 330, 351 (Del. 2013)).

certainty in the award of damages where a wrong has been proven and injury established," mere speculation is insufficient to provide the Court with a responsible estimate of damages.[265] Plaintiffs must prove their damages by a preponderance of the evidence.[266] "[W]hen acting as the fact finder, this Court may not set damages based on mere 'speculation or conjecture' where a plaintiff fails to adequately prove damages."[267]

Even assuming the cGMP violations delayed Alexion's progress by a year,[268] and even if the cost of that delay would put Alexion back in the position it expected to be in but for the breaches of Section 4.13, Alexion did not provide any estimate for the cost of that delay at trial. Alexion first tried to prove it was out half the purchase price through an expert witness, but that expert was excluded before trial because his report was untimely.[269] At trial, Alexion's lead negotiator and later CFO, Dr. Aradhana Sarin, testified the delay had some unquantified effect on the value of

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[265] *Delaware Exp. Shuttle, Inc. v. Older,* 2002 WL 31458243, at *17 (Del. Ch. Oct. 23, 2002).

[266] *Beard Rsch., Inc.*, 8 A.3d at 613.

[267] *Id.* (quoting *Medek v. Medek,* 2009 WL 2005365, at *12 n.78 (Del.Ch. July 1, 2009)).

[268] Sarin Tr. 974.

[269] D.I. 272 (striking the expert report and precluding expert testimony from Yogesh Bahl); *see* D.I. 257 ¶¶ 22–31 (arguing Alexion did not identify its diminution of value theory, which Bahl was going to present, until after the expert disclosure deadline); D.I. 266 ¶¶ 17–23; D.I. 269.

the deal. Sarin testified:

> [H]ad we known that we would not have cGMP product to start studies right away and it would be a year later that we would actually be able to dose patients, you know, it would have had an impact on value, it would have had an impact on whether we even pursued it or not. You don't want to be fourth to market. That's just not a good position to be in. So I think it would have been very different had we known that we wouldn't be able to start right away, and it would take -- you know, would be delayed by a year. That's a very different value and commercial proposition.[270]

Sarin testified knowledge of the cGMP manufacturing issues would have impacted the "commercial sensitivity" of the deal, including the net present value ("NPV") of the deal.[271] Sarin also testified that the success rate of Alexion's sensitivity models factored in the potential success rate of clinical trials.[272] Sarin did not quantify the value of the one-year delay.

There is no record evidence in the record of that value. Alexion's argument that it is entitled to approximately $350 million in damages relies solely on Sarin's testimony on the impact the problematic DS and DP Lots had on Syntimmune's value. Alexion concedes it did not quantify these damages, as it was relying on the

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[270] Sarin Tr. 974–75.

[271] *Id*. 977–79 (testifying to the commercial sensitivity reflected on JX 609 at 29); *see* JX 609 at 29.

[272] Sarin Tr. 1021–22.

expert who was excluded before trial.[273] Alexion's contentions as to the value of Syntimmune's breach are entirely speculative and insufficient under Delaware law.[274]

E. Conclusion

For the foregoing reasons, Alexion is entitled to indemnification in the amount of $11,115,556.33. The parties shall confer and submit a proposed implementing order for the Court's consideration, and a final order and judgment for this case.

Sincerely,

/s/ Morgan T. Zurn

Vice Chancellor

MTZ/ms

cc: All Counsel of Record, via *File & ServeXpress*

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[273] DB Exp. 20 n.77.

[274] *E.g.*, *In re Mobilactive Media, LLC*, 2013 WL 297950, at *24 (Del. Ch. Jan. 25, 2013); *Doft & Co. v. Travelocity.com Inc.*, 2004 WL 1152338, at *5–6 (Del. Ch. May 21, 2004) (finding management projections unreliable in the context of an appraisal action because, among other reasons, management themselves did not regard them as reliable); *OptimisCorp v. Waite*, 2015 WL 5147038, at *82 (Del. Ch. Aug. 26, 2015) (holding that the court cannot award speculative damages), *aff'd*, 137 A.3d 970 (Del. 2016); *Ivize of Milwaukee, LLC v. Compex Litig. Supp., LLC*, 2009 WL 1111179, at *11 (Del. Ch. Apr. 27, 2009) (same); *Am. Gen. Corp. v. Cont'l Airlines Corp.*, 622 A.2d 1, 12 (Del. Ch. 1992) (same); *Twardowski v. Jester*, 163 A.2d 242, 224 (Del. Ch. 1960) (same).