IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GALDERMA LABORATORIES L.P.
and TCD ROYALTY SUB LP,

Plaintiffs,

v. No. 21-cv-1710

LUPIN INC. and LUPIN LTD.,

Defendants.

Jack B. Blumenfeld, Jeremy A. Tigan, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, Delaware; Andrew J. Cochran, Gerald J. Flattman, Jr., CAHILL GORDON & REINDEL LLP, New York, New York.

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MEMORANDUM OPINION

March 22, 2024

BIBAS, *Circuit Judge*, sitting by designation.

Speculation is not science. Scientific theories need evidence to back them up. Without evidence, they are mere conjecture.

Galderma has a theory but no proof. It alleges that Lupin infringed its patents. But it did not back that theory up with evidence, relying instead on conclusory conjecture. So I reject its patent-infringement claim.

I. GALDERMA SUES LUPIN FOR PATENT INFRINGEMENT

A. Galderma treats rosacea using its patented doxycycline capsule, Oracea

Rosacea, a form of acne, causes a distinctive reddening of the face. Tr. 75:22–23. It can mirror the look of an alcohol flush, leading to inflamed, rosy cheeks. Tr. 137:20–138:4.

Fortunately for sufferers of rosacea, Galderma has a treatment. It holds several patents for a once-daily doxycycline capsule. *See* U.S. Patent No. 7,749,532; U.S. Patent No. 8,206,740. Together, the '532 and '740 patents are called the Chang patents. Tr. 13:12–14. And the commercial embodiment of the Chang patents is Galderma's drug, Oracea. Tr. 84:10–13.

In higher doses, doxycycline has an antibiotic effect. Tr. 77:2–7. But Oracea releases too little doxycycline to cause that effect. Tr. 138:5–18. Instead, its smaller dose serves as an anti-inflammatory, reducing redness in the cheeks and providing relief from rosacea. *Id.*

To ensure a consistent dose, Oracea releases some doxycycline up front and the rest over time. PTX-001, at 8; PTX-002, at 12. That lets it maintain steady-state blood levels of doxycycline between 0.1 and 1.0 μg/ml. PTX-162, at 5. To do that, Oracea has an immediate-release portion of 30 mg and a delayed-release portion of 10 mg. *Id.* The delayed-release portion is covered by an enteric coat that prevents it from releasing until it is exposed to a higher pH. Tr. 113:1–21.

The two-step release tracks the path of a capsule through the digestive system. When taken, a capsule travels quickly to the stomach. Tr. 67:8–68:1, 623:6–624:8. There, the low pH causes the immediate-release portion to break down into liquid form. Tr. 502:23–503:5. But the delayed-release portion's coating lets it remain in solid pellets. Tr. 503:13–18.

The liquid doxycycline and delayed-release pellets soon slide into the small intestine. Tr. 503:20–504:22. There, they first enter the duodenum. Tr. 73:13–14. Because the duodenum has a higher pH than the stomach, the delayed-release portion starts to break down. Tr. 254:16–24, 505:2–17. Eventually, whatever remains travels to the rest of the small intestine (or distal small intestine). Tr. 73:16–19. Any leftover solids then pass into the colon. Tr. 74:1–8.

Doxycycline absorbs into the bloodstream at different rates in different parts of the body. Absorption starts in the duodenum, where doxycycline absorbs into the bloodstream at a high rate. Tr. 73:19; PTX-176, at 175. But the rate falls off in the distal small intestine and even more so in the colon. PTX-176, at 175.

B. Galderma files this patent-infringement suit

Hoping to sell a rosacea treatment of its own, Lupin submitted an Abbreviated New Drug Application for a 40-mg doxycycline drug. DTX-027, at 1. Lupin claimed that its drug would have a 22-mg immediate-release portion and an 18-mg delayed-release portion. PTX-198, at 11; DTX-046, at 10. As part of its application process, Lupin manufactured and tested a large batch of around 230,000 capsules. DTX-046, at 11. In addition, it went on to manufacture a small batch of around 6,000 capsules

during this litigation. Tr. 357:23–358:5. Based on Lupin's testing, the FDA tentatively approved its drug as bioequivalent to Galderma's Oracea. DTX-027, at 1.

Galderma then sued Lupin under the Hatch-Waxman Act, asserting infringement of various claims of the Chang patents. D.I. 1, at 7–9. Galderma would later narrow its focus to four claims: claims 1 and 16 of the '532 patent plus claims 1 and 20 of the '740 patent. Tr. 79:11–14. Though the full text of these claims can be found in the appendix, claim 1 of the '532 patent is representative:

> An oral pharmaceutical composition of doxycycline, which at a once-daily dosage will give steady state blood levels of doxycycline of a minimum of 0.1 μg/ml and a maximum of 1.0 μg/ml, the composition consisting of (i) an immediate release (IR) portion comprising a drug, wherein the drug consists of about 30 mg doxycycline; (ii) a delayed release (DR) portion comprising a drug, wherein the drug consists of about 10 mg doxycycline, in which the DR portion is in the form of pellets coated with at least one enteric polymer; and (iii) one or more pharmaceutically acceptable excipients.

After a *Markman* hearing, I clarified several terms involved in these claims. I construed "immediate release" to mean "[a] dosage form that is intended to release substantially all of the active ingredient on administration with no enhanced, delayed, or extended release effect, where 'on' includes immediately after, and 'release' is a functional limitation referring to a release that alters the subject's steady-state blood level of doxycycline." *Galderma Lab'ys L.P. v. Lupin Inc.*, 2023 WL 2867215, at *2 (D. Del. Apr. 7, 2023) (emphasis omitted). In turn, immediate-release portion is "[a] functional limitation meaning any part of the claimed composition that releases drug immediately upon administration, with no enhanced, delayed or extended release effect.'" *Id.* at *4 (internal quotation marks omitted).

By contrast, delayed-release portion refers to "[a] functional limitation meaning any part of the claimed composition that delays release of a drug until a time other than immediately following oral administration, e.g., through coating, uncoated matrix, or other impediment to delay release." *Id.* (internal quotation marks omitted). I also noted that "if release is 'delayed' after thirty minutes, it is 'immediate' before then." *Id.* at *2. And because I defined the portions in functional terms, the thirty-minute threshold refers to time in the body, or *in vivo*. *Id.* at *2–3.

The patent-prosecution history also limits how to construe these claims. As noted by Judge Stark, a person of ordinary skill in the art "would understand that 'about 30 mg' of doxycycline represents at most a range of 27 to 33 mg of doxycycline." *Galderma Lab'ys, L.P. v. Sun Pharm. Indus. Ltd.*, 411 F. Supp. 3d 271, 282 (D. Del. 2019). Applying that same 10% plus-or-minus range to the delayed-release portion, a person of ordinary skill in the art would also understand "about 10 mg" of doxycycline to mean a range of 9 to 11 mg. Tr. 512:16–20.

C. At trial, Galderma's expert testified that Lupin infringed

Galderma called one expert witness at trial, Dr. Edward Rudnic. He testified that Lupin's drug infringed the Chang patents. Tr. 78:1–6. He began by describing the relevant practitioner for patent-infringement analysis: "[A] person of ordinary skill in the art is a person with education and experience in drug delivery and formulation science…. And that person could be any person with a Bachelor's degree with many years of experience or somebody with a higher degree with lesser years of experience." Tr. 77:10–15.

He then identified two peculiar elements of Lupin's drug design: (1) the use of methylene chloride; and (2) the coating having a weight gain of only 18% (the amount of weight added to the pellet by the coating). Tr. 91:12–16. In combination, Dr. Rudnic considered these design elements to be evidence of Lupin's intent to infringe Galderma's patents by creating a leaky enteric coating. Tr. 108:1–7.

To support his theory, he offered three pieces of evidence. First, he claimed that using methylene chloride in the coating process is uncommon because of its toxicity. Tr. 91:17–93:2; PTX-136, at 1–3. Second, he said that Lupin's 18% weight coating on its drug was the least possible coating that it could use to satisfy quality-control tests. Tr. 102:20–103:3. In support of that, Dr. Rudnic cited Lupin's test results showing that 16% and 17% weight-gain coatings had failed. Tr. 105:11–17; PTX-186, at 103. He contrasted that with Oracea's average weight gain of 30% and even higher weight gains on other drugs he had commercialized. Tr. 104:5–17. Third, he testified that scanning-electron-microscope images appeared to show the coat on Lupin's drug not adhering properly. Tr. 98:11–99:10; *see* DTX-083, at 14–15, 27.

From this evidence, Dr. Rudnic posited that Lupin had designed its drug to have a weak coating, which would lead about 8 mg of "delayed-release" pellets to leak and release immediately. Tr. 132:25–133:9. And he pointed to a test from Lupin's application that allegedly confirmed this hypothesis: the two-stage test. In that test, twelve of Lupin's drug capsules were first put in a pH-1.1 liquid for two hours. PTX-194, at 37. Then, a pH-11 liquid was added until the mixture reached pH 4.5. *Id.* The

capsules remained in that pH-4.5 liquid for another two hours. *Id.* The results of that test are shown below, comparing Lupin's results with Oracea's.

LUPIN INC. **Module 5**

PRODUCT: DOXYCYCLINE CAPSULES	**ORIGINAL ANDA**
Section	**5.3 – Clinical Study Report**
Subsection	**5.3.1 – Reports of Biopharmaceutics Studies**
Sub-subsection	**5.3.1.3 – In vitro In vivo Correlation Study Report**

Table 14 Comparative Dissolution Profile for Doxycycline Capsules, 40 mg Vs ORACEA® (doxycycline, USP) Capsules, 40 mg (RLD) [Multimedia Dissolution study - pH 1.1 HCl Followed by pH 4.5 phosphate buffer]

Product	Batch No.	Stage	Time in Min.	% Doxycycline Dissolved																Date of Analysis
				1	2	3	4	5	6	7	8	9	10	11	12	Min	Max	Mean	% RSD	
Doxycycline Capsules, 40 mg **[Test Product]**	M19 0018	**pH 1.1 HCl (Acid)**	**30**	46	53	50	50	50	53	52	51	49	50	49	49	**46**	**53**	**50**	**3.88**	02-Sept -2021
			60	49	54	54	53	52	54	54	54	52	52	50	51	**49**	**54**	**52**	**3.3**	
			120	52	53	55	55	54	54	54	54	54	54	52	53	**52**	**55**	**54**	**1.83**	
		pH 4.5 Phosphate (Buffer)	**150**	78	57	62	57	58	85	84	58	58	58	55	58	**55**	**85**	**64**	**17.63**	03-Sept -2021
			180	93	60	83	59	60	95	93	67	60	60	57	60	**57**	**95**	**71**	**21.98**	
			240	95	64	93	62	62	96	93	86	62	62	59	62	**59**	**96**	**75**	**21.48**	
ORACEA® (doxycycline, USP) Capsules, 40 mg **[RLD]**	AL238 9A	**pH 1.1 HCl (Acid)**	**30**	71	71	76	77	72	72	70	76	73	77	77	76	**70**	**77**	**74**	**3.69**	17-Aug-2021
			60	71	73	77	77	72	71	72	76	73	76	77	76	**71**	**77**	**74**	**3.31**	
			120	71	72	76	77	72	71	72	76	72	76	77	75	**71**	**77**	**74**	**3.29**	
		pH 4.5 Phosphate (Buffer)	**150**	63	64	63	71	65	71	64	71	66	69	73	67	**63**	**73**	**67**	**5.35**	
			180	65	64	64	72	63	72	64	71	67	69	72	68	**63**	**72**	**68**	**5.26**	
			240	65	65	64	71	65	71	65	72	67	72	69	67	**64**	**72**	**68**	**4.54**	

Seizing on Lupin's results at 150 minutes and beyond, Dr. Rudnic pointed out that five of Lupin's capsules had failed by releasing doxycycline prematurely. Tr. 116:11–21. He also noted that Lupin's capsules released 75 percent of their doxycycline by the end of 240 minutes. *Id.* And seventy-five percent of 40 mg is 30 mg, the exact amount of doxycycline that Oracea releases immediately. *Id.*; PTX-162, at 5.

Dr. Rudnic found this relevant because he testified that the pH of the stomach ranges from 2.2 to 5, with 3 being a good average. Tr. 64:25–65:3. Because pH 4.5 falls within that range, he concluded that these results show that Lupin's delayed-

release pellets would dissolve in the stomach and release immediately. Tr. 132:7–14. But he admitted that at pH 1.1, Lupin's drug released only 22 mg of doxycycline. Tr. 185:15–186:2.

He also disagreed with Lupin's suggestion that hotspots could have caused the unusual test results. Tr. 118:23–119:2. That theory suggests that adding a high-pH liquid during testing might lead to isolated pockets with very high pH values, or hotspots, causing pellets' coatings to fail. Tr. 119:10–22. But in Dr. Rudnic's opinion, hotspots are "ghost[s]" that "[n]o one has ever proven … exist[]." Tr. 118:25–119:1. And he discounted any testing on Lupin's small batch because the FDA had not tested it. Tr. 122:22–123:12.

D. Lupin's experts disagree with Dr. Rudnic

In response, Lupin called three witnesses. First was Makarand Avachat, its executive vice president of research and development. He disagreed with several of Dr. Rudnic's claims about Lupin's manufacturing process and the differences between the application and small batches. And he explained that any methylene chloride used in the manufacturing process evaporates away. Tr. 346:14–18.

Avachat further testified that the small batch was representative of the large batch. Tr. 366:9–11. And though Lupin had not submitted the small batch to the FDA for testing, he said that it did not have to. Tr. 366:25–367:6; *see also* Tr. 647:7–14. But he conceded that Lupin's manufacturing process had differed in some ways between the two batches, including different atomization, air pressure, air flow, spray rate, and equipment. Tr. 359:5–360:5; *see* DTX-613.

Next, Lupin called a dissolution expert, Vivian Gray. She testified that the two-stage test was unreliable. Tr. 398:16–18, 400:16–24. In particular, she noted several anomalies in the results. First, for many of the Oracea tablets, the percentage of dissolved doxycycline went *down* in the second stage. Tr. 399:12–17. Second, the test results for Lupin's drug had a high relative standard deviation (and showed much more variability than usual). Tr. 398:14–399:9. From these anomalies, she concluded that there might have been errors in the testing method. Tr. 400:18–20.

To verify that conclusion, Gray did a single-stage test on Lupin's small batch at pH 4.5. Tr. 407:7–14. After two hours, it had released 55.4% doxycycline on average and Oracea had released 73.7%. Tr. 408:21–409:9; DTX-054, at 2, 5. In other words, none of Lupin's delayed-release pellets dissolved in the single-stage pH-4.5 test. *See id.* (both sources). So, she reasoned, the two-stage test's anomalous results likely stemmed from hotspots that had developed in the testing vessels. Tr. 401:16–20.

Lastly, Lupin called its main expert, Dr. Graham Buckton. He largely disputed Dr. Rudnic's testimony. Dr. Buckton testified that pH in a *fed* stomach may be higher, but the pH of a *fasted* stomach ranges from 1 to 2. Tr. 485:15–486:5. That matters because patients must take Lupin's drug on a fasted stomach. Tr. 488:1–2. And though he admitted that the pH could be slightly higher after a person drinks water, he said that "pH 1.1 is undoubtedly biorelevant" for a fasted stomach. Tr. 486:10–487:14; 488:10.

Dr. Buckton also countered Dr. Rudnic's testimony about the coating of Lupin's drug. Although he agreed that a normal weight-gain range is 20–40%, he disagreed

that Lupin's 18% coating made for either a weak or incomplete coat. Tr. 537:16–538:4. Rather, he highlighted that the 18% weight coating had released no doxycycline when tested. Tr. 539:17–20. Likewise, he thought the scanning-electron-microscope images showed breakage typical of a capsule being split open, not an incomplete coating. Tr. 547:9–24, 561:10–562:19.

Finally, Dr. Buckton concluded that even though the two-stage test showed that some of Lupin's *capsules* had failed, it could not be used to draw inferences about the behavior of Lupin's delayed-release *pellets*. Tr. 524:1–526:14. And he testified that Dr. Rudnic's use of the mean release at 240 minutes was inappropriate, because "you can't take a mean with [a] bimodal distribution and say everything does that." Tr. 526:18–20.

II. GALDERMA'S PATENT-INFRINGEMENT CLAIM FAILS

Because Galderma claims patent infringement under federal patent law, I have subject-matter jurisdiction under 28 U.S.C. §§ 1331 and 1338(a). So I proceed to the merits.

A. Galderma cannot show direct infringement

To prove direct infringement, a plaintiff must show by a preponderance of the evidence either (1) literal infringement or (2) infringement under the doctrine of equivalents. *Pozen Inc. v. Par Pharm., Inc.*, 696 F.3d 1151, 1167 (Fed. Cir. 2012). A drug *literally* infringes if it contains every element of an asserted claim. *V-Formation, Inc. v. Benetton Grp., SpA*, 401 F.3d 1307, 1312 (Fed. Cir. 2005). A drug infringes under the doctrine of equivalents if it contains an element "identical or equivalent to

each claimed element of the patented [drug]." *Pozen*, 696 F.3d at 1167 (cleaned up). In other words, close counts in horseshoes, hand grenades, and the doctrine of equivalents.

Lupin agrees that its drug contains most elements of the asserted claims. Tr. 87:12–25. But it says that its drug releases 22 mg of doxycycline immediately and 18 mg after a delay. *See, e.g.*, Tr. 87:25–88:2. So it contests whether its drug has "an immediate release … portion … of about 30 mg doxycycline" and "a delayed release … portion of about 10 mg doxycycline." PTX-001, at 14. Infringement thus turns on that issue.

I evaluate whether Lupin has infringed from the perspective of a person of ordinary skill in the art, the "reasonable person" standard in patent law. *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). And I accept Dr. Rudnic's definition of a person of ordinary skill in the art. *See* Tr. 77:10–15.

1. Galderma cannot prove literal infringement. For literal infringement, Galderma must show that about 8 mg of Lupin's 18-mg delayed-release portion releases immediately. To do that, Galderma puts forth a simple syllogism: "Lupin designed its [drug] to have a weak enteric coat." Tr. 88:11. That weak coat leaks, causing "about 8 milligrams of doxycycline in the [delayed-release] portion … [to] immediately release[]." Tr. 133:5–6. And this "results in a 30:10 composition ratio," "infring[ing] the Chang patents." Tr. 88:12–13.

But Galderma does not show its work. Rather than wrestling with pesky facts, it instead appeals to authority—its expert, Dr. Rudnic. Unfortunately for Galderma, I found him unauthoritative. He repeatedly presented wild guesses as scientific fact,

failed to back up those guesses with hard evidence, and was remarkably combative when pressed on the lack of support for his claims. Though he is highly credentialed, credentials alone do not make a witness credible. By contrast, I found Dr. Buckton thoroughly credible. So aside from a few instances below, I wholly credit Dr. Buckton's testimony over Dr. Rudnic's.

In any event, Galderma's infringement theory does not hold water. Take its first premise: Lupin intentionally designed its drug to have a weak enteric coat. But Galderma's generalized argument about the toxicity of methylene chloride does not prove Lupin's intent, especially when the methylene chloride evaporates in the coating process. Tr. 346:12–19.

True, Lupin uses a lower-than-normal weight coating on its drug. PTX-186, at 103–04. So some delayed-release pellets likely get a coating of less than 18% weight gain. Tr. 102:1–4. Yet Dr. Rudnic did not even estimate how many pellets would get a lighter coating. Tr. 101:3–102:5. Nor did he give any evidence showing that nearly half of the delayed-release pellets would leak. *See id.* On the contrary, Lupin's data show that even at a 16% weight coating, only 1% of doxycycline leaks. PTX-186, at 103. That falls far short of what Galderma's theory requires.

Next, to support its premise that about 8 mg of delayed-release pellets leak, Galderma relies on the two-stage test. But that test does not patch up the holes in its leaky argument, for three reasons.

First, Galderma improperly tries to draw conclusions about *in vivo* behavior from the second-stage *in vitro* test results at pH 4.5. It argues that the first stage of the

test is only "a stress test" that "is not [at] a relevant pH in the stomach." Tr. 111:19–22. And it says that "the clock starts over again" once the second stage arrives, bringing with it the "physiologically relevant stomach pH" of 4.5. Tr. 71:14, 111:19.

But Galderma is wrong on both counts. Neither party disputes that, upon ingestion, a capsule travels quickly to the stomach, where it stays for less than an hour before entering the duodenum. Tr. 67:8–68:1; 623:6–624:8. I credit Dr. Buckton's testimony that the pH of a fasted stomach is between 1 and 2, though it could be slightly higher for a short time right after drinking water. Tr. 486:8–13; *see* PTX-149, at 5 ("Median pH value was 2.4 twenty minutes after administration of water and stabilized to 1.7 at later time points."). In the duodenum, the doxycycline confronts a pH of around 5.5. Tr. 489:18–22. So the first stage is not just a stress test: it represents the capsule's arriving in the stomach and spending time at pH 1.1, "the standard industry representation of the [fasted] human stomach." Tr. 480:19–20. And at that pH, even Dr. Rudnic agreed that Lupin's drug released only 22 mg immediately. Tr. 185:15–186:2.

Nor does the clock start over again at the second stage. As Dr. Buckton observed, "if you soak something in acid [for] two hours, you can't say [that] has done nothing." Tr. 527:6–7. Even if the enteric coat does not release at pH 1.1, the capsule "has at least hydrated in the acid for two hours." Tr. 527:8. And a capsule in the body would rarely if ever spend such a long time at pH 1.1 before passing into the duodenum. To say otherwise would require ignoring the "stress" in "stress test." *Cf.* PTX-145, at 2

("While these [quality-control] methodologies have existed for many years and have been used extensively, none accurately reflect[s] *in vivo* conditions.").

Plus, though the second-stage pH of 4.5 may exist in some stomachs, it is not a physiologically relevant pH for a fasted stomach. Indeed, pH 4.5 better approximates the pH of the duodenum than of a fasted stomach. *See* Tr. 486:8–13, 489:18–22. And the '532 patent confirms this: "With the enteric coated pellets, there is no substantial release of doxycycline in the acidic stomach environment of approximately *below* pH 4.5." PTX-001, at 11 (emphasis added). So Galderma cannot draw valid conclusions about *in vivo* behavior by looking to the second-stage results at pH 4.5.

Second, even if those test results could reliably show *in vivo* behavior, evident flaws in the data called for more investigation, not blind reliance. Not only did Lupin's drug have a high relative standard deviation, but also the percentage of the dissolved doxycycline went *down* for most of the Oracea capsules—an impossible result. Tr. 398:13–399:17; PTX-194, at 37. And as Galderma pointed out when cross-examining Dr. Buckton, the U.S. Pharmacopeia suggests that "the two most likely causes of … variability are the formulation itself … or artifacts associated with the test procedure." Tr. 640:7–10; DTX-101, at 5.

Given these two possible causes of variability, Galderma should have investigated further. Further investigation would have revealed a test in Lupin's application that used pH 1.1 followed by pH 5.5. *See* DTX-075, at 28. In that test, neither drug exhibited the same flaw as in the two-stage test, and Lupin's drug released 22 mg

immediately and 18 mg after a delay. *See id.* This should have been a clue that errors in Lupin's formulation do not explain the two-stage test results.

The more plausible explanation is "artifacts associated with the test procedure." Tr. 640:9–10. Perhaps hot spots developed in Lupin's mixture based on how quickly the higher-pH liquid was added. *See* DTX-313, at 1; Tr. 410:7–22. Or perhaps Galderma's capsules would have displayed the same behavior if the percentage of dissolved doxycycline had not declined. *See* PTX-194, at 37.

But I need not speculate, for Lupin gave yet another clue by doing more testing. In a single-stage test at pH 4.5, its capsules displayed none of the same issues as the two-stage test. DTX-054, at 5. The single-stage test also shows that Lupin's drug had a 22-mg immediate-release portion plus an 18-mg delayed-release portion. *Id.* Together, these clues are conclusive: The two-stage test results are anomalous. And all the evidence suggests that the anomaly resulted from testing error.

Galderma protests that there is no "general rule requiring one who alleges infringement of a claim containing functional limitations to perform actual tests or experiments on the accused product." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1374 (Fed. Cir. 2009). True. But neither is there a rule against it. And though Lupin performed the validation testing on its small batch, Galderma offers no evidence showing that batch differed from its large batch in any meaningful way. *See* DTX-613; *Par Pharms., Inc. v. Eagle Pharms., Inc.*, 44 F.4th 1379, 1384 (Fed. Cir. 2022) ("[C]ourts may look to other relevant evidence, *such as* data or samples the … filer has submitted to the FDA, to assess whether a proposed product will infringe."

(emphasis added)). Galderma should have known that a person of ordinary skill in the art would not have relied on just the anomalous two-stage test to show infringement.

Third, Galderma offers a confused, conflicted argument for how the test shows infringement. Dr. Rudnic first suggested in his opening expert report that because five out of twelve capsules (or 42%) fail, we could infer that around 42% of Lupin's delayed-release pellets would fail. D.I. 130-9, at 50 & n.16. Then, at trial, he argued that infringement is proved by the mean doxycycline release of all the capsules after exposure to pH 4.5. Tr. 116:15–17. And now, in its post-trial briefing, Galderma argues that the test shows infringement because Capsule 1 "released 78 percent of its doxycycline 30 minutes after exposure to pH 4.5." Pls.' Responsive Post-Trial Br. 5.

Yet any version of Galderma's everything-but-the-kitchen-sink argument fails. Galderma never explained how I can infer that a certain percentage of *pellets* will leak based on a certain percentage of *capsules* leaking. Tr. 526:9–14. And it seemed to abandon this theory at trial. Tr. 524:1–21. So I reject that argument as meritless.

Nor can I find that Galderma proved infringement by the mean doxycycline release at one or two hours after exposure to pH 4.5. The data reflects a bimodal distribution, with some capsules releasing nearly all their doxycycline and others releasing around 60%. *See* PTX-194, at 37. As Dr. Buckton correctly observed, the mean of a bimodal distribution is not a useful statistic. Tr. 526:15–20. If it were, taking 364 sugar pills with a once-yearly capsule containing a 10,950-mg immediate-release portion and a 3,650-mg delayed-release portion would infringe. Nonsense.

Admittedly, "an accused device that sometimes, but not always, embodies a claim nonetheless infringes." *Broadcom Corp. v. Emulex Corp.*, 732 F.3d 1325, 1333 (Fed. Cir. 2013) (cleaned up). So if I credited that Capsule 1's behavior at 30 minutes into the second stage reflects *in vivo* behavior at that time in the stomach, Galderma would have shown infringement. But as Dr. Rudnic stressed, "30 minutes into the [two-stage] test is not 30 minutes … in the body." Tr. 118:2–4; *see* Tr. 110:19–21, 112:3–5, 115:19–21. And Galderma never explained how time in the test relates to time in the body. Thus, Capsule 1's behavior thirty minutes after exposure to pH 4.5 does not show infringement.

Because I reject Galderma's premises, I also reject its conclusion. I find no evidence that Lupin's drug has about a 30-mg immediate-release portion and about a 10-mg delayed-release portion. Rather, the evidence confirms that Lupin's drug has a 22-mg immediate-release portion and an 18-mg delayed-release portion. So I rule that Lupin's drug does not literally infringe.

2. Galderma cannot show infringement under the doctrine of equivalents. Under the doctrine of equivalents, Galderma must show that Lupin's drug has the equivalent of a 30-mg immediate-release portion and a 10-mg delayed-release portion. There are two tests for equivalency. First, "the function-way-result test … asks whether an alleged equivalent performs substantially the same function in substantially the same way to obtain the same result." *Galderma Lab'ys, L.P. v. Amneal Pharms., LLC*, 337 F. Supp. 3d 371, 404 (D. Del. 2018). Second, "the substantial-differences test …

asks whether the substitute element plays a role substantially different from the claimed element." *Id.* (cleaned up).

For example, *Sun Pharmaceutical* held that Sun's drug was equivalent to Oracea. Sun's drug had an immediate-release layer of 26.4 mg and a modified-release layer of 13.6 mg, but the latter would release roughly 3.6 mg in the first thirty minutes. 411 F. Supp. 3d at 278–79, 310. So under the function-way-result test, Sun's product "perform[ed] substantially the same function (immediate release of about 30 mg doxycycline), in substantially the same way (releasing about 30 mg immediately after oral administration…), to achieve substantially the same result (bioequivalence to 30 mg IR, 10 mg DR…)." *Id.* at 310.

Sun's drug also failed under the substantial-differences test. Both it and Oracea released 30 mg of doxycycline within the first thirty minutes. That made Sun's drug "insubstantially different from a composition with an IR portion consisting of 30 mg of doxycycline." *Id.*

But unlike in *Sun Pharmaceutical*, Galderma did not show that Lupin's drug released either 30 mg immediately or 10 mg after a delay. Though Galderma argues that bioequivalence is all that it needs, that is only the same *result*. *See id.* That is not enough. And all reliable evidence points to Lupin's drug having a 22-mg immediate-release portion and an 18-mg delayed-release portion, making it substantially different from Oracea. So under either test, Galderma cannot show infringement.

B. Galderma cannot show indirect infringement

Indirect infringement includes both contributory infringement and induced infringement. But Galderma cannot show either because "[a]bsent direct infringement of the

patent claims, there can be neither contributory infringement, nor inducement of infringement." *Met-Coil Sys. Corp. v. Korners Unlimited, Inc.*, 803 F.2d 684, 687 (Fed. Cir. 1986). So without direct infringement, I cannot find indirect infringement.

* * * * *

Galderma's theory masquerades speculation as science. But it does not back up that theory with evidence. So I reject its patent-infringement claim.

Appendix

Claims for the '532 Patent

Claim 1	An oral pharmaceutical composition of doxycycline, which at a once-daily dosage will give steady state blood levels of doxycycline of a minimum of 0.1 μg/ml and a maximum of 1.0 μg/ml, the composition consisting of (i) an immediate release (IR) portion comprising a drug, wherein the drug consists of about 30 mg doxycycline; (ii) a delayed release (DR) portion comprising a drug, wherein the drug consists of about 10 mg doxycycline, in which the DR portion is in the form of pellets coated with at least one enteric polymer; and (iii) one or more pharmaceutically acceptable excipients.
Claim 15	A method for treating rosacea in a mammal in need thereof, comprising administering to the mammal a daily dose of an oral pharmaceutical composition of doxycycline, which at a once-daily dosage will give steady state blood levels of doxycycline of a minimum of 0.1 μg/ml and a maximum of 1.0 μg/ml, the composition consisting of (i) an immediate release (IR) portion comprising a drug, wherein the drug consists of about 30 mg doxycycline; (ii) a delayed release (DR) portion comprising a drug, wherein the drug consists of about 10 mg doxycycline, in which the DR portion is in the form of pellets coated with at least one enteric polymer; and (iii) one or more pharmaceutically acceptable excipients.
Claim 16	The method of claim 15, wherein the mammal is a human.

Claims for the '740 Patent

Claim 1 An oral pharmaceutical composition of doxycycline, which at a once-daily dosage will give steady state blood levels of doxycycline of a minimum of 0.1 μg/ml and a maximum of 1.0 μg/ml, the composition consisting of (i) an immediate release (IR) portion comprising 30 mg doxycycline; (ii) a delayed release (DR) portion comprising 10 mg doxycycline; and optionally, (iii) one or more pharmaceutically acceptable excipients.

Claim 19 A method for treating rosacea in a mammal in need thereof, comprising administering an oral pharmaceutical composition of doxycycline comprising [sic], which at a once-daily dosage will give steady state blood levels of doxycycline of a minimum of 0.1 μg/ml and a maximum of 1.0 μg/ml, the composition consisting of (i) an immediate release (IR) portion comprising 30 mg doxycycline; (ii) a delayed release (DR) portion comprising 10 mg doxycycline; and optionally, (iii) one or more pharmaceutically acceptable excipients.

Claim 20 The method of claim 19, wherein the mammal is a human.

PTX-001, at 13–14; PTX-002, at 17–18.