UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

JANSSEN BIOTECH, INC., Plaintiff, v. CELLTRION HEALTHCARE CO., LTD., CELLTRION, INC., and HOSPIRA, INC. Defendants.	No. 1:17-cv-11008 **CONFIDENTIAL** **FILED UNDER SEAL**

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION FOR SUMMARY JUDGMENT OF NON-INFRINGEMENT BASED ON ENSNAREMENT
[Leave to File 30 Page Brief Granted April 4, 2018, Dkt. 224]

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I. Introduction

The Court should end this case as a matter of law based on ensnarement—"the longstanding principle that the prior art restricts the scope of equivalency that the party alleging infringement under the doctrine of equivalents can assert." *Conroy v. Reebok Int'l, Ltd.*, 14 F.3d 1570, 1576 (Fed. Cir. 1994). To maintain its 12-way doctrine-of-equivalents theory, Janssen—not the Defendants—have the "burden of persuasion" to establish "that the asserted scope of equivalency would not ensnare the prior art," such that the "equitabl[y]" expanded claims are patentable inventions over the prior art. *Depuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1323-24 (Fed. Cir. 2009).

Ensnarement is particularly appropriate for summary judgment because it is a "legal limitation on the application of the doctrine of equivalents," one that is "determined by the court," that is "decid[ed] as a matter of law," and that may be disposed of "on a pretrial motion for partial summary judgment." *Depuy Spine*, 567 F.3d at 1323-24; *Gemalto S.A. v. HTC Corp.*, 754 F.3d 1364, 1374-75 (Fed. Cir. 2014). In fact, the Federal Circuit has repeatedly affirmed summary judgment opinions rejecting infringement under the doctrine of equivalents based on ensnarement.

Here, too, the law bars Janssen's theory outright. The asserted claims of the '083 patent cover a cell culture media with 52 required ingredients at specified concentration ranges. For its equivalents theory against the accused media, Janssen essentially ignores the claimed concentration ranges, maintaining that numerous concentration differences well outside the claimed ranges—some as high as 400% or more above the claimed range and as low as 10% of the claimed range—are "equivalent."

Under a proper ensnarement analysis, the claimed concentration ranges are expanded to match Janssen's equivalents theory. The result is that every "equivalent" concentration range in the '083 patent—without a single exception—overlaps with the concentration ranges disclosed in

a prior art patent application filed by GlaxoSmithKline or GSK. Such "overlapping ranges," "even a slight overlap," "establishes a *prima facie* case of obviousness" (*In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003)) and a "presumption of obviousness." *Ormco Corp. v. Align Tech. Inc.*, 463 F.3d 1299, 1311 (Fed. Cir. 2006).

Janssen has made no effort to overcome this presumption, which would require a showing that there was something "critical" about its claimed concentration ranges, "generally by showing… unexpected results relative to the prior art range." *In re Geisler*, 116 F.3d 1465, 1469-70 (Fed. Cir. 1997). Far from asserting the claimed ranges are "critical," Janssen's experts and lead inventor have sworn just the opposite—testifying that the claimed ranges were *not* "critical," that there's "a broad plateau of interchangeable concentrations," and that [redacted] Ex. 1 (Wurm Dep.) at 166:5-19; Ex. 2 (1/31/2018 Hr'g Tr.) at 11:15-22; Ex. 3 (1/30/2018 Hr'g Tr.) at 82:20-83:3; Ex. 4 (Epstein Dep.) at 230:12-21; SOF[1] ¶¶ 10-15.

That leaves Janssen with only two minor differences, neither of which can possibly salvage its expanded claims as a non-obvious invention. Fifty of the '083 patent's fifty-two required ingredients match exactly with ingredients in GSK's media. For the two remaining ingredients, the '083 patent supplies two nutrients important to cell growth—vanadium and iron—by using two well-established alternatives to specific ingredients that GSK used to provide the same two nutrients. This substitution of known alternatives is the very definition of obvious under the United States Supreme Court's decision in *KSR*, which holds that the "mere substitution of one element for another known in the field" that does no "more than yield a predictable result" is unpatentably

[1] Citations to "SOF" herein refer to Defendants' Rule 56.1 Statement of Undisputed Material Facts In Support of this motion.

obvious. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007).

GSK is not the only reference that blocks Janssen's use of the doctrine of equivalents. Another reference, Life Techs, discloses 47 of the 52 ingredients required by the '083 claims, and all but one with a concentration range that overlaps with the claimed ranges. For the five ingredients not expressly disclosed, Life Techs teaches that the ingredients it uses are "examples" that serve the purpose of providing the exact same active trace element provided by the five alternative ingredients claimed in the '083 patent. Again, the "substitution" of known ingredients to "yield a predictable result"—providing the same amount of active trace ingredient—is obvious. And nothing about the one difference in concentration ranges matters, since under Janssen's own positions, it would have required nothing more than routine optimization by a skilled artisan to arrive at an overlapping range. That is not a patentable distinction.

Janssen's doctrine-of-equivalents infringement theory fails as a matter of law, and summary judgment of non-infringement should be granted.

II. Factual Background

The '083 patent is directed to a media composition for culturing animal and human cells outside of the body.

A. Scientists Have Been Developing And Optimizing Cell Culture Media For Decades Before The '083 Patent

Scientists have used cell culture media to grow cells since the 1950s, starting with the seminal work of Harry Eagle. Ex. 5 (Glacken Op.) at ¶¶ 70-75; Ex. 6 (Frohlich) at ¶ 66; SOF ¶ 21. Over sixty years ago, Eagle figured out the essential "food" categories required to grow cells: "amino acids or proteins, an energy source such as glucose or other carbohydrates, elements such as iron, lipids or fats, vitamins, and other well-known factors." Ex. 5 (Glacken Op.) at ¶ 70; Ex. 6 (Frohlich) at ¶ 63; SOF ¶¶ 22-23. "For example, in 1959, Eagle introduced a minimal essential

medium (MEM) for the growth of mammalian cells which consisted of glucose, amino acids, and vitamins in a balanced salt solution." Ex. 7 (Butler Reb.) at ¶ 13; SOF ¶ 24.

Through his research, Eagle identified the specific nutrients necessary for basic cell growth: 13 amino acids, 8 vitamins, 6 salts, and glucose, along with serum. Ex. 5 (Glacken Op.) at ¶ 76; Ex. 7 (Butler Reb.) at ¶ 13; SOF ¶ 23. "The same categories of ingredients that Eagle identified in 1955 remain the same basic nutrient groups used in cell culture media to this day." Ex. 6 (Frohlich) at ¶ 65; SOF ¶ 23. In fact, Eagle's classic MEM is still sold commercially today. Ex. 5 (Glacken Op.) at ¶ 79; Ex. 6 (Frohlich) at ¶ 66; SOF ¶ 24.[2]

For decades, skilled scientists have also known that nutrients important to cell growth could be provided by various alternative ingredients. Under Janssen's theory of infringement, what matters is not the ingredient itself, but rather the important nutrient provided by that ingredient. For example, Dr. Butler explained that two different ingredients were "interchangeable" because they both provide the nutrient "asparagine":

> Q. Would you consider asparagine and asparagine hydrate to be interchangeable sources of asparagine?
>
> A. Certainly, yes. It's the same components. It's the same active component. Essentially it's the amino acid asparagine.

Ex. 3 (1/30/2018 Hr'g Tr.) at 59:9-12; Ex. 2 (1/31/2018 Hr'g Tr.) at 11:8-14; SOF ¶ 25. He made the same point regarding "L-histidine•HCl•H20" and "L-histidine free base," explaining that both ingredients provided cells with the "same active component (L-histidine)." Ex. 10 (Butler Op.) at ¶¶ 73-74; SOF ¶ 26. Janssen's other expert, Dr. Wurm, took the same position regarding the interchangeability of various ingredients:

[2] Ex. 8 (https://www.sigmaaldrich.com/life-science/cell-culture/classical-media-salts/mem-media.html); Ex. 9 (https://www.thermofisher.com/us/en/home/life-science/cell-culture/mammalian-cell-culture/classical-media/mem.html)

> [F]or a number of the ingredients for which the Celltrion Media are literally below the claimed range… the Celltrion Media contain other ingredients that supply the same active component in solution. These additional sources of the active component offset all or most of the literal concentration differences between the Celltrion Media and claim 1 for these ingredients.

Ex. 11 (Wurm Op.) at ¶ 52; SOF ¶ 27.

Before the priority date in 2004, numerous media formulations—all using the same basic formula with numerous overlapping and alternative ingredients—were being widely used for research and commercial purposes. Ex. 5 (Glacken Op.) at ¶¶ 67-260; SOF ¶ 28. This included media formulations free of any animal or human serum, which were sold by many companies, including Gibco/Invitrogen, HyClone, Irvine Scientific, Roche, and Sigma-Aldrich. *E.g.* Ex. 12 (Serum-Free Media For Cell Culture [CELLREM-0246022]). This also included "[c]hemically defined" media—meaning all the components are known and defined—such as CD Hybridoma and CD CHO offered by Gibco/Invitrogen. *Id.* at 030; SOF ¶ 29.

B. Janssen's '083 Patent Is Not New, Especially Under Its Unprecedented Dozen-Way Doctrine Of Equivalents Theory

Janssen asserts claims 1 and 2 of the '083 patent. Claim 1 recites a cell culture media formulation of 61 ingredients, each with its own specified concentration range. Claim 2 depends from claim 1 and further recites a "buffering molecule with a pK_a between 5.9 and 7.8 and a cell protectant." Ex. 13 ('083 Patent) at Claim 2; SOF ¶ 8.

Nine of the 61 claimed ingredients list a concentration range with a lower end of zero, meaning they are optional. "[O]ptional elements do not narrow the claim because they can always be omitted," and thus are not relevant to determining a claim's patentability. *In re Johnston*, 435 F.3d 1381, 1384 (Fed. Cir. 2006).

1. Janssen removed the purported benefits of the patent by successfully arguing against construing the claims as chemically defined.

When obtaining its patent from the Patent Office—unlike before this Court—Janssen was

not touting its "invention" as some supposedly unique combination of ingredients and concentrations. Rather, Janssen focused on allegedly "inventing" a *serum-free* and *chemically-defined* media. Its 2004 application was entitled "Chemically Defined Media Compositions," and Janssen emphasized throughout that its "present invention" related to "chemically defined media compositions for the culture of eukaryotic cells." Ex. 14 (Provisional App.) at 1:4-5 and 7:3-4; SOF ¶¶ 1-2; *see also* Ex. 15 ('083 Patent Application) at 1:10-11 and 6:38-7:1. Janssen told the Patent Office that chemically *un*defined media, such as media containing serum, posed a threat to patients through "adventitious particle contamination." Ex. 14 (Provisional App.) at 1:8-37. The inventors allegedly solved that problem by creating a an "animal component free cell culture media" that is "'chemically defined' such that the media compositions contain only known chemical compounds, and are free of all proteins--even those not of animal origin such as recombinant proteins." *Id.* at 1:32-37; SOF ¶ 3.

But then during the claim construction phase of this case, Janssen urged the Court to construe the claims in way that covered chemically ***undefined*** media, such as media that include serum:

> If the inventors had wished to limit the claimed invention to those "cell culture media" that are "chemically defined," they would have used the words "chemically defined" in the claim. They did not. The plain and ordinary meaning of the claim language contains no limitation to "chemically defined" cell culture media.

E.g. No. 15-10698 Dkt. 149 at 1; SOF ¶ 4.

2. None of the ingredients were new to cell culture media.

By 2004, there was nothing special or inventive about the claimed media, especially because it is required to be neither serum-free nor chemically-defined. None of the ingredients recited in claim 1 of the '083 patent are new. They all have been used in cell culture media long before 2004, as Dr. Butler, Janssen's expert, admitted:

> Q. You couldn't if I asked you right now to say can you pick out anything on this list which these inventors are using in a cell culture medium for the first time in 2004, can you identify one?
>
> A. No.

Ex. 16 (Butler Dep.) at 55:19-24; Ex. 3 (1/30/2018 Hr'g Tr. (Butler)) at 86:15-18 ("Q. [] None of the ingredients listed in Claim 1 were new for cell media preparations as of the invention date in 2004, correct? A. Correct."); SOF ¶ 30.

Dr. Butler further concedes that 49 of the 52 ingredients were "*commonly used* in cell culture medium prior to 2004," and that the other three were used "in a minority of culture media formulation." Ex. 16 (Butler Dep.) at 58:9-17, 57:6-19 (emphasis added); SOF ¶ 31. Dr. Butler likewise admitted that skilled scientists use these common and known ingredients to make useful cell culture media:

> Q. [] Do you agree that the claimed ingredients were known in the art and that skilled artisans generally knew how to combine different ingredients to make soluble compositions useful for making media?
>
> A. Yes.

Ex. 16 (Butler Dep.) at 72:13-20 (objection omitted); SOF ¶ 32.

Janssen has no legitimate basis for asserting there was anything "inventive" about using the 52 required ingredients. Multiple prior art references describe cell culture media that uses all of them, including references never considered by the Patent Office. This includes, for instance, the Life Technologies application from 1998 ("Life Techs") that describes a cell culture media using 47 of the 52 ingredients. Ex. 17 (WO 98/15614) at Table 1; App'x B (comparing Life Techs to '083 Patent Claim 1); SOF ¶¶ 40, 59. Indeed, the five "missing" ingredients are present in Life Technologies in different chemical forms that provide the same active component. Ex. 5 (Glacken Op.) at ¶ 237; SOF ¶ 41.

The GSK international patent application from March 2004—the primary subject of this motion and a reference never considered by the Patent Office—similarly discloses as "common ingredients" 50 of the 52 required ingredients in one example media. Ex. 18 (GSK) at 21:5-6 ("An ex[e]mplary advantageous fresh culture medium comprises all or most of the common ingredients as listed in Table 3."); SOF ¶ 35; *see* App'x A (comparing GSK to '083 Patent Claim 1).

The nearly complete overlap of these ingredients is not surprising given the common knowledge of skilled artisans about useful ingredients, as Dr. Butler conceded:

> Q. Do you recall that you've gone through this analysis and have confirmed that this prior art media has 50 of the 52 required ingredients from the '083 patent?
>
> A. I believe that that was the case, but I can't see it from my picture here.
>
> Q. Yeah. Fair enough. And the reason for that is because folks that make cell media, there's a convergence of ideas and a convergence of opinions on what kind of ingredients ought to be included in the mix, right?
>
> A. Right.
>
> Q. And that's why it's not surprising that GSK in the prior art made a similar, not the same, exactly the same, but made a similar cell culture media as the inventors of the '083 patent, correct?
>
> A. Correct.

Ex. 3 (1/30/2018 Hr'g Tr. (Butler)) at 88:11-25; Ex. 16 (Butler Dep.) at 273:22-274:22; SOF ¶ 36.

While conceding that "GSK's cell culture media from the '955 patent includes fifty of the 52 ingredients required by Claim 1 of the '083 patent," Dr. Butler emphasized that there are two missing ingredients: "ammonium vanadate and ferric ammonium citrate." Ex. 16 (Butler Dep.) at 269:14-270:8; SOF ¶ 37. Both these supposedly "missing" ingredients are simply common alternatives to supply two nutrients the GSK reference *does* disclose—vanadium supplied by sodium metavanadate and chelated iron supplied by ferric fructose. Ex. 18 (GSK) at Table 3 ("$NaVO_3$ [sodium metavanadate] 0.00001-0.2") and 24:3-4 ("In Table 3 above, an iron complex

(ferric fructose) is also used as an iron source in addition to an inorganic iron."); SOF ¶ 37.

Ammonium Metavanadate vs. Sodium Metavanadate. Long before 2004, skilled artisans knew sodium metavanadate (the GSK application, and Life Techs) and ammonium metavanadate (the '083 patent) were interchangeable sources of vanadium. Replacing one with the other is simply not an invention. For instance, a 1983 article reports the "substitut[ion]" in one media recipe of "$NaVO_3$" (sodium metavanadate) "for NH_4VO_3" (ammonium metavanadate) simply "for reasons of convenience." Ex. 19 (Cleveland 1983) at Table 1; SOF ¶ 42.

Janssen has not contended otherwise. It has never claimed there was anything "inventive" about replacing GSK's source of vanadium (sodium metavanadate) for another common source of vanadium (ammonium metavanadate). The '083 patent itself makes no such argument. It simply lists ammonium metavanadate among the laundry list of ingredients without suggesting there's anything special about that particular source of vanadium. Ex. 13 ('083 Patent) at 5:27; SOF ¶ 43.

[redacted][3]; Ex. 5 (Glacken Op.) at ¶ 258, Ex. 21 (Glacken Reb.) at ¶ 109; SOF ¶ 44. Janssen's Dr. Butler admitted the same thing:

> Q. Folks in 2004 would also know that one way to deliver vanadium to cells is to use ammonium vanadate, correct?
>
> A. I would presume that's correct, yes.

Ex. 16 (Butler Dep.) at 311:16-20; *id.* at 155:23-156:6; SOF ¶ 45; *see also* Ex. 10 (Butler Op.) at ¶ 55 (function of ammonium metavanadate is to provide vanadium).

[3] All objections omitted unless otherwise noted.

In short, there is nothing in the record, nor any claim by Janssen, that using ammonium metavanadate produces any unknown benefits or unexpected results, or otherwise is anything other than a routine choice for supplying vanadium.

Ferric Ammonium Citrate vs. Ferric Fructose and Ferric Citrate. Similarly, long before 2004, it was well known that ferric fructose (the GSK application), ferric citrate (Life Techs) and ferric ammonium citrate (the '083 patent) were alternative sources of chelated iron, often to replace transferrin. *E.g.*, Ex. 5 (Glacken Op.) ¶¶ 243, 256-57; SOF ¶¶ 46, 48-49. So replacing one with the other is not an invention. Again, prior art references explicitly disclose the interchangeability of various sources of iron.

For example, the '083 patent cites to a published patent application filed in 2002 that states "[t]he chelated salts such as ferric citrate and *ferric ammonium citrate are preferred*." Ex. 13 ('083 Patent) at Cover; Ex. 22 (WO 03/046162) at 18:28-31; SOF ¶ 47. Another reference, Keenan 1996, similarly references various iron sources, including ferric ammonium citrate. Ex. 23 (Keenan) at 452; SOF ¶ 48. Another, Kitano's 1991 chapter on serum-free media, explained:

> Two highly water soluble iron salts, ***ferric ammonium citrate*** and ferric ammonium sulfate, can completely replace transferrin [an iron rich component of natural serum] to support the growth of human leukemic cell lines (Titeux et al. 1984). Kovar and Franek (1987) succeeded in establishing a chemically defined protein-free medium for mouse hybridomas by replacing transferrin with high concentration of ferric citrate.

Ex. 24 (Kitano) at 83 (emphasis added); SOF ¶ 49.

Janssen's expert Dr. Butler agrees: "FAC is a particular form of iron—a chelated iron… [and] a replacement for transferrin," which is an iron rich component of natural serum. Ex. 7 (Butler Reb.) at ¶ 81; SOF ¶ 50. [redacted]

GSK likewise discloses ferric fructose, not as some particularly preferred ingredient, but merely as a routine option for providing iron. Ex. 5 (Glacken Op.) at ¶ 256, Ex. 21 (Glacken Reb.) at ¶ 109; SOF ¶ 52. GSK explains its use of ferric fructose is "an iron source," one that will serve to replace the iron-rich component transferrin found in serum. Ex. 18 (GSK) at 1:29-32 ("Serum is a major source for… iron (transferrin)."); *id.* at 24:3-4 ("In Table 3 above, an iron complex (ferric fructose) is also used as an iron source."; *see* lack of transferrin in Table 3); Ex. 5 (Glacken Op.) at ¶ 257, Ex. 21 (Glacken Reb.) at ¶ 109; SOF ¶ 52.

In short, there is nothing in the record, nor any claim by Janssen, that ferric ammonium citrate produces any unknown benefits or unexpected results, or otherwise is anything other than a routine choice for supplying iron.

Manganese, Selenium, and Tin. The prior art likewise recognized that there were alternative ingredients available to provide other claimed trace metals. Life Techs, for example, expressly disclosed the purpose of the media was to provide trace metals, including: "manganese [Mn(II)], … selenium [SeO_3(II)], [and] … tin [Sn(II)]." Ex. 17 (Life Techs) at 12:23-13:2; SOF ¶ 53. To accomplish this, Life Techs states: "These ions may be provided, for example, in trace element salts such as… $MnCl_2.4H_2O$ [providing manganese]… H_2SeO_3 [providing selenium]… [and] $SnCl_2$ [providing tin]." *Id.*

Yet alternative chemical forms of manganese, selenium, and tin, and specifically those recited in the '083 patent, were all known in the literature as common sources used to provide these active trace elements. *E.g.* Ex. 26 (Hamilton 1977) at Table 1 ("$MnSO_4$•$5H_2O$… manganese," "$SnCl_2 \cdot 2H_2O$"); Ex. 27 (WO 98/08934 to Life Technologies) at Table 2 ("manganous sulfate•H_2O [$MnSO_4$•H_2O]," "sodium selenite [Na_2SeO_3]," and "stannous chloride•$2H_2O$ [$SnCl_2.2H2O$]"); SOF ¶ 54.

There is nothing in the record, nor any claim by Janssen, that $MnCl_2 \cdot 4H_2O$, H_2SeO_3, and $SnCl_2$ produce any unknown benefits or unexpected results, or otherwise are anything other than routine choices for supplying the trace metals manganese, selenium, and tin.

3. Janssen argues the ranges are not critical.

Claim 1 also requires specific concentration ranges, but nothing in the specification suggests there is anything critical about those specific ranges.

To the contrary, according to Janssen, "there's a broad plateau of interchangeable concentrations in cell media." Ex. 2 (1/31/2018 Hr'g Tr.) at 11:17-18; SOF ¶ 10. Janssen has argued that the range of "interchangeable concentrations" is "sometimes … extremely broad, 2500 times, sometimes it's six times" and "never very, very tight." Ex. 2 (1/31/2018 Hr'g Tr.) at 11:17-22; SOF ¶ 11. Dr. Butler likewise argued that the specific ranges claimed in the '083 patent "don't define the thresholds of that plateau," and further that "the precise concentrations of the trace element-containing ingredients a[s] not critical." Ex. 3 (1/30/2018 Hr'g Tr. (Butler)) at 82:20-83:3; Ex. 10 (Butler Op.) at ¶ 42; SOF ¶ 12.

Janssen's other expert, Dr. Wurm, agreed. He was specifically asked about "the ranges that are specified in claim 1" and whether "you have to be in that range, it's critical?" to which he replied: "I cannot say critical." Ex. 1 (Wurm Dep.) at 166:5-19; SOF ¶ 13. [redacted]

In fact, to determine the ranges listed in claim 1, the '083 inventors [redacted]

Ex. 4 (Epstein Dep.) at 220:2-221:10 (emphasis added); SOF ¶ 15.

Moreover, the range of useful concentrations for the ingredients depends on the kind of cell being grown, such that the optimal concentration ranges of ingredients for one cell line will differ from the optimal ranges for another. Ex. 16 (Butler Dep.) at 274:23-275:13 ("for any particular cell you need a particular set of ingredients and a particular concentration of each of those ingredients"); ; SOF ¶ 16. The claims of the '083 patent, however, broadly cover media for growing any kind of cell.

4. The Prior Art is closer to the asserted claims than the accused products.

Given how the ingredients and concentration ranges were identified, it is not surprising that media from the prior art is highly similar—and, in fact, GSK's and Life Techs' media are *closer* to the '083 patent claims than the Defendants' accused media.

As the Court is aware, Janssen asserts that two accused products, Celltrion Growth Medium ("CGM") and Celltrion Production Medium ("CPM"), infringe claims 1 and 2 under the doctrine of equivalents. But it is undisputed that there are many concentration differences—12 for CPM and 13 for CGM—and some substantial differences extending as high as over 400% *above* the '083 patent's claimed range and as low as only 10% of the claimed ranged. *See* Ex. 11 (Wurm Op.) at ¶ 49 (shown at right); SOF ¶ 19-20. Yet Janssen contends that all these concentrations differences are "substantially equivalent" under the doctrine of equivalents.

'083 Patent Claim 1		CGM	CPM
Ingredient	**Amount (per liter)**	**Amount (per liter)**	**Amount (per liter)**
NaCl	5000-7500 mg	literally within range	4556.83 mg
NaH2PO4•H2O	30-100 mg	227.17 mg	262.97 mg
Na2HPO4	30-100 mg	374.15 mg	432.64 mg
CuSO4•5H2O	0.001-0.005 mg	0.000536727 mg	0.00062087 mg
CoCl2•6H2O	0.001-0.10 mg	0.000369 mg	0.00043 mg
(NH4)6Mo7O24•4H2O	0.001-0.005 mg	0.000964 mg	literally within range
NiSO4•6H2O	0.000025-0.0005 mg	0.00094471 mg	0.00109275 mg
SnCl2•2H2O	0.000025-0.0005 mg	0.000008 mg	0.00001 mg
NH4VO3	0.0001-0.0025 mg	0.000046 mg	0.00005 mg
L-arginine•HCl	200-5000 mg	63.34 mg	73.27 mg
L-asparagine•H2O	40-250 mg	3.22 mg	3.72 mg
L-histidine•HCl•H2O	100-500 mg	13.52 mg	15.64 mg
L-methionine	50-500 mg	37.57 mg	43.43 mg
L-valine	100-1000 mg	90.56 mg	literally within range

GSK's disclosed media is much closer to the '083 patent than the Defendants' accused media. Not only is GSK's ingredient list basically identical to the '083 patent's list—with just two alternative ingredients to deliver the same two nutrients—but the concentrations literally overlap for all but one ingredient. *See* App'x A (comparing GSK to '083 claim 1); SOF ¶¶ 55, 60. As to GSK's two alternative ingredients, both provide concentration ranges of the active component that overlap with the '083 patent's claimed concentration ranges. *Id.* Likewise, Life Techs is closer to the patent than the accused products, as it discloses concentrations that overlap for all but one ingredient, and for the five ingredients not identically present in Life Techs, it discloses known substitutes that yield an overlapping amount of the active trace elements.

In GSK, the only non-overlapping concentration is L-histidine.HCl.H_2O. GSK discloses using 15-70 mg/L of that ingredient, which is 30 mg/L below the '083 patent's claimed range of 100-500 mg/L. App'x A; SOF ¶ 57. But for that difference, the Defendants' accused media are *farther away* and well below GSK's upper range of 70 mg/L—13.52 mg/L for CGM and 15.64 mg/L for CPM. SOF ¶ 58. Yet Janssen maintains that these two concentrations are substantially equivalent to the claimed range.

III. Legal Standards

A. Summary Judgment

Summary judgment should be granted when "there is no genuine dispute as to any material fact" and "the movant party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). An issue is "genuine" when a reasonable fact-finder could find for the non-moving party; a fact is "material" when it might affect the outcome of the suit under the applicable law. *Morris v. Gov't Dev. Bank of P.R.*, 27 F.3d 746, 748 (1st Cir. 1994). The non-moving party bears the burden of placing at least one material fact into dispute after the moving party shows the absence of any disputed material fact. *Mendes v. Medtronic, Inc.*, 18 F.3d 13, 15 (1st Cir. 1994) (discussing *Celotex Corp. v. Catrett*, 477 U.S. 317, 325 (1986)).

B. The "Ensnarement" Principle Is A Fundamental Limit On The Doctrine Of Equivalents

"A doctrine of equivalents theory cannot be asserted if it will encompass or 'ensnare' the prior art." *Jang v. Boston Sci. Corp.*, 872 F.3d 1275, 1285 (Fed. Cir. 2017). This is because the doctrine of equivalents does not exist "to give a patentee something which he could not lawfully have obtained from the PTO had he tried." *Wilson Sporting Goods Co. v. David Geoffrey & Assocs.*, 904 F.2d 677, 683-686 (Fed. Cir. 1990).

The "burden of persuasion is on the patentee to establish…that the asserted scope of

equivalency would not ensnare the prior art." *Depuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1323-24 (Fed. Cir. 2009) (citing *Wilson Sporting Goods*, 904 F.2d at 685).

The ensnarement doctrine is a "legal limitation[] on the application of the doctrine of equivalents," one that is to "be determined by the court," that is decided "as a matter of law," and that may be disposed of "on a pretrial motion for partial summary judgment." *Depuy Spine*, 567 F.3d at 1323. The Federal Circuit has repeatedly affirmed summary judgment on ensnarement. *Gemalto S.A. v. HTC Corp.*, 754 F.3d 1364, 1374-75 (Fed. Cir. 2014) (affirming summary judgment of non-infringement under the doctrine of equivalents, explaining "the doctrine of equivalents cannot be applied to encompass the prior art"); *Icon Health & Fitness, Inc. v. Octane Fitness, LLC*, 496 Fed. App'x 57, 64-65 (Fed. Cir. 2012) (affirming summary judgment of non-infringement because patentee's equivalence theory ensnared the prior art), reversed as to denial of attorney's fees, 134 S. Ct. 1749, 1758 (2014); *K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1368-69 (Fed. Cir. 1999) (affirming summary judgment of non-infringement, explaining that "[t]o hold otherwise would allow the [asserted] patent, through the doctrine of equivalents, to cover subject matter that could not have been legally patented in the first instance"); *Cortland Line Co. v. Orvis Co.*, 203 F.3d 1351, 1360 (Fed. Cir. 2000) (affirming summary judgment of non-infringement under the doctrine of equivalents, noting "the great similarity between" the prior art and the accused product); *Marquip, Inc. v. Fosber Am., Inc.*, 198 F.3d 1363, 1368 (Fed. Cir. 1999) (affirming summary judgment of non-infringement because equivalents theory would ensnare the prior art).

IV. Argument

Determining "whether an equivalent would impermissibly ensnare the prior art" is typically resolved through a "hypothetical claim analysis." *Jang*, 872 F.3d at 1285. There are two steps: the first is to "construct a hypothetical claim that literally covers the accused device"; the second is to

determine whether the Patent Office would have found the hypothetical claim to be "patentable over the prior art." *Id.* (quoting *Intendis GmbH v. Glenmark Pharms. Inc., USA*, 822 F.3d 1355, 1363 (Fed. Cir. 2016)). In constructing the hypothetical claim, the patentee "may not add any narrowing limitations" to try to avoid the prior art. *Id.* at 1286. "Ultimately, if such a [hypothetical] claim would be unpatentable under 35 U.S.C. §§ 102 [*i.e.*, anticipation] or 103 [*i.e.*, obviousness], then the patentee has overreached, and the accused device is noninfringing as a matter of law." *Depuy Spine*, 567 F.3d at 1325.

As set forth below, the hypothetical claim analysis confirms that Janssen's equivalents theory would impermissibly ensnare the prior art GSK and Life Techs references, such that the accused formulations are non-infringing as a matter of law.

A. A Hypothetical Claim That Literally Encompasses the Accused Media Is Unpatentably Obvious In View Of GSK

A patent claim is invalid for obviousness "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1237 (Fed. Cir. 2010).

International publication WO 4/078955, assigned to GlaxoSmithKline Biologicals S.A. ("GSK"), renders the hypothetical claims unpatentably obvious. GSK was filed on March 1, 2004 and published September 16, 2004, and thus constitutes prior art under at least 35 U.S.C. § 102(a) and (e). SOF ¶ 33.

Here, there is no dispute over the scope of the prior art, the level of skill in the art, and the differences between the prior art and the claims at issue. The parties agree that the GSK prior art at Table 3 discloses 50 of claim 1's 52 required ingredients with only one concentration difference

(L-histidine.HCl.H_2O) and only two alternative ingredients (ferric fructose and sodium metavanadate) to supply the same important nutrients as the '083 patent, iron and vanadium at overlapping concentrations. These minor differences do not render the hypothetical '083 claims patentably distinct from GSK.

1. GSK's Concentration Of L-histidine.HCl.H_2O Is Closer To The Claimed Range Than The Accused Products Are

A hypothetical claim for purposes of evaluating ensnarement requires expansion to cover the accused product for each of the 12 (CGM) or 13 (CPM) differences. *See e.g.*, *Abbott Labs. v. Dey, L.P.*, 287 F.3d 1097, 1105 (Fed. Cir. 2002) (extending limit of claimed range to encompass accused product).

Doing so eliminates the one concentration difference between the '083 patent and the GSK prior art. This is because the hypothetical claim concentrations (shown in black) overlap with GSK's concentration range (shown in blue) for L-histidine.HCl.H_2O (15-70 mg/L), given that the lower end of the hypothetical claims is 13.52 mg/L for CGM and 15.64 mg/L for CPM.

Figure 1: Comparison of L-histidine.HCl.H2O Concentrations (mg/L)

In other words, for an ensnarement analysis, the '083 patent and the GSK application have overlapping ranges for all 52 required ingredients, including the two alternative ingredients. App'x A. "Where a claimed range overlaps with a range disclosed in the prior art, there is a presumption of obviousness." *Ormco*, 463 F.3d at 1311; *see also Peterson*, 315 F.3d at 1329 ("In cases

involving overlapping ranges, we and our predecessor court have consistently held that even a slight overlap in range establishes a *prima facie* case of obviousness.").

Given the overlapping ranges, the presumption of obviousness applies here. Yet Janssen has offered no evidence to overcome the presumption. According to the Federal Circuit, "[w]hen an applicant seeks to overcome a prima facie case of obviousness by showing improved performance in a range that is within or overlaps with a range disclosed in the prior art, the applicant must 'show that the claimed range is ***critical***, generally by showing that the claimed range achieves unexpected results relative to the prior art range.'" *In re Geisler*, 116 F.3d 1465, 1469-70 (Fed. Cir. 1997) (original emphasis, citation omitted); *accord Ormco*, 463 F.3d at 1311 ("The presumption can be rebutted if it can be shown that the prior art teaches away from the claimed range, or the claimed range produces new and unexpected results."); *In re Applied Materials, Inc.*, 692 F.3d 1289, 1297 (Fed. Cir. 2012) ("[A] prima facie case of obviousness established by the overlap of prior art values with the claimed range can be rebutted by evidence that the claimed range is 'critical' because it 'achieves unexpected results.'") (citation omitted).

Far from attempting overcoming the presumption, Janssen has conceded it *cannot.* Janssen's Dr. Wurm admitted the claimed ranges were *not* "critical." Ex. 1 (Wurm Dep.) at 166:5-19; SOF ¶ 13. Janssen similarly argued that there is "a broad plateau of interchangeable concentrations in cell media," sometimes "extremely broad" plateaus, that are *not* limited to the ranges recited in claim 1. Ex. 2 (1/31/2018 Hr'g Tr.) at 11:15-22; Ex. 3 (1/30/2018 Hr'g Tr.) at 82:20-83:3; SOF ¶ 11. [redacted]

Even if Janssen argued the '083 patent recited the optimum concentration ranges (which

as shown above, is not what happened), it would not save Janssen. "[I]t is not inventive to discover the optimum or workable ranges by routine experimentation." *Geisler*, 116 F.3d at 1469-70; *Applied Materials*, 692 F.3d at 1295. There can be no genuine dispute that Janssen cannot overcome the presumption of obviousness. *See Wilson Sporting Goods*, 904 F.2d at 683-686 (reversing denial of ensnarement where ranges did not overlap but were close); *Ineos USA LLC v. Berry Plastics Corp.*, 783 F.3d 865, 869 (Fed. Cir. 2015) (prior art anticipatory "if it describes the claimed range with sufficient specificity such that a reasonable fact finder could conclude that there is no reasonable difference in how the invention operates over the ranges").

2. The '083 Patent's Composition Merely Recites Obvious Variants Of Two Ingredients Expressly Disclosed In The Prior Art GSK Reference

The only remaining difference between the hypothetical claims and the GSK prior art is the recitation of (i) ferric ammonium citrate and (ii) ammonium metavanadate. But GSK discloses known alternative ingredients that provide the exact same active trace elements at overlapping concentration ranges. This is not an invention as a matter of law.

Substituting one known ingredient for another, when both were known to provide the same trace element, is textbook obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 415-17 (2007). "[A] patent for a combination which only unites old elements with no change in their respective functions…obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." *Id.* (quoting *Great Atlantic & Pacific Tea Co. v. Supermarket Equip. Corp.*, 340 US. 147, 152-53 (1950)). "This is a principal reason for declining to allow patents for what is obvious." *Id.* "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *Id.* Likewise, the "mere substitution of one element for another known in the field" that does no "more than yield a predictable result" is unpatentably obvious. *Id.*

Thus, where, as here "a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious." *Id.; see also Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1364 (Fed. Cir. 2012) (affirming summary judgment of obviousness where the claimed elements were all known in the prior art, and "all that was required to obtain [the claimed] combination was to substitute one well-known cooling agent for another"); *In re Omeprazole Patent Litig.*, 483 F.3d 1364, 1374 (Fed. Cir. 2007).

KSR's mandate controls here. The purpose of each claimed ingredient—ferric ammonium citrate and ammonium metavanadate—is to provide an active trace element. GSK discloses the use of alternative ingredients—ferric fructose and sodium metavanadate—to provide the very same active trace elements, chelated iron and vanadium. "A simple substitution of one known element for another known element in the field to obtain predictable results is obvious" as a matter of law. *In re Lackey*, 371 Fed. Appx. 80, 82 (Fed. Cir. 2010), *accord KSR*, 550 U.S. at 417.; *Wrigley*, 683 F.3d at 1364.

Notably, Janssen's expert Dr. Butler, in asserting that the accused media infringe under the doctrine of equivalents, took advantage of the "active component" principle with respect to other trace metal containing ingredients:

> Claim 1 requires between 0.001-0.005 mg of $CuSO_4 \cdot 5H_2O$… The function the $CuSO_4 \cdot 5H_2O$ ingredient performs in the context of claim 1 is to provide a trace amount of free copper in its +2 oxidation state (*i.e.*, copper(II), or cupric copper) for the cells in culture.… Adding together the $CuSO_4 \cdot 5H_2O$ and $CuCl_2 \cdot 2H_2O$ in the Celltrion Media, the total concentration of the active component (copper (II)) supplied by the Celltrion Media is within the range of that total concentration of copper (II) supplied by claim 1 of the '083 patent.

E.g. Ex. 10 (Butler Op.) at ¶ 57-60.

Ammonium Metavanadate vs. Sodium Metavanadate. Janssen has never argued that using ammonium metavanadate (the '083 patent) as a substitute for sodium metavanadate (the

GSK prior art) was anything but obvious. [redacted]; SOF ¶ 44. And the prior art has long taught that they were interchangeable, and that they could be substituted simply "for reasons of convenience." Ex. 19 (Cleveland 1983) at Table 1; *accord* Ex. 26 (Hamilton 1977) at Table 1 ("NH_4VO_3… 0.001170 [mg]"); Ex. 28 (Darfler 1990) at Table 1 ("NH_4VO_3… [0.00060 mg]") and 773 ("ammonium vanadate, which appeared to have a significantly beneficial effect"); SOF ¶ 42.

At no point has Janssen ever contended that it was "inventive" to make that substitution, or that doing so yielded any kind of surprising or unexpended results. Thus, the use of ammonium metavanadate as a vanadium source cannot salvage the '083 patent's hypothetical claims.

Ferric Ammonium Citrate vs. Ferric Fructose. The same reasoning applies for the '083 patent's use of ferric ammonium citrate as a substitute for GSK's use of ferric fructose. Again, both ingredients have the same function of supplying chelated iron. [redacted]

The prior art—including art cited by the '083 patent—has likewise long identified ferric ammonium citrate as an option for providing iron, even a "preferred" option. Ex. 13 ('083 Patent) at Cover; Ex. 22 (WO 03/046162) at 18:28-31; Ex. 23 (Keenan) at 452 (identifying ferric ammonium citrate as a source of iron); Ex 23 (Kitano) at 83 ("[t]wo highly water soluble iron salts, ferric ammonium citrate and ferric ammonium sulfate, can completely replace transferrin to support the growth of human leukemic cell lines"); SOF ¶¶ 47-49. Janssen has never offered any evidence that ferric ammonium citrate produces any unknown benefits or unexpected results, or otherwise is anything other than a routine choice for supplying chelated iron.

Because it cannot genuinely dispute that ferric ammonium citrate was a known source of iron, Janssen contends that a single reference among all the prior art, Keenan 1996, "teaches away from using [ferric ammonium citrate] as a transferrin replacement." Ex. 7 (Butler Reb.) ¶ 82. According to Janssen, although Keenan 1996 discloses using ferric ammonium citrate as a source of iron, it nevertheless suggests that four other sources of iron performed better and were thus "preferable," while "FAC is inferior." Ex. 7 (Butler Reb.) at ¶ 84. Janssen quotes Keenan's discussion of selecting four compounds "for further analysis," and asserts that Keenan thus "discarded" ferric ammonium citrate for further testing, such that one of skill in the art would have affirmatively avoided the ingredient. *Id.* ¶ 83. Janssen's selective misreading of Keenan doesn't hold up, and its teaching away argument fails as a matter of law.

As an initial matter, Keenan never once refers to "discarding" anything, and certainly not ferric ammonium citrate. Keenan simply discloses testing seven compounds that it refers to as "simple iron compounds or iron chelators" that were known to be used "to replace transferrin." Ex. 23 (Keenan) at 451; SOF ¶ 48. And Keenan found that all of them worked—several stimulated growth from 92-100% of the growth shown by transferrin, and others stimulated growth from 74-75% of the growth shown by transferrin. Ex. 23 (Keenan) at 452; SOF ¶ 48. Importantly, in selecting four compounds "for further analysis," Keenan says nothing—disparaging or otherwise—about the usefulness of the others to act as transferrin replacements. Rather, in discussion near the end of the article, Keenan concludes that "all" of the compounds tested were successful:

> In summary, ***all*** the factors tested were able to exert a concentration-dependent, growth-promoting effect on MDCK cells in single-stage growth assays. These factors have previously been used as transferrin replacements with various degrees of success…

Ex. 23 (Keenan) at 453; SOF ¶ 48.

In fact, Keenan even invited further investigation into all of the compounds, explaining that although his tests were only conducted on MDCK cells—which are *not* the kinds of cells used by either Defendants or Janssen for their infliximab products— "it should be noted that the effectiveness of any of these factors will depend not only on the cell line but also the culture system being used[.]" Ex. 23 (Keenan) at 453; SOF ¶ 48. The fact that other cell culture media *after* Keenan used ferric ammonium citrate as a source of iron, including for example, [redacted]; SOF ¶ 51), refutes the suggestion that skilled artisans had abandoned ferric ammonium citrate.

At best for Janssen, Keenan merely expresses a preference for four of the seven tested compounds over ferric ammonium citrate for MDCK cells. "But the teaching away inquiry does not focus on whether a person of ordinary skill in the art would have merely favored one disclosed option over another disclosed option." *Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316, 1327-28 (Fed. Cir. 2017). "In assessing whether prior art teaches away, that 'better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes.'" *Id.* (quoting *In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012)). "[T]he fact that there may be reasons a skilled artisan would prefer one over the other does not amount to a teaching away from the lesser preferred but still workable option." *Id.* Likewise, "[a] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F. 3d 551, 553 (Fed. Cir. 1994); *Apple Inc. v. Samsung Elecs. Co.*, 816 F.3d 788, 801-02 (Fed. Cir. 2016) ("Indeed, we have found a reference to not teach away when, for example, it described a particular composition 'as somewhat inferior to some other product for the same use.'"), vacated, 839 F.3d 1034, 1050-58 (Fed. Cir. 2016) (en banc).

Ultimately, Janssen is merely arguing that Keenan suggests that there are "better alternatives" than ferric ammonium citrate for MDCK cells, but art describing a known option as "inferior" does not somehow render using that option a patentable invention. *Bayer*, 874 F.3d at 1327-28.

In re Omeprazole, 483 F.3d at 1373-74, is right on point. In that case, the asserted claim covered a method of making the drug omeprazole. It recited the use of certain alkaline salts as an "alkaline reaction component" (ARC) to stabilize omeprazole. *Id.* at 1343. The prior art did not disclose the exact alkaline salts recited in the asserted claim, but rather disclosed the use of arginine as the active "alkaline reaction component." *Id.* There was no genuine dispute that both arginine and the claimed alkaline salts were "generally known as" alkaline reactive compounds, that they acted "'just like' other ARCs" as stabilizing agents, and that "it is easy to substitute" one for the other. *Id.* at 1373-74. The district court found, and the Federal Circuit affirmed, that the patented invention was obvious over the prior art: "it would have been obvious to one skilled in the art to substitute one ARC for another." *Id.* at 1374. So too here.

3. There Is No Evidence Of Secondary Considerations That Could Legally Avoid Obviousness

The obviousness inquiry must also account for objective indicia of non-obviousness or secondary considerations, including for example, commercial success of the claimed invention. Here, however, there is no such evidence.

At one point, Janssen pointed to an alleged long-felt need for a "chemically defined cell culture media" (Ex. 7 (Butler Reb.) at ¶ 156), even though such media already existed in the prior art, [redacted]; Ex. 12 (CELLREM-0246022) at 022 and 030 (referring to CD CHO and CD Hybridoma as

"[c]hemically defined" and "entirely free of animal-derived components"); Ex. 6 (Frohlich) at ¶ 70; SOF ¶ 29. But "secondary considerations" are "only significant if there is a nexus" to "the claimed invention." *Ormco*, 463 F.3d at 1311-12 ("[S]econdary considerations, is only significant if there is a nexus between the claimed invention and the commercial success.").

Here, Janssen successfully argued during claim construction that the '083 patent is not limited to "chemically defined" media, thus erasing any possibility of the required nexus between the alleged long-felt need and the scope of the claimed invention. *E.g.* No. 15-cv-10698, Dkt. 149 at 1. Having successfully read any such limitation out of the claims, Janssen cannot turn around to rely on it an effort to salvage its case.

In any event, this case presents the type of "strong prima facie case of obviousness" such that evidence of secondary considerations "simply cannot overcome" an obviousness finding. *Wyers*, 616 F.3d at 1246. As in *Wyers*, because the '083 claims "represent[] no more than 'the predictable use of prior art elements according to their established functions,'" any "secondary considerations are inadequate to establish nonobviousness as a matter of law." *Id.*

4. Claim 2 Is Likewise Unpatentable Over GSK

GSK also renders dependent claim 2 obvious. Claim 2 adds two additional limitations: "a buffering molecule with a pK_a between 5.9 and 7.8" and "a cell protectant." Ex. 13 ('083 Patent) at Claim 2. GSK teaches both.

As to the first, GSK includes HEPES, which is a well-known buffering molecule with a pKa of 7.3 (*i.e.* between 5.9 and 7.8). Ex. 5 (Glacken Op.) at ¶ 231, 253; Ex. 18 (GSK) at Table 3; SOF ¶ 62. Janssen does not dispute this.

As to the second, GSK discloses use of "oxidation stabilizers" to prevent the media from oxidizing and thus damaging the cells. Ex. 18 (GSK) at 11:21-12:2; Ex. 5 (Glacken Op.) at ¶ 254; SOF ¶ 63. That is undisputed. However, Janssen argues that these oxidation stabilizers are not a

"cell protectant," which it claims must "prevent [] damage 'by shear forces or the effects of gas bubble sparging in a bioreactor vessel." Ex. 7 (Butler Reb.) at ¶ 152. But that is not what the term means according the '083 patent's specification, which states: "[t]he term 'cell protectant' as used herein and in the claims means a substance that protects eukaryotic cells from damage." Ex. 13 ('083 Patent) at 4:25-27; SOF ¶ 9. Janssen's attempt to import limitations into the claims from the specification contradicts clear Federal Circuit precedent. *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) ("[P]articular embodiments and examples appearing in the specification will not generally be read into the claims."); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005) ("[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments."). In any event, the limitations that Janssen seeks to import are themselves denoted as merely exemplary in the specification, being introduced by the phrase "for example." Ex. 13 ('083 Patent) at 4:27-29.

B. A Hypothetical Claim That Literally Encompasses the Accused Media Is Unpatentably Obvious In View Of Life Technologies Inc.

International publication WO 98/15614, assigned to Life Technologies Inc. ("Life Techs"), likewise renders the hypothetical claims unpatentably obvious. Life Techs was published on April 16, 1998, and thus constitutes prior art under at least 35 U.S.C. § 102(b). SOF ¶ 38.

Of the 52 ingredients required by claim 1 of the '083 patent, the media disclosed in Life Techs expressly contains 47 of them. App'x B; SOF ¶ 61. For the other 5 ingredients, the Life Techs media contains an alternative ingredient that provides the same active component, and does so in a concentration of the active component that overlaps with the concentration of the active component provided by the corresponding ingredients of the '083 patent:

Active Component	'083 Patent		Life Techs	
	Ingredient	Amount Of Active Component (µmol/L)	Ingredient	Amount Of Active Component (µmol/L)
Chelated iron	ferric ammonium citrate	$1.53x10^{-1}$–$7.63x10^{2}$	ferric citrate	$4.10x10^{-2}$–$8.16x10^{1}$
Manganese (Mn(II))	$MnSO_4•H_2O$	$4.14x10^{-4}$–$4.73x10^{-2}$	$MnCl_2•4H_2O$	$5.05x10^{-6}$–$5.05x10^{-3}$
Selenium (SeO_3(II))	Na_2SeO_3	$2.31x10^{-2}$–$4.05x10^{-1}$	H_2SeO_3	$7.75x10^{-5}$–$3.88x10^{-2}$
Tin (Sn(II))	$SnCl_2$.2H2O	$1.11x10^{-4}$–$2.22x10^{-3}$	$SnCl_2$	$5.27x10^{-6}$–$5.27x10^{-4}$
Vanadium	NH_4VO_3	$8.55x10^{-4}$–$2.14x10^{-2}$	$NaVO_3$	$8.20x10^{-5}$–$8.20x10^{-3}$

Ex. 5 (Glacken Op.) ¶¶ 234-239, 244-247; Ex. 21 (Glacken Reb.) ¶104; SOF ¶ 41.

There is no genuine dispute that the five ingredients recited in the '083 patent are known alternative sources of the active component, interchangeable with the ingredients used in Life Techs. As discussed above, ferric ammonium citrate and ferric citrate were both known options for transferrin replacement. *E.g.* Ex. 22 (WO 03/046162) at 18:28-31 ("[t]he chelated salts such as ferric citrate and ferric ammonium citrate are preferred."); Ex. 23 (Keenan) at 453; SOF ¶¶ 48-49, 52. Likewise, Life Techs itself recognized the goal was to provide the trace metals "manganese [Mn(II)],… selenium [SeO_3(II)], vanadium [VO_3],… tin [Sn(II)]" and gave the particular chemical forms as "example[s]." Ex. 17 (Life Techs) at 12:23-13:2; SOF ¶ 53. And the chemical forms of manganese, selenium, vanadium, and tin were all known in the literature to provide these ingredients. *E.g.* Ex. 26 (Hamilton 1977) at Table 1 ("$MnSO_4•5H_2O$… manganese," "$SnCl_2·2H_2O$," and "NH_4VO_3… vanadium,"); Ex. 27 (WO 98/08934 to Life Technologies) at Table 2 ("manganous sulfate•H_2O [$MnSO_4•H_2O$]," "sodium selenite [Na_2SeO_3]," and "stannous chloride•$2H_2O$ [$SnCl_2.2H_2O$]".) ; SOF ¶ 54. The hypothetical claims merely substitute one known ingredient for another to provide a known active ingredient; that is the Supreme Court's very definition of obviousness. *KSR*, 550 U.S. at 415-17.

As to the claimed ingredients expressly disclosed in Life Techs, the concentration range of all but one ingredient overlaps with the ranges required by the hypothetical claims. That leaves as the only remaining difference between the hypothetical claims and Life Techs the concentration range of putrescine.2HCl. Life Techs recites using 0.0001-0.01 mg of putrescine.2HCl, while the range of the hypothetical '083 patent claim is 0.025-0.25 mg.

But the mere fact that the concentration amount for putrescine.2HCl in Life Techs is roughly 40% below the hypothetical claim range does not render the claims patentable, at least when considering Janssen's position of what matters. As set forth above, Janssen has no evidence that there is anything "critical" about the claimed ranges in general, nor does it have any regarding this ingredient in particular. To the contrary, under Janssen's theory, "the precise concentrations of the trace element-containing ingredients ***are not critical***" and that "these [ranges] were meant to be the ***guidelines for estimation*** of that plateau… ***they're not precise*** insofar as they don't define the thresholds of that plateau." Ex. 10 (Butler Op.) at ¶ 42; Ex. 3 (1/30/2018 Hr'g Tr.) at 82:20-83:3; Ex. 2 (1/31/2018 Hr'g Tr.) at 11:15-20 ("[T]here's a broad plateau of interchangeable concentrations in cell media, you know, sometimes it's extremely broad, 2500 times, sometimes it's six times. But it's never very, very tight."); SOF ¶ 10-12. [redacted] Life Techs plainly satisfies that requirement, as it discloses that its media is "capable of supporting the *in vitro* cultivation of animal cells." Ex. 17 (Life Techs) at Abstract; SOF ¶ 40.

As to asserted claim 2, Life Techs recites HEPES and Pluronic-F68. Ex. 17 (Life Techs) at 11:26-12:5, 15:10, 38:8-9; Ex. 5 (Glacken Op.) at ¶ 231, 238; SOF ¶¶ 64-65. As discussed above, HEPES is a buffering molecule with a pKa of 7.3 (*i.e.* between 5.9 and 7.8) as required by claim

2. Likewise, the ’083 patent identifies Pluronic-F68 as a cell protectant. Ex. 13 (’083 Patent) at 7:14-15 (“Examples of cell protectants are non ionic surfactants such as Pluronic-F68.”); SOF ¶ 65. There is thus no dispute that Life Techs satisfies the additional limitations of claim 2.

V. Conclusion

For the reasons above, the Court should grant summary judgment of non-infringement.

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Respectfully submitted,

Celltrion Healthcare Co., Ltd., Celltrion, Inc., and Hospira, Inc.

By their attorneys,

/s/*Andrea L. Martin, Esq.*
Dennis J. Kelly (BBO # 266340)
Andrea L. Martin (BBO #666117)
BURNS & LEVINSON LLP
125 Summer Street
Boston, MA 02110-1624
Tel: 617-345-3000
dkelly@burnslev.com
amartin@burnslev.com

James F. Hurst, P.C. (*pro hac vice*)
Bryan S. Hales, P.C. (*pro hac vice*)
Elizabeth A. Cutri (*pro hac vice*)
Gregory B. Sanford (*pro hac vice*)
KIRKLAND & ELLIS LLP
300 North LaSalle
Chicago, IL 60654
Tel: (312) 862-2000
james.hurst@kirkland.com
bryan.hales@kirkland.com
elizabeth.cutri@kirkland.com
gregory.sanford@kirkland.com

Ryan Kane (*pro hac vice*)
James McConnell (*pro hac vice*)
KIRKLAND & ELLIS LLP
601 Lexington Avenue
New York, NY 10022
Tel: (212) 446-4800
ryan.kane@kirkland.com
james.mcconnell@kirkland.com

Noah S. Frank (*pro hac vice*)
KIRKLAND & ELLIS LLP
655 Fifteenth St., N.W.
Washington, DC 20005
Tel: (202) 879-5000
noah.frank@kirkland.com

Charles B. Klein (*pro hac vice*)
WINSTON & STRAWN LLP
1700 K Street, N.W.
Washington, D.C. 20006-3817
Tel: (202) 282-5000
cklein@winston.com

Samuel S. Park (*pro hac vice*)
Dan H. Hoang (*pro hac vice*)
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, IL 60601-9703
Tel: (312) 558-7931
spark@winston.com
dhoang@winston.com

Attorneys for Defendants Celltrion Healthcare Co., Ltd., Celltrion, Inc., and Hospira, Inc.

CERTIFICATE OF SERVICE

I, Andrea L. Martin, hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non-registered participants on April 6, 2018.

/s/Andrea L. Martin, Esq.
Andrea L. Martin, Esq.