IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JANSSEN BIOTECH, INC. and NEW YORK UNIVERSITY Plaintiffs, v. CELLTRION HEALTHCARE CO., LTD. , CELLTRION, INC., and HOSPIRA, INC. Defendants.	)	Civil Action No. 1:15-cv-10698-MLW Civil Action No. 1:16-cv-11117-MLW

JANSSEN'S OPPOSITION TO DEFENDANTS' MOTION TO EXCLUDE THE OPINIONS OF JANSSEN'S EXPERTS, DR. WURM AND DR. BUTLER, ON INFRINGEMENT

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I. INTRODUCTION

As Defendants note, there are, at least in theory, "countless possible powders" that can be used for cell culture media in which to grow drug-producing cells. Br. (Dkt. No. 340) 1. Out of all of the "countless powders" that can be used, Defendants chose to use cell culture media that have ***every single one*** of the 52 ingredients required by claim 1 of the '083 patent, and seven of the nine optional ingredients. Forty-seven (or in the case of one of the accused products, forty-six) of the ingredients are literally present in Defendant's media within the exact ranges of concentration recited in the claim. For the 12 (or 13) remaining ingredients, the exact same ingredient is present in the Celltrion Media, but in concentrations that are outside the ranges recited in the claims. The question for trial is whether those concentration differences are insubstantial such that the Celltrion Media infringe the '083 patent under the doctrine of equivalents (DOE). Defendants' motion to exclude Janssen's evidence on this question fails.

First, the infringement analyses of Janssen's expert witnesses Dr. Michael Butler and Dr. Florian Wurm do not vitiate the concentration elements of the '083 patent. On the contrary, the entire point of their analyses is to assess, on an element-by-element basis, whether the concentrations of particular ingredients in the Celltrion Media are insubstantially different from the concentration ranges specified in the claims for those same particular ingredients. Rather than vitiating the claim limitations, Janssen's experts use them as a benchmark for analyzing equivalence. Meanwhile, the experiments performed by Dr. Wurm affirmatively prove that the claim limitations are not vitiated. In a negative control experiment that Defendants ignore, the claimed ingredients were reduced by 80% and the results, on all variables, were substantially different from the Celltrion Media. There is no vitiation.

Second, the experiments conducted by Dr. Wurm are scientifically reliable and will assist

the jury in assessing infringement under the DOE. Defendants' contention that Dr. Wurm did not properly compare the accused product to the claimed invention is internally contradictory and wrong. Dr. Wurm's well-controlled experiments compared the Celltrion Media to variants of the media that were altered, on an element-by-element basis, to literally meet the concentration limitations of the '083 patent. Defendants' criticisms of Dr. Wurm's methodology fall flat. Accepting Defendants' various recommendations would have been in some respects physically impossible, in other respects unscientific, and in the remaining respects ill-advised. Nevertheless, Defendants would have been free to present their own experiments at trial, had they conducted them, and they are free to present their criticisms of Dr. Wurm's methodology to the jury. What they should not be permitted to do is prevent the jury from hearing relevant and meaningful scientific evidence on the question of infringement.

II. THE OPINIONS OF JANSSEN'S EXPERTS

At trial, Janssen will present the expert testimony of two world-renowned cell biologists in support of its infringement case under the DOE. Dr. Michael Butler, a leading cell culture media scientist based in Ireland, will present Janssen's comprehensive infringement analysis, including his element-by-element analysis of the insubstantiality of the particular differences between the accused products and the asserted patent claims, and his interpretation of the results of laboratory experiments that support this opinion. Dr. Florian Wurm, a Switzerland-based scientist with expertise in cell culturing and process development, conducted the laboratory experiments, and his testimony will focus on the methodology and results of those experiments. Celltrion has not challenged the impressive credentials of either scientist and it cannot. Both experts' testimony is relevant to infringement under the doctrine of equivalents, and neither's testimony should be excluded under Federal Rule of Evidence 702 and *Daubert*.

A. Dr. Butler's Infringement Analysis

Dr. Butler will testify at trial that he compared the formulations of the accused Celltrion Media to the patent claims. Ex. 1 (Butler Rep.) ¶¶ 35-38 & Table 1. The Celltrion Media contain each and every ingredient required by the claims, in precisely the same form (as well as seven of the nine optional ingredients). *Id.* ¶ 37. Of the 61 claimed concentration ranges, the accused products literally meet all but 12 or 13 of them. *Id.* ¶ 38. With respect to the differences, Dr. Butler will testify that "each of the literal differences between the Celltrion Media and claimed range is insubstantial" and that "the ingredients in the Celltrion Media perform substantially the same if not the identical function in substantially the same if not the identical way as the corresponding ingredients in the claim, and experimentation shows that they achieve substantially similar results." *Id.* ¶ 40. In other words, Dr. Butler will apply the two well-established tests for determining infringement under the DOE – the "insubstantial differences" test and the "function-way-result" test – and conclude that both tests are met.

1. Assessment of each individual difference in concentration

Dr. Butler's DOE analysis proceeds in two parts. *See* Ex. 2 (Butler Reply Rep.) ¶ 16. The first part of Dr. Butler's analysis, which focuses on the "insubstantial differences" test and the "function" and "way" portions of the function/way/result test, is a detailed assessment of the differences between the Celltrion Media and the concentration ranges recited in the '083 patent, taking into account the nature of each ingredient and the magnitude of each difference in view of his knowledge, expertise and 30 years of experience in the field of cell culture media. Ex. 1 (Butler Rep.) ¶¶ 42-97.

Dr. Butler begins by grouping the ingredients in the Celltrion Media whose concentrations are literally outside the claimed ranges into three basic categories: trace element-

containing ingredients, amino acid-containing ingredients, and the inorganic salts sodium phosphates and sodium chloride. *Id.* Dr. Butler then goes one by one through each of the individual ingredients, discussing their function, how they work, and what factors are relevant to assessing differences in their concentrations. *Id.* Dr. Butler concludes that the differences between the concentrations in the Celltrion Media and those recited in the '083 patent are "insubstantial." *Id.* ¶ 46; *see also id.* ¶¶ 49, 52, 55, 58, 61, 67, 70, 74, 79, 84, 89, 92, 95, 97. Furthermore, applying the function/way/result test, Dr. Butler concludes that because the ingredients are exactly the same, both in and out of the range, the function of these ingredients and the way they work are exactly the same, not merely substantially the same, as the patent claim. *E.g.*, *id.* ¶ 46. Dr. Butler also states that he would "expect, subject to experimentation, that mammalian cells would perform similarly in the Celltrion Media as in media that were otherwise identical" but had concentrations literally within the range claimed by the patent. *Id.*

2. Reliance on Dr. Wurm's experiments

The second part of Dr. Butler's infringement analysis, focused on the result prong of the function/way/result test, relies on Dr. Wurm's experiments. Having determined that he would ***expect*** the Celltrion Media to perform similarly in cell culture to otherwise identical media that literally met the limitations of the claims, Dr. Butler states that Dr. Wurm's laboratory testing "confirms" this expectation. *E.g.*, *id.* ¶ 47. Later in his report, Dr. Butler examines Dr. Wurm's experiments in more detail, explaining that, in his view, they confirm experimentally that each of the individual concentration differences between the Celltrion Media and the '083 patent is insubstantial and meets the function-way-result test. *Id.* ¶¶ 98-129. In addition to providing proof on the "result" prong of the function/way/result test, Dr. Wurm's experiments also

provided support for Dr. Butler's conclusion that the differences between the Celltrion Media and the claim limitations were not substantial. *E.g.*, *id.* ¶¶ 47, 112.

B. Dr. Wurm's Experiments

As Dr. Wurm will explain at trial, the laboratory experiments that he performed (and on which Dr. Butler relied in part) were well-controlled, scientifically reliable experiments designed to assess the effect of each difference between the Celltrion Media and the claims of the '083 patent on the performance of cell culture media. Dr. Wurm carried out two analogous sets of experiments, one for each of the two Celltrion Media: the Celltrion Growth Medium ("CGM") and the Celltrion Production Medium ("CPM").

1. Preparation of cell culture media for testing

The guiding principle of Dr. Wurm's experimental design was to isolate each of the twelve individual concentration differences and to test whether that difference affected the performance of drug-producing mammalian cells in cell culture. First, Dr. Wurm prepared cell culture media using the recipe of ingredients and concentrations in the Celltrion Media. *See* Ex. 3 (Wurm Rep.) ¶¶ 13, 58. Then, Dr. Wurm prepared twelve variants of the Celltrion Media for testing. *Id.* ¶ 58. Each of the variants was identical to the Celltrion Media except with respect to one ingredient whose concentration literally differed from the patent claim; that ingredient's concentration was adjusted to the claimed range. *Id.*[1]

For both of the Celltrion Media, Dr. Wurm also created an "All Changes" variant, in which all ingredients for which the Celltrion Media were literally outside the claimed concentration ranges were moved into the claimed ranges. *Id.* ¶ 60 n.6. The "All Changes"

[1] In the CGM experiment, for example, the [redacted] variant was identical to the CGM media except with respect to the concentration of [redacted]: in the variant it was [redacted] (a claimed amount), while in CGM, it was [redacted] (the concentration in the accused product). *Id.* ¶ 59.

variants literally met each of the limitations of claim 1 and literally infringed the claim.

Besides testing the Celltrion Media and the variants, Dr. Wurm also included a negative control in the experiments. A negative control is part of good science and assesses whether the experiment is capable of detecting substantial differences. Dr. Wurm's negative control replicated the Celltrion Media, but reduced the concentration of the ingredients by 80%. *Id.* ¶ 65.

2. Addition of necessary ingredients

In addition to the ingredients in the Celltrion Media powders, Dr. Wurm added to the media certain ingredients that are not recited in claim 1 of the '083 patent, but were necessary for the cells to grow properly. Since cells will not grow in a dry powder, Dr. Wurm added water to achieve the concentrations specified in the patent. Ex. 4 (Wurm Reply Rep.) ¶ 8; Ex. 5 (Wurm Tr.) 72:13-20; *see also* Ex. 2 (Butler Reply Rep.) ¶ 65. To each of the tested media (the Celltrion Media and the variants), Dr. Wurm also added L-glutamine (1.022 g/L) and sodium bicarbonate (2.1 g/L). Ex. 3 (Wurm Rep.) ¶ 61. Like water, L-glutamine and sodium bicarbonate are routinely added to powdered formulations of cell culture media. However, these ingredients are typically not included in the powdered formulation, because they "are unstable under the conditions usually used to prepare powdered media." *Id.*; Ex. 4 (Wurm Reply Rep.) ¶ 9; Ex. 5 (Wurm Tr.) 173:3-174:4; *see also* Ex. 6 (Glacken Tr.) 248:20-21. Indeed, the concentrations of L-glutamine and sodium bicarbonate that Dr. Wurm added to the tested media are those expressly taught by the '083 patent. *See* '083 patent, at col. 8:8-9, 8:22-26. Celltrion also adds both ingredients to the Celltrion Media prior to use in cell culture, in similar concentrations as taught by the patent. Ex. 3 (Wurm Rep.) ¶ 31; Ex. 7 (Glacken Reb. Rep.) ¶ 147 & n.35.

In addition, Dr. Wurm added mycophenolic acid (0.5 mg/L), hypoxanthine (2.5 mg/L), and xanthine (50 mg/L) to the tested media, a trio of ingredients referred to as "MHX." Ex. 3

(Wurm Op. Rep.) ¶ 63. The ’083 patent teaches adding MHX in these precise concentrations to the patented cell culture media. ’083 patent, at col. 8:29-34; claims 4, 9. The MHX trio is used to culture cells with a specific genetic selection system (the “GPT” system) since MHX selects for cells that incorporate the GPT system. Ex. 3 (Wurm Rep.) ¶ 22. The cell line described in the ’083 patent and used in Dr. Wurm’s experiments, known as “C743B,” *id.* ¶ 62; *see* ’083 patent, at col. 9:40-col. 10:43, incorporates the GPT selection system and therefore requires MHX. Ex. 3 (Wurm Rep.) ¶ 63. Celltrion’s cell line does not use the GPT selection system and Celltrion thus does not add MHX to its cell culture media. Ex. 4 (Wurm Reply Rep.) ¶ 10. (The ’083 patent is not limited to any particular cell line; since Celltrion’s proprietary cell line was unavailable, Dr. Wurm used the exemplary cell line identified in the patent).

Importantly, Dr. Wurm added the same amount of water, L-glutamine, sodium bicarbonate, and MHX to every single cell culture media that he tested: the two Celltrion Media and each of the variants of those two media. Thus, these ingredients were well controlled in Dr. Wurm’s experiments. Any observed differences among the various cell culture media that Dr. Wurm tested cannot be attributed to water, L-glutamine, sodium bicarbonate or MHX, because these ingredients were present in the same concentrations in each of the tested media.

3. Cell culture testing

Once the cell culture media were prepared for testing, C743B cells were added to each of the media and their growth and productivity was observed. To minimize external sources of error, each of the various cell cultures were performed side-by-side and simultaneously in the same incubator under the same culture conditions. Ex. 3 (Wurm Rep.) ¶ 64. The cultures were initiated in each vessel with a uniform amount of cells from a single population. *Id.* The testing was performed in triplicate, meaning that for each of the tested media, cells were grown in three

separate flasks and the results were averaged. *Id.* ¶ 66.

Dr. Wurm assessed the performance of the tested cell culture media by periodically measuring three variables: (1) the viable cell density (*i.e.*, the number of living cells present); (2), the percent viability (*i.e.*, the percentage of the cells in the culture that were alive); and (3) the antibody titers (*i.e.*, the amount of biologic drug that the cells produced). These three performance measures are those reported in Examples 1 and 2 of the '083 patent, and are the most important measures by which to assess the performance of a cell culture medium designed for growing cells engineered to produce a biopharmaceutical product. *See* Ex. 1 (Butler Rep.) ¶ 98. Dr. Wurm's tests showed no substantial differences between the Celltrion Media and any of its variants. *Id.* ¶¶ 104, 116; Ex. 3 (Wurm Rep.) ¶¶ 71, 83. The results for the negative control, however, were substantially different from the other variables tested. Ex. 3 (Wurm Rep.) ¶¶ 72, 84; Ex. 1 (Butler Rep.) ¶¶ 105, 117.

4. Omission of galactose from one set of experiments

In one of the two sets of experiments (the CGM experiments, but not the CPM experiments), Dr. Wurm inadvertently omitted galactose – an unclaimed ingredient. As both Dr. Wurm and Dr. Butler explained, because galactose is an unclaimed ingredient and was omitted from both the CGM media and the twelve variants to which it was compared, the CGM experiments validly tested the effect of each of the differences between CGM and the patent claim. *See* Ex. 8 (Supp. Wurm Decl.) ¶ 3; Ex. 9 (Supp. Butler Decl.) ¶ 2; Ex. 10 (Butler Tr.) 163:12-165:25. Notably, galactose was not omitted in the CPM experiments. The tested CPM and each of its variants contained galactose. As noted, in both experiments, the results were the same: there were no substantial differences between the performance of the Celltrion Media and the individual variants or the all-changes variant. Ex. 3 (Wurm Rep.) ¶¶ 71, 83.

C. Dr. Butler's Deposition Testimony

At his deposition, Dr. Butler confirmed that his infringement opinion was based on "two assessments" – his independent analysis of the concentration differences and Dr. Wurm's experiments.

> Q. So let's talk about the way that you conducted your analysis. You had an expectation about what would be important and what wouldn't be important, and then you relied on Dr. Wurm's testing to reach your ultimate opinion, right?
>
> A. Yes.
>
> Q. Was Dr. Wurm's testing important? Could you come to a conclusion without Dr. Wurm's testing about whether the cell culture media would be equivalent or not?
>
> A. I would have to rely on those two assessments.

Id. 101:12-102:1.[2]

With respect to the first part of his analysis, Dr. Butler testified at length at his deposition about the various considerations that informed his opinion that the differences in question were insubstantial. For example, when asked how he analyzed sodium chloride (NaCl), Dr. Butler explained that he considered the effect on osmolality (*i.e.*, the overall concentration of all the salts dissolved in the medium) to be the key issue:

> A. The importance of sodium chloride is in the osmolality. So the critical factor here is how that sodium chloride -- that concentration relates to other salts in the media. The important thing is to maintain an osmolality of around 300 which is the typical value.
>
> Q. So how low would the concentration, then, of sodium chloride have to go before you would deem it to be not equivalent, something greater than an insubstantial difference and therefore not equivalent?

[2] It is possible, of course, for a scientist to draw a conclusion about equivalents without scientific testing, as Dr. Butler explained in his expert report. "Infringement can be assessed by comparing the Celltrion Media formulations to the claim and seeing, based on knowledge and experience in the art, that the literal differences – differences in the concentration of a small minority of ingredients – would not be expected to have a substantial impact." Ex. 2 (Butler Reply Rep.) ¶ 27. With Dr. Wurm's experiments to consider as well, Dr. Butler properly also relied upon the experiments in forming his expert opinion.

> A. Typically I would expect that the performance of the media would start decreasing if the osmolality decreases by 10 to 20%. So if you keep all the other ingredients in the media constant and only reduce the sodium chloride, then it's at that sort of level of decrease that you'll get a decrease in osmolality which will potentially affect the performance of the cells. . . .

Id. at 75:21-76:16. In similar fashion, Dr. Butler explained how he analyzed the substantiality of other ingredients about which he was asked by Defendants' counsel. *See, e.g.*, *id.* at 76:17-78:10, 85:12-100:14, 139:11-146:20.

Defendants' counsel then asked Dr. Butler a series of hypothetical questions as to whether he would consider differences more extreme than those at issue here to be equivalent ***if*** Dr. Wurm's testing showed them to perform equivalently. Although Celltrion argues that Dr. Butler's answers to these hypotheticals show that his infringement analysis vitiates claim elements, they do nothing of the sort. For example, Dr. Butler was asked about a hypothetical medium with ***all the required ingredients*** but with different concentrations. *Id.* at 109:5-16, 113:15-25. Dr. Butler testified that ***if and only if*** Dr. Wurm's well-controlled testing of one ingredient at a time showed substantially the same results, he understood that to constitute proof under the doctrine of equivalents. *Id.* That hardly makes concentration irrelevant. Rather, its relevance is the subject of scientific testing. Indeed, as the testing of the negative control proved, there are limits beyond which the concentration may not be varied, and experiments can demonstrate that.

Later, and irrelevantly, Dr. Butler was asked – without reference to the legal test for DOE – whether a hypothetical medium with missing ingredients that was proved equivalent to the claim in well-controlled experiments "would be an equivalent media" and he agreed that it would. *Id.* at 151:7-16. This testimony is scientifically accurate; a media experimentally shown to be equivalent to another media is equivalent as a matter of science. Dr. Butler never

suggested, however, that his analysis ***of the Celltrion Media*** relied solely on Dr. Wurm's experimental results. On the contrary, Dr. Butler testified, as he disclosed in his report, that his opinion was based on "two assessments": (1) the insubstantiality of the concentration differences based on his element by element analysis, and (2) the experimental results confirming that the differences in fact did not affect performance. *Id.* at 101:12-102:1. (Although Dr. Wurm's trial testimony will be limited to his experiments and will not include a formal DOE analysis, he was asked similar hypotheticals and gave similar responses at deposition.)

III. THE DOE ANALYSIS BY JANSSEN'S EXPERTS DOES NOT VITIATE CLAIM LIMITATIONS

Neither the infringement opinions presented by Dr. Butler nor the experiments conducted by Dr. Wurm vitiate the concentration elements of the '083 patent. Janssen's experts rigorously analyze, on an ingredient-by-ingredient basis, whether the concentrations in the Celltrion Media are insubstantially different from those recited in claim 1 of the patent. Meanwhile, the results for the negative control provide affirmative proof that the concentration ranges are not vitiated.

A. The Law on Vitiation

If "a theory of equivalence would entirely vitiate a particular claim element," then the doctrine of equivalents is not available as a matter of law. *Warner-Jenkinson Co. v. Hilton David Chem. Co.*, 520 U.S. 17, 39 n.8 (1997). The vitiation concept "derives from the requirement that the doctrine of equivalents must be applied to the claims 'on an element-by-element basis,' so that every element of the invention – or its equivalent – is present in the accused product." *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349, 1356 (Fed. Cir. 2012) (quoting *Warner-Jenkinson*, 520 U.S. at 40). "Of course, in every case applying the doctrine of equivalents, at least one claimed element is not literally present in the accused product." *Id*. As a result, the "vitiation test cannot be satisfied merely by noting that the equivalent substitute is outside the

claimed limitation's literal scope." *Brilliant Instruments, Inc. v. GuideTech, LLC*, 707 F.3d 1342, 1347 (Fed. Cir. 2013).

"Rather, vitiation applies when . . . limitations are not interchangeable, not insubstantially different, and when they do not perform substantially the same function in substantially the same way, to accomplish substantially the same result." *Id.* "'Vitiation' is not an exception to the doctrine of equivalents, but instead 'a legal determination that the evidence is such that no reasonable jury could determine two elements to be equivalent.'" *Deere*, 703 F.3d at 1356 (quoting *Warner-Jenkinson*, 520 U.S. at 39 n.8). "In short, saying that a claim element would be vitiated is akin to saying that there is no equivalent to the claim element in the accused device based on the established 'function-way-result' or 'insubstantial differences' tests." *Brilliant Instruments*, 707 F.3d at 1347.

B. The Doctrine of Equivalents Is Available Where an Accused Product Does Not Literally Meet Claim Limitations Reciting a Numeric Range

The starting point of Defendants' vitiation argument is the assertion that, because the claimed concentration ranges are recited in "precise" quantitative terms, Janssen's experts are vitiating the concentration elements of the claim by asserting that equivalent media with concentrations outside the claimed ranges infringe under the DOE. Br. 17. But "the fact that a claim recites numeric ranges does not, by itself, preclude . . . [reliance] on the doctrine of equivalents.'" *U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1378 (Fed. Cir. 2007) (quoting *Abbott Labs v. Dey, L.P.*, 287 F.3d 1097, 1107-08 (Fed. Cir. 2002)); *see also Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1292 (Fed. Cir. 2010) ("The mere existence of a numerical value or range in the claim, absent more limiting language in the intrinsic record, does not preclude application of the doctrine of equivalents.").

The doctrine of equivalents is available where limitations reciting a numeric value or range are not met literally. For example, in *Warner-Jenkinson*, 520 U.S. 17, the Supreme Court allowed assertion of the doctrine of equivalents for a claim limitation reciting a pH range "from approximately 6.0 to 9.0." *Id.* at 22, 32-33; *see also U.S. Philips*, 505 F.3d at 1378 ("[R]esort to the doctrine of equivalents is not foreclosed with respect to the claimed concentration range."); *Abbott*, 287 F.3d at 1100, 1107-08 (a claim limitation reciting an "overall phospholipid content [of] 68.6–90.7%" was not vitiated by the application of the doctrine of equivalents); *Jeneric/Pentron, Inc. v. Dillon Co.*, 205 F.3d 1377, 1384 (Fed. Cir. 2000) (stating that the issue of equivalents for a claim limitation reciting 0.5–3% lithium oxide needed to be resolved on the evidence at trial); *Eastman Kodak Co. v. Agfa-Gevaert, N.V.*, No. 02-CV-6564T, 2005 U.S. Dist. LEXIS 32108, at *10 (W.D.N.Y. June 28, 2005) ("[T]here is no bright line rule against allowing a patent holder to assert a doctrine of equivalents infringement claim against an alleged infringer even where the patentee has used precise numerical terms in defining the literal meets and bounds of the claimed invention.").

C. Janssen's Experts Assess Equivalence on an Element-by-Element Basis and Their Analysis Does Not Vitiate Claim Elements

Defendants argue that the opinions of Janssen's experts supposedly "analyze DOE based on the claims as a whole," Br. 12, and not on an element-by-element basis as required by controlling authority. Defendants are mistaken.

1. Dr. Butler's assessment of individual concentration differences does not vitiate the concentration elements of the claim

At trial, Dr. Wurm's testimony will focus on the methodology and results of his experiments, and Dr. Butler will present the formal analysis of infringement under the doctrine of equivalents. As discussed above, Dr. Butler conducted a two-part analysis that began by

assessing each of the individual ingredients and concentration differences one by one in light of the scientific literature and his knowledge and experience and concluded that they are insubstantial. Ex. 1 (Butler Op. Rep.) ¶¶ 42-95; Ex. 10 (Butler Tr.) 75:21-78:10, 85:12-100:14, 139:11-146:20. Although this detailed analysis occupies more than twenty pages of Dr. Butler's infringement report, Defendants ignore this portion of Dr. Butler's infringement opinion in their brief. That omission is fatal to their motion.

Plainly, Dr. Butler's analysis of each of the individual ingredients that are literally outside the claimed ranges does not improperly assess the DOE based on the "claim as a whole." On the contrary, this part of Dr. Butler's analysis is addressed solely to the nature and function of each individual ingredient. Nor does Dr. Butler's ingredient-by-ingredient analysis render the concentration limitations of the patent irrelevant. Indeed, Dr. Butler's analysis would make no sense without taking into account the patented concentration ranges, as without those benchmarks there would be no concentration differences to assess. By ignoring Dr. Butler's analysis of each individual concentration difference, Defendants attack a straw-man version of Dr. Butler's opinions that is different from what he disclosed in his reports, described in his deposition, and will testify about at trial. Their motion must be denied for that reason alone.

2. The experiments conducted by Dr. Wurm and relied on by Dr. Butler do not vitiate the concentration elements of the claim

The second part of Dr. Butler's infringement analysis, relying on Dr. Wurm's experimental results, also does not improperly focus on the claim as a whole. As explained above, the whole point of Dr. Wurm's experiments was to isolate each individual difference in concentration and measure its effect on performance. *See supra* Part II.B. That is why Dr. Wurm tested twelve or thirteen separate variants for each of the two Celltrion Media. Had Dr. Wurm only been interested in comparing the Celltrion Media to the claim as a whole, he would

have only had to test one variant for each media: the "All Changes" variant that literally meets all the limitations of claim 1. Over 90% of the work that Dr. Wurm did was directed at measuring performance on an element-by-element basis.

Defendants argue that because Dr. Wurm's experiments assess overall measures of cell culture performance such as cell growth and antibody production, his experiments somehow ignore the individual concentration limitations. Br. 17. In support of this argument, Defendants repeatedly quote Dr. Wurm's testimony that his experiments measured the "sum of everything" in the media. Br. 10, 17. This testimony does not support their point. It is true, as Dr. Wurm testified, that the performance measures he tested do "not teach us which component in the medium provides the growth potential." Ex. 5 (Wurm Tr.) 156:21-157:3. But Dr. Wurm's study design ensures that any ***differences*** in performance that are observed among the variants can be attributed to the particular concentration differences being tested. *See id.* at 110:20-25 (stating that the "element-by-element approach" was "crucial" because it "isolate[s] an effect to a certain component"). Furthermore, the performance measures that Dr. Wurm selected are those that appear in the specification of the '083 patent, *see* col. 9:40-col. 8:20, which is the appropriate way to measure equivalence under the function-way-result test. *See Interactive Pictures Corp. v. Infinite Pictures, Inc.*, 274 F.3d 1371, 1383 (Fed. Cir. 2001) (holding that in applying the function-way-result test, "we look to the way in which [the] functions are accomplished and the attendant results in the specification").

In contending that Dr. Wurm's experiments vitiate claim elements, Defendants assume that well-controlled experiments are meaningless exercises that cannot be relied upon as proof of what they are designed to isolate and test. In fact, Dr. Wurm's experiments were fully capable of measuring whether a particular cell culture media did or did not produce substantially similar

results to the Celltrion Media. The negative control proved exactly that for an 80% deviation from the concentrations in the accused media. *See, e.g.*, Ex. 3 (Wurm Op. Rep.) ¶¶ 65, 72, 75, 78. Not only were Janssen's experiments properly designed to test equivalence on an element-by-element basis, their results demonstrate that the experiments were able to capture substantial differences where they existed. This demonstrates that the experiments do not vitiate any elements of the claim.

3. The experts' deposition testimony does not vitiate the concentration elements of the claim

Defendants selectively quote a handful of statements made by Janssen's experts at their depositions, and assert that these out-of-context statements show that they "completely disregard[ed] the concentration limitations for each individual ingredient." Br. 17.
But the testimony about which Defendants complain was hypothetical and unrelated to Janssen's proof against the Celltrion Media. The testimony does not suggest that Janssen's infringement theory vitiates the elements of the asserted claims.

Defendants repeatedly cite Dr. Butler's testimony that as he "underst[ood] the doctrine of equivalents," any individual concentration difference that displayed equivalent performance as shown in Dr. Wurm's experiments "would be deemed equivalent" "regardless of what concentration a person uses." Ex. 10 (Butler Tr.) 113:15-25; *see* Br. 2, 10, 17, 18. According to Defendants, this means that Dr. Butler "ignored the concentration limitations" and "focused entirely on the end result of a given cell culture medium." Br. 18. As shown above, however, that is simply untrue. *See supra* Part II.C. Dr. Butler's testimony was in response to an explicitly counterfactual, hypothetical line of questioning in which he was instructed to "assume" that cell culture media with compositions and concentrations different from the Celltrion Media would be shown to be equivalent in Dr. Wurm's experiments. Ex. 10 (Butler Tr.) 102:7-113:25.

Dr. Butler testified that as he understood the DOE, a media could be deemed equivalent based on Dr. Wurm's experiments alone regardless of concentration. Dr. Butler did not testify, however, that his analysis ***of the Celltrion Media*** was based solely on Dr. Wurm's experiments. On the contrary, Dr. Butler testified that his analysis was based on "two assessments": the magnitude and nature of the differences in light of his knowledge and experience, and the experimental results. *Id.* at 101:12-102:1.

An argument much like the one Defendants raise was considered – and rejected – by the Federal Circuit in *Abbott*. In that case, Abbott asserted that a 94.5% phospholipid concentration in the accused product met the relevant claim, which recited "68.6–90.7% phospholipid." 287 F.3d at 1101. The defendant relied on testimony by Abbott's expert, that "very close to a hundred percent could still work," in arguing Abbott's DOE theory vitiated the claim limitation by "improperly reading out the phospholipid range limitation altogether." *Id.* at 1107. The Federal Circuit rejected that argument as "irrelevant," (*id.*):

> Abbott only asserts an upper limit of 94.5%. An examination of what happens in the extreme outer ranges of phospholipid content is **therefore irrelevant** to the scope of equivalents asserted by Abbott. (Emphasis added).

The reason the expert's testimony as to the "extreme outer ranges" of phospholipid content was "irrelevant" in *Abbott* is that these extreme conditions did not match either the facts of the case or the plaintiff's assertions. It is axiomatic that although experts can be asked hypothetical questions, their answers to those questions are irrelevant unless the hypothetical is based on the actual facts. *See, e.g., Eaton v. Hancock Cnty.*, No. 1:08-cv-00370-JAW, 2011 U.S. Dist. LEXIS 67092, at *6 (D. Me. June 22, 2011) ("As a basic matter, the Court agrees that defense counsel should not ask a hypothetical question which assumes facts which will not be admitted into evidence."); *Larue v. Nat'l Union Elec. Corp.*, 571 F.2d 51, 58 (1st Cir. 1978)

(affirming district court's decision to strike expert's opinion based on a hypothetical fact for which the record "failed to provide an independent basis"). Here, Dr. Butler's actual opinion, based on his two-part analysis, is that the specific concentrations in the Celltrion Media are equivalent to those recited in the claim. The "extreme outer ranges" of what would be considered equivalent are irrelevant. And Janssen's assertion – its legal theory – is that the analysis of those particular ingredients and concentrations combined with well-controlled experiments is sufficient to prove infringement under the doctrine of equivalents. Its theory affirms the importance of the concentration ranges; it does not vitiate them.

Even if it were not directed to a counterfactual hypothetical, Dr. Butler's testimony would not vitiate the claim's concentration elements. Dr. Butler did not testify that any concentration would infringe. That would vitiate the concentration ranges. Rather, he testified that a concentration that was ***proved in Dr. Wurm's experiments*** to be an equivalent could be deemed an equivalent. As the results of the negative control demonstrate, Dr. Wurm's experiments are fully capable of distinguishing insubstantial concentration differences from substantial ones.

However, the Court does not need to decide whether Dr. Butler's infringement opinion would vitiate claim elements if it were based on Dr. Wurm's experiments alone, because his opinion is based on much more than that. If an opinion based on experiments alone would vitiate (which it would not), Dr. Butler's answers to hypothetical questions would, at most, suggest that he did not correctly understand the legal concept of vitiation. *See Abbott GmbH & Co., KG v. Centocor Ortho Biotech, Inc.*, 971 F. Supp. 2d 171, 184 n.4 (D. Mass. 2013) (because the Court applies the law, "it is of no consequence that defendant's experts did not set forth the precise legal test"). It would not mean that Dr. Butler's opinions in this case, which are based on "two assessments" operating together, are inadmissible. Ex. 10 (Butler Tr.) 101:12-102:1.

4. Defendants rely on inapposite case law

Defendants rely on inapposite cases where the plaintiffs, instead of identifying an equivalent for a particular limitation or limitations in the accused product, offered an incorrect theory that Janssen does ***not*** raise, i.e., that particular limitations were unnecessary to the claim. In *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1160 (Fed. Cir. 1998), for example, the plaintiff did not attempt to show that a hemispherical cup in the accused product was substantially equivalent to the claimed conical cup in a hip prosthesis; rather, the plaintiff offered only "conclusory" testimony that a "any . . . shape" would "function[] almost exactly the same way" once implanted. The same principle guided the decisions in *Forest Labs., Inc. v. Abbott Labs.*, 239 F.3d 1305, 1313 (Fed. Cir. 2001) (declining to treat a limitation related to the percentage of water in a composition as "irrelevant") (citing *Tronzo*, 156 F.3d at 1160), and *Revlon Consumer Prods. Corp. v. Estee Lauder Co.*, No. 00 Civ. 5960 (RMB)(AJP), 2003 U.S. Dist. LEXIS 13004, at *141-44 (S.D.N.Y. July 30, 2003) (Peck, M.J.) (finding that plaintiff failed to established equivalence for the limitation requiring "100% coating" where it asserted that "the degree of coating is irrelevant" and did not establish the degree of coating in defendant's products).

Here, Janssen does ***not*** assert that the specific concentrations of the claimed ingredients are "irrelevant." Instead, Janssen has offered evidence specific to each element in the Celltrion Media that falls outside the claimed range to demonstrate that the concentration in the Defendants' product is substantially equivalent to the claimed concentration. It is hard to imagine a more appropriate way of demonstrating that the equivalent of "every element" of the '083 media "is present in the accused product." *Deere & Co.*, 703 F.3d at 1356.

Nor have Janssen's experts asserted the "same" theory as the plaintiff in *Chiron Corp. v. SourceCF Inc*., 431 F. Supp. 2d 1019 (N.D. Cal. 2006). In *Chiron*, the plaintiff argued that the

total dose of an ingredient, not the concentration, was the relevant measure of infringement: "[f]or example, if 100 mg in 1 ml is within the claim, Chiron argues that 100 mg in 2 ml should also be deemed within the claim since the total dose is still 100 mg." *Id.* at 1035. This interpretation would have entirely eliminated concentration at the expense of total dose and thereby rendered the concentration limitation "meaningless." *Id.* Unlike in *Chiron*, Janssen's experts do not assert that something other than concentration is the relevant measure of infringement. They simply opine that on the facts presented here, the concentrations in the Celltrion Media are equivalent to those in the claim.

D. The Magnitude of the Deviations from the Range Recited in the Claims Does Not Preclude Application of the Doctrine of Equivalents

Celltrion also argues that the concentration of some ingredients in the accused product is so far from the range recited in the claims, in one direction or the other, that applying the doctrine of equivalents would vitiate the claim limitations. Br. 6-7, 14-15. Thus, Celltrion argues that "one ingredient [redacted] . . . is ***433%*** of the claimed maximum construction, and another [redacted] . . . is about ***8%*** of the claimed minimum concentration . . . ." Br. 6-7 (emphasis in original). This argument is misleading[3] and, in any event, misses the mark.

1. Multi-fold differences in quantity can be equivalent

What is important for the doctrine of equivalents is not the magnitude in the abstract of any variation from the claimed concentration ranges, but rather, the significance of that variation, if any, in the context of the facts of the particular case. *See, e.g., Intendis GmbH v. Glenmark*

[3] As Dr. Butler explains in his expert report, part of the reason that the [redacted] concentration in the Celltrion Media is equivalent to the concentration recited in the claim is that the Celltrion Media have another form of [redacted]. Ex. 1 (Butler Rep.) ¶¶ 81-83. Considering the two sources of [redacted], the total amount of [redacted] in the Celltrion Media is actually within the claimed range. *Id.*

Pharm. Inc., USA, 822 F.3d 1355, 1364 (Fed. Cir. 2016) ("'What constitutes equivalency must be determined against the context of the patent, the prior art, and the particular circumstances of the case . . . .'") (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 609 (1950)). On the facts of a given case, variations from a recited numerical value as large or larger than those at issue here can be insubstantial and can have substantially the same function/way/result as a number or numeric range recited in the claims. *See Warner-Jenkinson*, 520 U.S. 17; *Jeneric/Pentron*, 205 F.3d at 1384; *U.S. Philips Corp*, 505 F.3d at 1378. Decisions by the Supreme Court and the Federal Circuit make this clear.

For example, in *Warner-Jenkinson*, the jury had found infringement under the doctrine of equivalents on the ground that a pH of 5.0 was insubstantially different from a pH within the claimed range of "approximately 6.0 to 9.0." 520 U.S. at 22. The Supreme Court pointed out that pH is measured "on a logarithmic scale, with each whole number difference representing a ten-fold difference in acidity." *Id*. at 22 n.1. In percentage terms, a ten-fold difference is a difference of ***1000*** percent. Nevertheless, the Supreme Court noted that the "practical significance" of this 1000% difference "depend[ed] on the context," *id*., and remanded for further proceedings, *id*. at 41. On remand, the Federal Circuit upheld the jury's finding of infringement. *Hilton Davis Chem. Co. v. Warner-Jenkinson Co.*, 114 F.3d 1161, 1164 (Fed. Cir. 1997).

Similarly, in *Jeneric/Pentron*, the accused product had lithium oxide in a concentration of 0.041% – only ***8.2%*** of the lower end of the claimed range of 0.5–3% lithium oxide. The Federal Circuit held that it was a question of fact "whether that [twelve-fold difference] is insubstantial." 205 F.3d at 1384. And in *U.S. Philips*, the Federal Circuit vacated the district court's ruling that a finding of infringement would vitiate the claim limitation despite the fact that the accused

product had halogen in a concentration 200% higher than the upper end of the claimed range. 505 F.3d at 1377-78 (citing *Abbott*, 287 F.3d at 1100, 1107-08; *Warner-Jenkinson*, 520 U.S. at 32-33).

Here, as in *Warner-Jenkinson*, "the practical significance" of the variations from the range recited in the claims can only be determined in the context of the facts of this case, including evidence on whether the concentrations in Defendants' media have substantially the same function/way/result as concentrations in the claimed ranges. 520 U.S. at 22 n.1. That determination can only be made on a full record as developed at trial.

2. Defendants' cases do not establish quantitative limits on the doctrine of equivalents

The cases Defendants cite on this issue do not support a different conclusion. In *Talbert Fuel Sys. Patents Co. v. Unocal Corp.*, 347 F.3d 1355, 1358-60 (Fed. Cir. 2003), and *Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd.*, 476 F.3d 1321, 1328 (Fed. Cir. 2007), for example, the Federal Circuit relied on the doctrine of prosecution history estoppel in rejecting the plaintiffs' claims under the doctrine of equivalents. Defendants have not relied on prosecution history estoppel in this case, because there would be no basis for doing so.

Additionally, in *Ortho-McNeil*, 476 F.3d at 1329, and *Conopco, Inc. v. May Dept's Stores Co.*, 46 F.3d 1556, 1561 (Fed. Cir. 1994), unlike this case, the numerical ranges in the claim limitations were described in the patent's specification or prosecution history as "critical" to the patented inventions.[4] Here, in contrast, nothing in the specification or prosecution history states

[4] *Conopco* is also inapposite because it predated the Supreme Court's decision in *Warner-Jenkinson*. The Federal Circuit's jurisprudence on the doctrine of equivalence was in flux before *Warner-Jenkinson* and has largely been superseded by more recent case law applying controlling Supreme Court precedent. *See* 5B-18 Chisum on Patents § 18.04(1)(a)(iii)-(iv) (discussing split in Federal Circuit over the DOE prior to *Warner-Jenkinson*).

that the limitations for which Janssen asserts the DOE are critical. Defendants rely on the opinions of their expert, Dr. Glacken, and the testimony of Dr. Butler to suggest that the claimed concentration limitations ***in general*** are important. Br. 5-6 (citing Glacken Reb. Rep. ¶¶ 60-68; Butler Tr. 60:18-61:10). But the claim recites 61 ingredients, each with a range of concentrations. As one of the inventors of the '083 patent, David Epstein, explained at his deposition, a person of skill in the art would know that some variation outside of the claimed concentration ranges was possible and that each specific concentration limitation was not critical. Ex. 11 (Epstein Tr.) 226:4-25. Dr. Butler agreed. Ex. 10 (Butler Tr.) 64:17-65:3, 104:9-23. Meanwhile, defendants' expert Dr. Glacken does not opine that the twelve (or thirteen) specific concentrations ranges that the Celltrion Media fall outside of are critical to the invention.

Advanced Steel Recovery, LLC v. X-Body Equipment, Inc., 808 F.3d 1313 (Fed. Cir. 2015), is similarly inapposite. The relevant limitation there did not involve a numerical requirement or range. Rather, it was a structural limitation requiring a "container packer" be located at the "proximate end" of a shipping container. The accused product had the container packet located in the "bottom middle" of the container, changing the manner in which the container physically functioned. This case does not involve remotely similar facts.

Finally, in *Amazin' Raisins, Int'l, Inc. v. Ocean Spray Cranberries, Inc.*, 306 F. App'x 553, 557-59 (Fed. Cir. 2008), the relevant limitation recited "dried fruit" which was construed to mean fruit having a moisture content of "about 10% to 18%." The Federal Circuit found that applying the DOE to fruit with a moisture content of 87% to 90% would vitiate the requirement that the fruit be "dried." In contrast, Janssen will demonstrate, limitation by limitation and based on substantial evidence, that the accused product does have equivalents to the claimed ranges.

IV. DR. WURM'S EXPERIMENTS VALIDLY COMPARED THE ACCUSED CELLTRION MEDIA TO THE CLAIM ON AN ELEMENT-BY-ELEMENT BASIS

In addition to their flawed vitiation arguments, Defendants also contend that the jury should be prevented from hearing testimony about Dr. Wurm's experiments. Br. 19-28. This argument falls of its own weight. On the one hand, Defendants contend that Dr. Wurm should have tested the actual Celltrion Media made by HyClone and should not have added ingredients that are necessary for cell growth (and that Celltrion itself adds for cell growth), ignoring the facts that this would have made the experiments physically impossible to conduct and that cells would not have grown without the added ingredients. On the other hand, Defendants argue that Dr. Wurm should have somehow compared the Celltrion Media to the claimed invention through an experimental design in which the Celltrion Media was not actually studied. In short, Defendants argue that Dr. Wurm should have conducted impossible and scientifically flawed experiments rather than the sophisticated, valid experiments that he actually carried out.

A. Dr. Wurm's Experiments Use Valid Replicas of the Celltrion Media

Defendants' first argument against Dr. Wurm's experiments focuses on the fact that he made replicas of the Celltrion Media and added certain necessary ingredients to them rather than testing the actual Celltrion Media made by HyClone. Br. 20-24. This argument faults Dr. Wurm for failing to do the impossible. It should be rejected out of hand.

1. It would have been impossible to conduct element-by-element experiments starting with a HyClone-manufactured powder

Defendants challenge Dr. Wurm's decision to make his own media using Celltrion's recipes, rather than obtaining samples of the actual media powders that Celltrion purchases from HyClone. Br. 20-21. It took Janssen months even to obtain the formula for the Celltrion Media and to receive permission to share that information with Dr. Wurm. Obtaining samples of the

actual powder would surely have delayed matters for so long as to make the experiments impossible.

More to the point, the actual media would have been useless for the experiments. It would have been physically impossible for Dr. Wurm to conduct his twelve-variant experiments using a HyClone-produced powder. This is because some ingredients (*e.g.*, [redacted]) are present in the Celltrion Media in higher concentrations than those recited in claim 1 of the '083 patent. Ex. 1 (Butler Op. Rep.) ¶ 48; Br. App'x A, at 3-4. In order to create variants of the Celltrion Media that literally fell within the lower concentration range of the claim, Dr. Wurm would have had to ***remove*** material from the HyClone powders. It is impossible, however, to isolate and subtract specific ingredients from a powder that is composed of a mixture of multiple ingredients; it would be like trying to remove baking soda from pancake mix. *See* Ex. 5 (Wurm Tr.) 204:6-7; Ex. 10 (Butler Tr.) 159:18-24, 160:20-21. As a result, the only possible way for Dr. Wurm to conduct his experiments was to create media from scratch according to Celltrion's recipes as he did.[5] Defendants' argument that Dr. Wurm should have acted differently is not to be taken seriously.

2. Adding ingredients to the powder formulation was necessary to grow productive cells

Defendants' suggestion that Dr. Wurm should not have added L-glutamine, sodium

[5] Even if it were possible to prepare variant media from the HyClone powders, doing so would have been scientifically invalid. As Dr. Wurm testified at his deposition, a comparison of variants prepared in his laboratory with samples of the accused Celltrion Media made by HyClone would have been a comparison of "[a]pples against pears," because his media were freshly prepared in his laboratory, while the powder "may be made half a year ago sitting in a warehouse maybe for delivery to Celltrion." Ex. 5 (Wurm Tr.) 205:5-9. There would also have been no way of verifying that the ingredients in the HyClone powders were from the same sources as those prepared in Dr. Wurm's lab or that the media had been prepared under similar conditions. *Id.* at 62:23-63:12. In contrast, Dr. Wurm's experiments, in which all the tested media were prepared at the same time by the same people from identically sourced ingredients, were well controlled. *Id.* at 203:8-16.

bicarbonate, or MHX to his test media is also specious. Br. 21-24. As discussed above, L-glutamine and sodium bicarbonate are added to powdered formulations to enable the formulation to grow cells. The '083 patent discloses their use and Celltrion itself adds them to its media. Col.8:7-12, 8:22-26. Indeed, Defendants' expert Dr. Glacken agreed that "you would have to add glutamine and [sodium] bicarb[onate] to do a reasonable experiment." Ex. 6 (Glacken Tr.) 248:20-21. Similarly, there is no dispute that MHX is needed in order for C743B cells, the type of cells that Dr. Wurm used in his experiments, to be productive. Ex. 5 (Wurm Tr.) 191:11-23, 194:5-8. The presence of these necessary ingredients to cell growth does not mean that Dr. Wurm failed to test "reliable" replicas of the HyClone powders. Br. 23. The extra ingredients that Dr. Wurm added to his experimental media would also need to be added to the HyClone powders in order to grow productive C743B cells. This fact proves nothing helpful to Defendants' case.

Izumi Products Co. v. Koninklijke Philips Electronics NV, 315 F. Supp. 2d 589 (D. Del. 2004), on which Defendants rely, is completely inapposite. In *Izumi*, the court excluded the plaintiff's expert witness because he had merely "reviewed" two products and then delivered an opinion about their function "based solely on his subjective belief." *Id.* at 602. The expert did not "perform any testing on any of the accused infringing electric rotary razors or, for that matter, on an electric rotary razor manufactured by Izumi," and "likewise did not cite any literature reference to substantiate" his opinion. *Id.* Here, Dr. Wurm performed sophisticated scientific experiments, testing each difference element-by-element. Dr. Wurm's experiments are not a matter of "subjective belief," but of scientific fact.[6]

[6] The other cases cited by Defendants are equally irrelevant. In *Thermapure, Inc. v. RxHeat, LLC*, 35 F. Supp. 3d 968 (N.D. Ill. 2014), the plaintiff's expert relied solely on reviewing the "documents and

B. Dr. Wurm Properly Compared the Celltrion Media to the Claimed Invention on an Element by Element Basis

After arguing that Dr. Wurm should have tested the actual HyClone-produced powders without adding or subtracting any ingredients, Defendants abruptly switch gears and contend that Dr. Wurm should have conducted his experiments in a completely different way. Br. 25-28. Defendants contend that Dr. Wurm should have removed the 29 ingredients that are present in the Celltrion Media but not in the claim. Defendants also argue that instead of starting with the Celltrion Media and altering the concentrations one-by-one to match the claimed concentrations, Dr. Wurm should have started with a hypothetical media that literally infringed the claim and changed the ingredients in ***that*** media (which is not accused of infringement) one-by-one. These arguments are in direct contradiction to Defendants' first set of criticisms of Dr. Wurm's reports and would result in experiments that are not scientifically valid. They do not remotely provide a basis for excluding Dr. Wurm's experiments.

1. Removing 29 unclaimed ingredients from the Celltrion Media would not have tested the accused product

Defendants challenge Dr. Wurm's experiments on the ground that when constructing his replica of the accused product and the variants for testing, Dr. Wurm did not remove 29

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specifications" of how the allegedly infringing product worked. *Id.* at 984. Like *Izumi*, *Thermapure* does not remotely suggest that testimony based on sophisticated scientific experiments can be excluded as unreliable. In *Hoffman v. Ford Motor Co.*, 493 F. App'x 962 (10th Cir. 2012), the Tenth Circuit endorsed the testing of a product that was similar but not identical to the one at issue, holding that the testing of a "similar buckle[] . . . is a valid scientific method." *Id.* at 975. The issue was only that the expert failed to test how that buckle would behave in a real-world setting. *Id.* In both of the other cases cited, the expert testimony was excluded because it failed to replicate the conditions relevant to the disputed issue. *Phillips v. Am. Honda Motor Co.*, 238 F. App'x 537, 540 (11th Cir. 2007) (where fact in issue was temperature of foot, expert testimony excluded because test did not demonstrate that dummy foot responded to temperature in the same way as a human foot); *Bogosian v. Mercedes-Benz of N. Am., Inc.*, 104 F.3d 472, 479 (1st Cir. 1996) (holding that expert testimony properly excluded where expert's test did not replicate circumstances of accident). Here, none of the differences between the Dr. Wurm's tested and the accused product are relevant to infringement.

ingredients that are actually present in the Celltrion Media but are not claimed in the ’083 patent. This is preposterous. Had Dr. Wurm done this, he would not have tested the accused product. It was necessary that Janssen test the accused product.

Celltrion admits that the 29 unclaimed ingredients are present in the Celltrion Media and the ’083 patent permits the addition of such unclaimed ingredients, as the Court recognized on claim construction. Dkt. No. 233 (8/17 Hearing Tr.), at 105, 115. Therefore, any accurate replica of the Celltrion Media would need to contain these 29 unclaimed ingredients. Elsewhere, Defendants seem to agree. Indeed, as discussed above, they assert that Dr. Wurm should have tested media made from powders obtained directly from HyClone. *See supra* Part IV.A.1. The HyClone powders, of course, contain the 29 unclaimed ingredients. Indeed, as noted above, it would be impossible to remove these 29 ingredients from the HyClone powders. Dr. Wurm’s experiments were well controlled. The 29 unclaimed ingredients from the Celltrion Media are present in both the Celltrion Media and the variants, and they therefore had no effect on the outcome of the experiments. Other than speculation, Dr. Glacken identifies no such effect.

2. Dr. Wurm properly isolated each concentration difference in the Celltrion Media

As discussed above, Dr. Wurm created replicas of the Celltrion Media and then, for each of the twelve (or thirteen) ingredients with concentrations outside the ranges recited in the patent, he created a variant medium with the concentration moved within the claimed ranged. *See supra* Part II.B. Because the two Celltrion Media have twelve (or thirteen) differences in concentration from those recited in the claim, changing the concentrations one by one results in variants that each have eleven (or twelve) differences from the claim. Defendants argue that Dr. Wurm failed to compare the Celltrion Media to the claimed invention. Br. 25-26. Defendants are wrong.

As a preliminary matter, Defendants' contention that Dr. Wurm did not "compare [the accused products] to media made according to asserted claim 1" is incorrect. Br. 25. Dr. Wurm did exactly that, creating an "All Changes" variant that met all the limitations of claim 1 and comparing that literally-infringing variant to the Celltrion Media. He found no substantial differences. *See* Ex. 3 (Wurm Rep.) ¶¶ 71, 74, 77; *id.* Ex. B, at 18. Defendants ignore this variant when they contend that none of Dr. Wurm's replicas meets all the limitations of the '083 patent. Their contention that Janssen did not test the claimed invention is wrong.

The problem with relying exclusively on the "All Changes" experiment, however, is that it does not evaluate the effect of the individual concentration differences on an element-by-element basis, as required by law. To do that, the twelve (or thirteen) concentration differences have to be varied one at a time, as Dr. Wurm did in his experiments. In their brief, Defendants do not say what they believe Dr. Wurm should have done differently to test the relevant concentration differences one-by-one. In Dr. Glacken's report, however, he argues that Dr. Wurm should have done the inverse of what he did. Instead of beginning with the Celltrion Media and altering the concentrations one by one to the claimed ranges, Dr. Glacken suggests that Dr. Wurm should have started with the "All Changes" variant as a control – the variant that meets all the limitations of the '083 patent – and change the concentrations one by one to those in the Celltrion Media. Ex. 7 (Glacken Reb. Rep.) ¶ 166. Indeed, Celltrion argues that Janssen should have used an "All Changes" variant with the 29 unclaimed ingredients also removed.

The problem with this approach is apparent. Dr. Wurm's variants (other than the "All Changes" variant) each had one difference from the accused Celltrion Media and eleven differences from the claim, and was compared to the accused Celltrion Media. The variants proposed by Dr. Glacken would each have one difference from the claim and ***eleven differences***

from the Celltrion Media. It would be compared to a control that had ***twelve differences*** from the Celltrion Media. (If the 29 unclaimed ingredients were also removed, this experiment would compare each variant to a composition that had ***42 differences*** from the accused product). As a result, Dr. Glacken's proposed experiments would not test the Celltrion Media, or anything like it, even though it is the accused product. Therefore, these experiments would not, and could not, isolate each individual difference between the Celltrion Media and the claim. The proposed experiments are a random exercise unrelated to the infringement issues in this case. Of course, Dr. Glacken was free to undertake these experiments if he so chose, but he did not do so.

In any event, there is no basis to suggest that Dr. Wurm somehow generated scientific results that are not reliable by choosing to conduct a controlled experiment ***of the accused Celltrion Media*** rather than of a hypothetical media not at issue in this case. Plainly, Dr. Wurm's experiments provide useful information about the insubstantiality of the differences between the Celltrion Media and the claims. There is no basis to exclude testimony about these experiments.

V. CONCLUSION

For the above reasons, Defendants' motion should be denied.

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EXHIBITS 1-11

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