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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CELLTRION, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2016-01667
Patent 7,976,838 B2

Before ERICA A. FRANKLIN, SHERIDAN K. SNEDDEN and JACQUELINE T. HARLOW, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Celltrion, Inc. ("Petitioner") filed a Petition (Paper 2; "Pet.") to institute an *inter partes* review of claims 1–14 of US 7,976,838 B2 (Ex. 1001; "the '838 patent"). Genentech, Inc. ("Patent Owner") filed a Patent Owner Preliminary Response. Paper 13[1] ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a).

Upon consideration of the Petition and Preliminary Response, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim. 35 U.S.C. § 314(a). Accordingly, we deny the Petition and decline to institute an *inter partes* review.

A. Related Proceedings

The parties inform us that there are no pending proceedings concerning the'838 patent. Pet. 2; Paper 5, 2. Previously, the'838 patent was challenged in IPR2015-00417, by a different petitioner, and an *inter partes* review was instituted for claims 1–14. Case IPR2015-00417, Paper 11. Thereafter, the case was terminated upon a request by that petitioner. Case IPR2015-00417, Paper 18. Prior to termination, Celltrion, Inc. filed a petition challenging the '838 patent in IPR2015-01733 and a motion for

[1] Patent Owner filed a Motion to Seal its Patent Owner Preliminary Response and certain exhibits, and for Entry of a Protective Order. Paper 12. With respect to those items, this decision refers only to the unsealed, redacted paper and exhibits.

joinder with IPR2015-00417. Case IPR2015-01733, Papers 2, 3. Subsequently, the Celltrion, Inc. petition was dismissed without prejudice upon a request by Celltrion, Inc. Case IPR2015-01733, Paper 12. The dismissal decision explains, "a dismissal without prejudice does not modify or otherwise alter the application of statutory and regulatory requirements to a filed petition, including the Board's discretionary considerations when deciding whether to institute an *inter partes* review." *Id*. at 2–3.

B. The '838 patent

The '838 patent discloses methods of treating rheumatoid arthritis ("RA") in a human patient who experiences an inadequate response to a TNFα-inhibitor. Ex. 1001, Abstract, 4:3–24. The methods of the claimed invention involve administration of an antagonist that binds to a B cell surface marker, such as CD20. *Id.* at 4:60–65. The Specification describes treating patients who have experienced an inadequate response to a TNFα-inhibitor. *Id.* at 6:64–7:12. The Specification expressly defines the term "inadequate response to a TNFα-inhibitor" as follows:

> [A]n inadequate response to previous or current treatment with a TNFα-inhibitor because of toxicity and/or inadequate efficacy. The inadequate response can be assessed by a clinician skilled in treating the disease in question.

Id. at 5:25–29. Commercial examples of TNFα-inhibitors include Etanercept (ENBREL®), Infliximab (REMICADE®) and Adalimumab (HUMIRA™). *Id.* at 5:19–24.

C. Illustrative Claims

Claims 1, 2, 8, 10 and 11 are the independent claims among the challenged claims, and are reproduced below:

1. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient an antibody that binds to CD20, wherein the antibody is administered as two intravenous doses of 1000 mg.

2. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient an antibody which binds to CD20 in an amount that is effective to provide an ACR50 response at week 24, ACR70 response at week 24, or no erosive progression at weeks 24 and beyond, wherein the antibody is administered as two intravenous doses of 1000 mg.

8. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient rituximab, wherein rituximab is administered as two intravenous doses of 1000 mg.

10. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient rituximab, and methotrexate, wherein the patient has no erosive progression at weeks 24 and beyond, and wherein rituximab is administered as two intravenous doses of 1000 mg.

11. A method of achieving a clinical response selected from the group consisting of ACR50 response at week 24, ACR70 response at week 24, and no erosive progression at weeks 24 and beyond, in a human rheumatoid arthritis patient who experiences an inadequate response to a TNFα-inhibitor, comprising administering to the patient rituximab, and methotrexate, wherein rituximab is administered as two intravenous doses of 1000 mg.

Claims 3–7 depend from claim 2, either directly or indirectly. Claim 9 depends directly from claim 8. Claims 12–14 depend directly from claim 11.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–14 of the '838 patent on the following grounds:

Reference[s]	Basis	Claims challenged
Edwards[2]	§ 102	1–5, 7–14
Edwards and Tuscano[3]	§ 103(a)	1–14
Goldenberg,[4] Curd,[5] and De Vita[6]	§ 103(a)	1–14

[2] JCW Edwards et al., *Efficacy and Safety of Rituximab, a B-Cell Targeted Chimeric Monoclonal Antibody: A Randomized, Placebo-Controlled Trial in Patients with Rheumatoid Arthritis*, Abstracts of the American College of Rheumatology 66th Annual Meeting, Oct. 24-29, 2002 (New Orleans, LA). Ex. 1033 ("Edwards").

[3] Joseph M. Tuscano, *Successful Treatment of Infliximab-Refractory Rheumatoid Arthritis with Rituximab*, 46 ARTHRITIS RHEUM 3420, LB11 (2002). Ex. 1034 ("Tuscano").

[4] Patent Application Publication No. WO 00/74718 A1 by David M. Goldenberg et al., published Dec. 14, 2000. Ex. 1038 ("Goldenberg").

[5] Patent Application Publication No. WO 00/67796 A1 by John G. Curd et al., published Nov. 16, 2000. Ex. 1031 ("Curd").

[6] S De Vita et al., *Ruolo Patogentico Dei Linfociti B Nella Sinovite Reumatoide: Il Blocco Selettivo B Cellulare Puo Indurre Risposta Clinica In Pazienti con Artrite Reumatoid Refrattaria*, OFFICIAL JOURNAL OF THE ITALIAN SOCIETY OF RHEUMATOLOGY, Vol. 53, No. 3 (Suppl. No. 4) (2001) [ENGLISH TRANSLATION]. Ex. 1051 ("De Vita").

Petitioner also relies on the Declarations of Maarten Boers, M.D., Ph.D. (Ex. 1002), M. Laurentius Marais, Ph.D. (Ex. 1039), and Jack Goldberg, M.D. (Ex. 1036).

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc*., 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner does not contend that the claim recitation of "a patient who experiences an inadequate response to a TNFα-inhibitor" is not entitled to patentable weight. Rather, Petitioner asserts that the broadest reasonable construction of that claim phrase is "a patient who, due to the characteristics of the patient and her individual disease presentation, either (1) did not or would not respond to treatment with TNFα-inhibitor or (2) did or would experience a toxicity upon such treatment." Pet. 24. In other words, Petitioner's proposed construction does not require a patient to have *actually* experienced an inadequate response, but encompasses those patients who

theoretically "would" not respond to treatment or experience toxicity, based upon some "inherent characteristic of the patient herself." *Id*. at 25. According to Petitioner, its proposed construction is consistent with the Specification. *Id*.

We disagree with Petitioner. The Specification expressly defines the term "inadequate response to a TNFα-inhibitor" as "an inadequate response to previous or current treatment with a TNFα-inhibitor because of toxicity and/or inadequate efficacy." Ex. 1001, 5:25–28. We determine that definition is "set forth with reasonable clarity, deliberateness, and precision," *see In re Paulsen*, 30 F.3d at 1480, so as not to require further construction.

In view of our analysis, we determine that no additional claim terms require construction for the purpose of this Decision. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (Only terms which are in controversy need to be construed, and only to the extent necessary to resolve the controversy).

B. Anticipation by Edwards

Petitioner asserts that Edwards discloses a method that meets each element of claims 1–5 and 7–14. Pet. 31–45. Patent Owner disagrees. Prelim. Resp. 30–33.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987). "Inherency … may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *MEHL/Biophile Int'l. Corp. v. Milgraum*,

192 F.3d 1362, 1365 (Fed. Cir. 1999) (*quoting In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981)).

1. Edwards

Edwards discloses the results of a study involving 161 patients with RA, all of whom were rheumatoid factor positive and receiving methotrexate. Ex. 1033. The patients were separated into four patient groups: Group A (continuing methotrexate alone); Group B (rituximab alone); Group C (rituximab and cyclophosphamide); and Group D (rituximab plus continuing methotrexate). *Id.* Patients receiving rituximab were given two intravenous doses of 1000mg. *Id.* In addition, all groups received a 17-day course of corticosteroids. *Id.* All three rituximab regimens were "well tolerated" and produced "substantial clinical benefit in RA," with the combination therapies producing "the highest levels of ACR20, 50, and 70 responses." *Id.* Edwards does not discuss whether the study subjects had experienced an inadequate response to a TNFα-inhibitor.

2. Analysis

Petitioner contends that claims 1–5 and 7–14 of the '838 patent are anticipated by Edwards. Pet. 31–45. In particular, Petitioner asserts that Edwards inherently discloses treating RA with rituximab "in a human patient who experiences an inadequate response to a TNFα-inhibitor," an element required by each of the challenged claims. *Id*. at 32. In support of that assertion, Petitioner relies the declarations of Drs. Marais and Boers. *Id*. (citing Ex. 1002 ¶¶ 87–91).

Dr. Marais calculated "the probability" that Edwards' final sample of study participants would include at least one RA patient who experiences an inadequate response to a TNFα-inhibitor, i.e., an "RA-IR patient." Ex. 1039

¶ 4. He also determined a "statistically valid prediction" of the minimal actual number of RA-IR patients in the study sample. *Id*. Dr. Marais described the assumptions made for his calculations and provided a table of results showing that "the probability of including at least one RA-IR patient in a sample of "*n*" RA patients is virtually 100%." *Id*. ¶ 7.

Dr. Boers provided testimony based upon a belief that "patients who experience 'an inadequate response' [to a TNFα-inhibitor] are not limited to patients who have actually been treated with a TNFα-inhibitor." Ex. 1002 ¶ 27. Dr. Boers explains that "many patients inherently have an inadequate response to TNFα-inhibitor" and that such a response is innate to one's physiology. *Id*. ¶ 87. According to Dr. Boers, "it is virtually certain, based on my clinical and epidemiological understanding of the RA patient population, that at least one patient who received that dose belongs to the population that innately experiences an inadequate response to TNFα-inhibitor treatment." *Id*. ¶ 88. Dr. Boers states that the "probabilities calculated by Dr. Marais confirm my opinions." *Id*. at 91.

Patent Owner asserts that Petitioner's inherency position is insufficient, as it is based upon probabilities.[7] Prelim. Resp. 31–32. We agree. It is well established that "inherency does not follow even from a very high likelihood that a prior art method will result in the claimed invention." *In re Montgomery*, 677 F.3d 1375, 1384 (Fed. Cir. 2012), citing *Glaxo Inc. v. Novopharm Ltd*., 52 F.3d 1043, 1047 (Fed.Cir.1995) (holding

[7] Patent Owner asserts also that Edwards and Tuscano (asserted in an obviousness ground) are not prior art with respect to certain challenged claims. Prelim. Resp. 19–30, 34. Based on the dispositive issues analyzed in this decision, we do not reach Patent Owner's prior invention contentions.

that even though the defendant's experts reproduced a prior art method "thirteen times and each time they made [the claimed] crystals," the patentee's chemists twice produced different crystals from the same method, thus precluding inherency).

Thus, upon review of Petitioner's analysis and declaratory evidence, we determine that Petitioner has not established that Edwards discloses inherently "treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor," as required by each of claims 1–5 and 7–14.

Accordingly, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing that Edwards anticipates claims 1–5 and 7–14. Consequently, we decline to institute an *inter partes* review of any of those claims based on this ground.

C. Obviousness over Edwards and Tuscano

Petitioner asserts that claims 1–14 are rendered obvious by the combined teachings of Edwards and Tuscano. Pet. 45–50. Patent Owner disagrees. Prelim. Resp. 34–41.

A conclusion that the claimed subject matter is obvious must be supported by evidence, as shown by some objective teaching in the prior art or by knowledge generally available to one of ordinary skill in the art that would have led that individual to combine the relevant teachings of the references to arrive at the claimed invention. *See In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). Obviousness grounds must be supported with "articulated reasoning with some underpinning" and not by "mere conclusory statements." *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S 398, 418 (2007).

1. Tuscano

Tuscano discloses the results of "a clinical trial using rituximab alone for the treatment of erosive RA in patients that have previously failed multiple DMARD's including infliximab." Ex. 1034 (emphasis added). Rituximab was administered in an escalating dose starting at 100 mg on week one, 375 mg/m^2 on week two, and then 500 mg/m^2 on weeks three and four. *Id*. After five months of treatment, all seven patients had improved joint scores, and three patients had achieved an ACR20 response. *Id*. Tuscano concludes, "[w]hile the current patient numbers are small, and enrollment is ongoing, this data supports the hypothesis that B lymphocytes mediate pathology in RA, and that rituximab is a promising agent for patients with DMARD and infliximab-refractory RA." *Id*.

2. Analysis

Petitioner contends that claims 1–14 of the '838 patent are obvious over the combination of Edwards and Tuscano. Pet. 45–50. In particular, Petitioner maintains that Edwards discloses every limitation of the challenged independent claims, including administering two intravenous doses of 1000 mg of rituximab, and treating a patient who experiences an inadequate response to a TNFα-inhibitor. Pet. 46. In the combination, however, Petitioner relies on Tuscano as *expressly* disclosing treating a patient who experiences an inadequate response to a TNFα-inhibitor. *Id*. According to Petitioner, a person of skill in the art would have been motivated to administer rituximab according to the regimen disclosed in Edwards to the inadequate responders of TNFα-inhibitor in Tuscano, with a reasonable expectation of success, "because Edwards [] disclosed that the regimen is an effective therapy for RA." *Id*.

Petitioner acknowledges that Tuscano used a higher total dose of rituximab than Edwards, and asserts that "the claimed doses are obvious, as the lower doses were successfully used in Edwards." *Id*. at 48. Additionally, Petitioner asserts that that a skilled artisan would have had a reasonable expectation of success using Edwards dosing on Tuscano's patients based upon "[o]ther studies, which report using about 2000 mg total dose of rituximab to treat RA successfully." *Id*. (citing Ex. 1002 ¶ 128, Ex. 1035[8]). Further, Petitioner asserts "there is nothing critical about the claimed total dose of 2000 mg." *Id*. According to Petitioner, it would have been a matter of routine optimization for a POSA . . . to adjust the doses of rituximab to achieve the desired clinical outcome." *Id*.

At first glance, it appears as though Petitioner has addressed the deficiency in Edwards' disclosure, i.e., treating RA in a human patient who experiences an inadequate response to a TNFα-inhibitor, by combining Tuscano's teaching that rituximab may be used to treat RA in inadequate responders to a TNFα-inhibitor. Each challenged claim, however, requires administering to those inadequate responders a specified number of rituximab doses, in a specified dosage amount, i.e. two intravenous doses of 1000 mg.

Petitioner asserts that a person of skill in the art would have been motivated to use Edwards' regimen of administering two doses of rituximab 1000 mg, with a reasonable expectation of successfully treating RA in patients who experience an inadequate response to a TNFα-inhibitor because

[8] M. J. Leandro et al., *Clinical outcome in 22 patients with rheumatoid arthritis treated with B lymphocyte depletion*, 61 ANN RHEUM DIS 883–888, (2002). Ex. 1035 ("Leandro").

the regimen was effective for Edwards' patients. Pet. 46 (citing Ex. 1002 ¶ 126). Edwards, however, does not describe any of those patients as being part of a population that has inadequately responded to a TNFα-inhibitor. Petitioner's reference to Dr. Boer's declaration is unavailing, as he mentions two additional studies involving treating inadequate responders with rituximab, without a discussion of the dosing involved. Ex. 1002 ¶ 126.

Although Petitioner has reasonably described the level of skill in the art, *see* Pet. 45–46, Petitioner has not explained persuasively why a person of skill in the art would have expected the regimen that was effective in Edwards' patients to be effective in Tuscano's inadequate responders. As Petitioner acknowledges, the total dosage amount shown to be effective in Tuscano's inadequate responders was higher than that administered in Edwards. Pet. 20, 48. According to Petitioner, it matters only that "the lower doses were successfully used in Edwards." *Id*. at 48. That explanation is insufficient. What remains missing is some articulated reasoning why Edwards' results would have provided a skilled artisan a reasonable expectation of successfully treating RA in inadequate responders with Edwards' dosing regimen. The assertion by Petitioner and Dr. Boers that Leandro describes "using about 2000 mg total dose of rituximab to treat RA successfully," is not helpful, as Leandro does not describe treating patients who experience an inadequate response to a TNFα-inhibitor. Ex. 1035, 883–884. Nor do we find persuasive the contention by Petitioner and Dr. Boers that the claimed dosage is not critical, as elsewhere they suggest that the recited dosage is an amount effective to provide the intended clinical response. *Compare* Pet. 48–49 (citing Ex. 1002 ¶ 128) *with* Pet. 26–27 (citing Ex. 1002 ¶ 83).

Moreover, Tuscano's successful regimen differs from Edwards in the number of doses given, the manner by which those doses were determined, and the escalation of dosage amounts administered. Specifically, Tuscano discloses administering "100mg on wk #1, followed by 375mg/m2 on wk #2, and 500mg/m2 on wks 3 and 4.'" Ex. 1034. In other words, Tuscano administered four doses, wherein the treatment began with a low dose that was progressively increased with the second and third doses, wherein three of the doses were determined as a function of patient size, i.e. body surface area. Petitioner has not addressed sufficiently why a person of ordinary skill in the art would have expected another treatment regimen, involving a reduced number of treatments, a reduced total dosage, and a dosage not based, in part, on a patient's size would have successfully treated RA in Tuscano's inadequate responders.

Therefore, based upon our review of the Petition and the cited declaration testimony, we determine that Petitioner has not demonstrated a reasonable likelihood of prevailing in showing the unpatentability of claims 1–14 over the combined teachings of Edwards and Tuscano, as each of those claims require administering two doses of 1000 mg of rituximab to a patient who experiences an inadequate response to a TNFα-inhibitor.

Consequently, we decline to institute an *inter partes* review of claims 1–14 based on this ground.

D. Obviousness over Goldenberg, Curd, and De Vita

1. Goldenberg

Goldenberg discloses, in an example, treating a patient, who obtains only minor relief on a TNFα-inhibitor (Enbrel), with 300 mg of rituximab intravenously each week, for five weeks. Ex. 1038, 22 (Example 5). Goldenberg describes observing significant improvement in measures of disease activity. *Id*.

2. Curd

Curd discloses, in an example, administering rituximab intravenously to a patient with a clinical diagnosis of RA. Ex. 1031, 25:9–28 (Example 1). Curd describes treating RA according to any of the following dosing schedules:

(A) 50mg/m^2 IV day 1
150 mg/m^2 IV on days 8 15 & 22
(B) 150 mg/m^2 IV day 1
375 mg/m^2 IV days 8, 15 & 22
(C) 375 mg/m^2 IV days 1, 8, 15 & 22

Id. at 17–23.

Curd also discloses optionally further treating the patients with one or more agents, including methotrexate and corticosteroids. *Id*. at 25:10–16.

3. De Vita

De Vita discloses the administration of rituximab to two rheumatoid arthritis patients who were non-responsive to a TNFα-inhibitor. Ex. 1051. The rituximab treatment involved 4 intravenous infusions per week of 375 mg/m^2 each. *Id*. One patient achieved an ACR 20 response in month +5. *Id*. The patients were allowed to take low doses of steroids also. *Id*.

4. Analysis

Petitioner contends that claims 1–14 of the '838 patent would have been obvious over the combination of Goldenberg, Curd, and De Vita. Pet. 51–59. Petitioner asserts that both Goldenberg and De Vita teach treating a patient who experiences an inadequate response to a TNFα-inhibitor with rituximab. *Id*. at 51. Petitioner asserts also that both Goldenberg and Curd teach combining methotrexate with rituximab therapy. *Id*. Petitioner does not allege that Goldenberg, Curd, or De Vita teaches the claimed dosage of rituximab, i.e., two intravenous doses of 1000 mg. *Id*. at 52 ("The prior art does not teach the exact claimed dose of rituximab."). Rather, Petitioner asserts a person of ordinary skill in the art "would have been motivated to optimize the dose of rituximab used to treat RA." *Id*. at 53. In support of that contention, Petitioner asserts that the total dosage administered in the claimed methods, i.e., 2000 mg, falls squarely between the successful total dose of 1500 mg disclosed in Goldenberg and the successful total dose of 2550 mg disclosed in De Vita. *Id*.

Insofar as Goldenberg administers its dose in a total of five intravenous administrations, while De Vita administers a total of four intravenous administrations, Petitioner asserts that a person of skill would have been motivated to administer rituximab in as few doses as possible to increase patient compliance and convenience because rituximab is administered intravenously in a doctor's office or infusion center." *Id*. at 53 (citing Ex. 1002 ¶ 136). According to Petitioner, "Curd would also have motivated a skilled artisan to optimize the selection of an appropriate dose and scheduling." *Id*. (citing Ex. 1031, 23:28–29). Petitioner and Dr. Boers conclude that a skilled artisan would have known how to optimize the

dosage amount and schedule to treat RA patients with rituximab. *Id*. (citing Ex. 1002 ¶ 135).

Patent Owner asserts that Petitioner has not provided any evidence that a person of skill in the art would have arrived at the claimed dosing regimen through routine optimization. Prelim. Resp. 45. According to Patent Owner, Petitioner's argument relies on impermissible hindsight reconstruction and not a proper demonstration of routine optimization. *Id*. at 46.

We agree with Patent Owner. In particular, as Patent Owner has asserted, the claimed dosing regimen involves a number of variables that differ from the cited prior art, such as: dose-sizing option, i.e., fixed dosing vs. dosing based upon body surface area (Curd and De Vita); total dose; number of infusions; and amount of each infusion. Prelim. Resp. 47. Petitioner has not demonstrated that each of those parameters represents a result-effective variable, such that a person of skill in the art would have had a reason to optimize it. *See In re Antonie*, 559 F.2d 618, 620 (CCPA 1977). Moreover, Petitioner has not explained adequately that the alleged routine optimization would result in modifying each parameter in a manner so as to arrive at the claimed dosage regimen.

To the extent that Petitioner or Dr. Boers offers some explanation in that regard, it lacks a rational underpinning. For example, Dr. Boers explains that a skilled artisan would have wanted to reduce the number of infusions in Goldenberg or De Vita to improve patient compliance, Ex. 1002 ¶ 136. However, according to Dr. Boers, the skilled artisan would not have reduced the number of infusions to a single infusion because the artisan "would have been concerned that giving a single, high dose of rituximab to

patients may result in toxic reactions, and therefore, would have reached the dosing schedule of 2 doses." Ex. 1002 ¶ 136. As Patent Owner persuasively asserts, Prelim. Resp. 53, Dr. Boers does not explain why the artisan would have only been concerned the potential toxicity from a single infusion of 2000 mg and not two high dose infusions of 1000 mg. In that same vein, Dr. Boers has not explained why a skilled artisan would not have considered an optimized dose to include three infusions or some number of infusions with differing, e.g., escalating, dosage amounts. Thus, we consider Dr. Boer's opinion that arriving at the claimed dosage regimen "would have been a matter of routine optimization" to be conclusory and unpersuasive. *See Office Patent Trial Practice Guide*, 77 Fed. Reg. 48,756, 48763 (Aug. 14, 2012) (a declaration expressing an opinion of an expert without disclosing underlying facts may be given no weight).

Therefore, based upon our review of the Petition and the cited declaration testimony, we agree with Patent Owner that Petitioner has not demonstrated a reasonable likelihood of prevailing in showing the unpatentability of claims 1–14 over the combined teachings of Goldenberg, Curd, and De Vita, as each of those claims require administering two doses of 1000 mg of rituximab. Consequently, we decline to institute an *inter partes* review of claims 1–14 based on this ground.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing in showing the unpatentability of any challenged claim.

ORDER

Accordingly, it is hereby:

ORDERED that Petitioner's request for an *inter partes* review of claims 1–14 of the '838 patent is *denied*.

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