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Paper 9
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

REGENERON PHARMACEUTICALS, INC.,
Petitioner,

v.

KYMAB LTD.,
Patent Owner.

IPR2019-01579
Patent 9,447,177 B2

Before ZHENYU YANG, KRISTI L. R. SAWERT, and MICHAEL A. VALEK, *Administrative Patent Judges.*

SAWERT, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Regeneron Pharmaceuticals, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") requesting *inter partes* review of claims 1–5 of U.S. Patent No. 9,447,177 B2 ("the '177 patent"). Kymab Ltd. ("Patent Owner") timely filed a Preliminary Response (Paper 6, "Prelim. Resp."). On our authorization, Petitioner filed a Reply (Paper 7, "Reply") and Patent Owner filed a Sur-Reply (Paper 8, "Sur-Reply") directed to the applicability of 35 U.S.C. § 325(d) to this case.

We have authority under 35 U.S.C. § 314 to determine whether to institute an *inter partes* review. The standard for instituting an *inter partes* review is set forth in § 314(a), 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." Applying those standards, and upon consideration of the information presented in the Petition, the Preliminary Response, the Reply, and the Sur-Reply, and for the reasons explained below, we exercise our discretion under § 325(d) and deny institution of *inter partes* review of the challenged claims.

II. BACKGROUND

A. Real Parties in Interest

Petitioner identifies Regeneron Pharmaceuticals, Inc., as the real party-in-interest. Pet. 67. Patent Owner identifies Kymab Ltd. as the real party-in-interest. Paper 4, 1.

B. Related Matters

The parties identify IPR2019-01577, IPR2019-01578, and IPR2019-01580 as related matters under 37 C.F.R. § 42.8(b)(2). Pet. 68; Paper 4, 1. Petitioner also names several pending patent applications that claim priority to the '177 patent, or to which the '177 patent claims priority. Pet. 68.

C. The '177 Patent

The '177 patent, titled "Transgenic Mouse Homozygous For Chimeric IgH Locus," relates to mice "that are engineered to contain exogenous DNA, such as human immunoglobulin gene DNA . . . for production of . . . antibodies and antibody chains." Ex. 1001, 1:30–36. The chimeric antibodies produced by these transgenic mice have a "non-human mammal [i.e., mouse] constant region and a human variable region." *Id.* at 2:66–67.[1]

Specifically, the '177 patent discloses mice in which an unrearranged "human IgH VDJ region" comprising "DNA from a human genome that encodes all the exons encoding human V, D and J portions and suitably also the associated introns," is inserted into the mouse genome "upstream of [the mouse] constant region, the latter comprising all of the DNA required to encode the full constant region or a sufficient portion of the constant region to allow the formation of an effective chimaeric antibody capable of specifically recognizing an antigen." Ex. 1001, 5:12–29.

According to the '177 patent,

> in the present invention, host [mouse] constant regions are maintained and it is preferred that at least one [mouse] enhancer

[1] The variable region of a human IgH locus comprises a number of V, D, and J gene segments separated by stretches of non-coding DNA. Ex. 1002 ¶ 28; Ex. 2008 ¶ 13. The mouse constant region contains gene segments encoding antibody constant domains. Ex. 1002 ¶ 28; Ex. 2008 ¶ 27.

> . . . is maintained in functional arrangement with the [mouse] constant region, such that the effect of the enhancer . . . as seen in the host mammal, is exerted in whole or in part in the transgenic animal.

Id. at 6:39–46. In one embodiment, insertion of the human IgH VDJ region "is targeted to the region between the J4 exon and the Cμ locus in the mouse genome" (the "J/C intron"). *Id.* at 5:53–55. The J/C intron includes the mouse enhancer. Ex. 1002 ¶ 33. The '177 patent provides that "[t]his approach . . . is designed to allow the full diversity of the human locus to be sampled [and] to allow the same high expression levels that would be achieved by non-human mammal control sequences such as enhancers." *Id.* at 6:47–50.

D. Illustrative Claims

Claim 1 is illustrative of the subject matter of the challenged claims:

1. A transgenic mouse whose genome comprises a homozygous chimeric immunoglobulin heavy chain (IgH) locus comprising unrearranged human IgH variable region gene segments at an endogenous mouse heavy chain IgH locus upstream of an enhancer and a constant (C) region comprising an endogenous CH gene segment;

wherein said human variable region gene segments in said chimeric IgH locus are operably linked to said C region at a human/mouse chimeric junction within the JC intron of said chimeric IgH locus;

wherein said homozygous chimeric IgH locus comprises in 5′ to 3′ transcriptional orientation:

(i) unrearranged human immunoglobulin heavy chain (IgH) variable region (VH) DNA comprising human IgH V gene

segments, human D gene segments DH and human JH gene segments comprising a human 3′ JH gene segment,

(ii) a chimeric J/C intron comprising human DNA downstream of and naturally contiguous with said human 3′ JH gene segment, which is contiguous with mouse JC intronic DNA, and

(iii) said enhancer and said C region,

wherein said human 3′ JH is less than 1 kb upstream of said chimeric junction,

wherein DNA between said chimeric junction and said enhancer comprises mouse 129 strain JC intronic DNA;

wherein said enhancer is a mouse 129 strain μ enhancer;

wherein said transgenic mouse is functional to form rearranged human VH, DH and JH gene segments and to express chimeric immunoglobulin heavy chain polypeptide comprising a human VH region and a mouse C region, and wherein said transgenic mouse is capable, upon stimulation with antigen, of producing an antibody comprising a chimeric Ig heavy chain comprising a human IgH variable region and said C region; and

wherein the genome of said transgenic mouse comprises all or part of the endogenous mouse IgH variable region, and is capable of breeding to produce subsequent generation mice having in their germline an IgH locus comprising unrearranged human IgH variable region gene segments positioned upstream of an IgH constant (C) region comprising an endogenous C gene segment of an IgH locus.

Ex. 1001, 133:2–134:16.

E. Asserted Evidence

Petitioner submits the following evidence:

Evidence	Exhibit No.
Declaration of Anthony L. DeFranco, Ph.D.	1002
Murphy, WO 02/066630 A1 (Aug. 29, 2002) ("Murphy")	1005
Morrison, US 5,807,715 (Sept. 15, 1998) ("Morrison")	1006
David J. Adams et al., *A genome-wide, end-sequenced 129Sv BAC library resource for targeting vector construction*, 86 GENOMICS 753–758 (2005) ("Adams")	1007

F. Asserted Ground of Unpatentability

Petitioner asserts that claims 1–5 of the '177 patent are unpatentable on the following ground:

Claim(s) Challenged	35 U.S.C. §	Reference(s)
1–5[2]	103(a)	Murphy, Morrison, Adams

Pet. 26–62.

III. DISCRETION UNDER 35 U.S.C. § 325

Section 325(d) gives us express discretion to deny a petition when "the same or substantially the same prior art or arguments previously were presented to the Office." 35 U.S.C. § 325(d); *see also Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) ("[T]he PTO is permitted, but never compelled, to institute an IPR proceeding."). In evaluating whether to exercise our discretion under § 325(d), we weigh the following non-exclusive factors:

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;

[2] Petitioner does not challenge claim 6 of the '177 patent. *See* Pet. 26.

> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
>
> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
>
> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
>
> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of prior art or arguments.

Becton, Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) ("the *Becton, Dickinson* factors").

Factors (a), (b), and (d) of the *Becton, Dickinson* factors relate to whether the art and arguments presented in the petition are the same or substantially the same as those previously presented to the Office. *Advanced Bionics, LLC v. Med-El Electromedizinishe Geräte GMBH,* IPR2019-01469, Paper 6 at 10 (Feb. 13, 2020) ("*Advanced Bionics*"). Factors (c), (e), and (f) "relate to whether the petitioner has demonstrated a material error by the Office" in its prior consideration of that art or arguments. *Id.* Only if the same or substantially the same art or arguments were previously presented to the Office do we then consider whether petitioner has demonstrated error. *Id.* "At bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." *Id.* at 9.

A. Becton, Dickinson Factors (a), (b), and (d)

We first determine whether the same or substantially the same art or arguments were presented previously to the Office. In its only ground of unpatentability, Petitioner relies on the combination of prior-art references Murphy, Morrison, and Adams to allege obviousness of claims 1–5 of the '177 patent. Pet. 29. There is no dispute that Murphy and Adams were presented previously to the Office during examination of the application leading to the '177 patent. Pet. 65 (acknowledging that the Examiner considered the teachings of Murphy and Adams); Prelim. Resp. 4 n.1. The parties dispute, instead, whether the combination of Murphy, Morrison, and Adams constitutes "substantially new art and arguments" that do not preclude application of § 325(d). Pet. 62, 64–65; Prelim. Resp. 5–12.

1. Murphy

Petitioner relies primarily on Murphy to allege unpatentability of the subject matter of claims 1–5. *See* Pet. 2 (arguing that "the claimed mouse [is] functionally indistinguishable from the prior art Murphy mouse"). Upon review of the Petition and the submitted Office Actions, we find that Petitioner's arguments about Murphy largely overlap with the Examiner's discussion of Murphy during prosecution.

For example, during prosecution, the Examiner repeatedly rejected the claims for obviousness over prior-art combinations that, like the ground in the Petition here, relied on Murphy as a primary reference. *See* Ex. 1038, 14–18 (obviousness rejections over Murphy and other references); Ex. 1041, 7–12 (accord); Ex. 1044, 2 (maintaining the rejections for reasons of record); Ex. 1046, 2 (accord). In making those rejections, the Examiner relied on Murphy for teaching a transgenic mouse that "appear[s] to be structurally

[the] same" as "those embraced by the instant claims." Ex. 1038, 14–15. Specifically, the Examiner described Murphy as teaching "a transgenic mouse having a genome comprising entirely human heavy chain variable region loci operably linked to entirely endogenous mouse constant region loci such that the mouse produces a serum containing an antibody comprising a human variable region and a mouse constant region in response to antigenic stimulation." Ex. 1038, 15.

Petitioner makes the same or substantially the same arguments in its Petition, contending that "the claimed mouse [is] functionally indistinguishable from the prior art Murphy mouse." Pet. 2. In particular, Petitioner argues that Murphy teaches a homozygous IgH locus comprising an endogenous mouse IgH variable region operably linked to a human IgH variable region to express antibodies upon antigen stimulation. Pet. 27–28. These arguments overlap with the Examiner's findings during prosecution. *See, e.g.*, Ex. 1038, 15.

For these reasons, as to Murphy, we find that, not only did the Examiner consider Murphy's teachings extensively, the Petition presents the same or substantially the same arguments previously considered during prosecution.

2. Morrison

Morrison was not before the Examiner during prosecution. *See, e.g.*, Prelim. Resp. 5. Petitioner contends that "Morrison's teachings establish that, for chimeric genes that utilize mouse and human sequences, each of (i) fully mouse, (ii) fully human, and (iii) *chimeric* J/C introns can be used," and that "the exact cite of linkage . . . is a matter of convenient design choice." Pet. 15 (citing Ex. 1002 ¶ 64); *see also id.* at 44 ("Morrison

establishes that a [person of ordinary skill in the art] knew well before July 2009 that using a chimeric J/C intron is one of a limited number of choices for effective designs, and is a 'matter of convenience'" (quoting Ex. 1002 ¶¶ 110–115)). Because Morrison's teachings were not previously considered, Petitioner contends that the Petition presents "a new art combination," and therefore, "the Board should not exercise its discretion under 35 U.S.C. § 325(d)." *Id.* at 65.

Patent Owner acknowledges that Morrison was not before the Examiner, but argues that Morrison is not relevant, or, at most, cumulative of the prior-art reference Tanamachi,[3] which was considered by the Examiner. *See* Prelim. Resp. 5–12. As to relevance, Patent Owner argues that Morrison "teaches a traditional 'chimeric' antibody made by fusing the variable region from a non-human species to a human constant region, and expressing the chimeric protein in a host cell" *in vitro*, as opposed to "modifying the germline of a mouse with human DNA to create a transgenic mouse, as claimed in the '177 patent." *Id.* at 6–7. For this reason, Patent Owner argues, Morrison is non-analogous art. *Id.* As to Morrison's alleged cumulative nature, Patent Owner argues that "[e]ven if it were appropriate to consider the non-analogous Morrison reference, the teaching of Morrison on which Petitioner relies is clearly cumulative of the much more relevant Tanamachi reference, a publication that is from the relevant field of transgenic mouse production useful for making libraries of antibodies." *Id.* at 8–9.

[3] Tanamachi, WO2007/117410 A2 (Oct. 18, 2007) ("Tanamachi"). Ex. 1030.

After considering the parties' respective arguments and evidence, we determine that Morrison's teachings are cumulative to the teachings of Tanamachi, and that Petitioner's arguments about Morrison largely overlap with arguments previously presented during prosecution. Specifically, Petitioner relies on Morrison for teaching that a chimeric J/C intron was a known option for joining a variable gene region to a constant gene region to produce functional antibody chains. Pet. 15. That Tanamachi also teaches a mouse/human chimeric DNA junction was presented and discussed during prosecution. *See* Ex. 1047, 29–30 (characterizing the chimeric DNA junction taught by Tanamachi); Ex. 1050 ¶ 4 (discussing the Examiner's Summary of a telephonic interview where "the Examiner noted the prior art reference[] . . . Tanamachi et al. (WO2007/117410) teach[es] the concept of mice having a chimeric IgH locus comprising . . . a human/mouse chimeric DNA junction"); *see also* Prelim. Resp. 9–10.

Petitioner also relies on Morrison for characterizing the exact site of linkage as "a matter of convenience where there is a convenient restriction site in the introns from the two sources." Pet. 15 (quoting Ex. 1006, 3:60–62). But this teaching does not provide a material, non-cumulative disclosure over Tanamachi. To the contrary, Petitioner acknowledges that Tanamachi, in fact, describes a chimeric junction resulting from ligating a mouse coding-region fragment into "a restriction site 3′ of the human VDJ region." Pet. 48–49 (citing Ex. 1030, 27:31–28:1). Thus, we find that,

although Morrison is relevant prior art,[4] Petitioner has not shown that it is any more relevant than Tanamachi.

We are also not persuaded by Petitioner's contention that the Final Office Action in related U.S. Patent Application No. 14/040,405 ("the '405 Office Action") "directly refutes" that Morrison is cumulative of Tanamachi. Reply 3–4 (citing Ex. 1080). Petitioner contends that the '405 Office Action, which mailed after the issuance of the '177 patent, "reflects a *material change* in the Examiner's position regarding the significance of the 'chimeric J/C intron'" based upon the Examiner's subsequent consideration of Morrison in that examination. *Id.* at 4. In particular, Petitioner contends that "the Examiner, now armed with Morrison, found that it was known in the art that a chimeric J/C intron was 'desirable,' and that the 'site for the chimeric JC intron is not critical to produce a functional antibody" (quoting EX1080, 12 (brackets omitted))).

We find that the '405 Office Action does not support Petitioner's contentions. Instead, the '405 Office Action, if anything, supports Patent Owner's argument that Morrison is cumulative of Tanamachi. The obviousness rejections in the '405 Office Action were based on combinations of references that included Murphy and Tanamachi, as well as other references, but not Morrison. Ex. 1080, 2–3, 7–8. Although the Examiner cited to Morrison, the Examiner did so only as "further support[]" for Tanamachi's teaching that "the concept of a chimeric JC [intron] was known to one of ordinary skill in the art." *Id.* at 12–13. Put differently, the

[4] We agree with Petitioner, *see* Reply 2–3, that Morrison is analogous art at least because it relates to the same general field of endeavor as Murphy and Adams.

Examiner relied on Tanamachi for teaching a chimeric J/C junction, and merely cited to Morrison as evidence supporting Tanamachi's teachings that chimeric J/C junctions were well known in the art. *Id.* Thus, the Examiner's reference to Morrison in the '405 Office Action does not support Petitioner's argument that Morrison is not cumulative of Tanamachi.

3. Adams

Turning to Adams, Petitioner relies on this prior-art reference for teaching mouse 129 strain ES cells. *See* Pet. 52 ("Adams establishes that mouse 129 strain embryonic stem ('ES') cells were well known and widely used for mouse genome modifications as of July 2009."). The Examiner also relied on Adams for the same disclosure during prosecution. *See, e.g.*, Ex. 1041, 10–11 ("Adams et al[.] reported that gene-targeting experiments in mice are routinely performed in 129Sv-derived embryonic stem (ES) cell lines, which are generally considered to be more reliable at colonizing the germ line than ES cells derived from other strains."). Thus, we find that the Petition presents the same or substantially the same arguments previously considered during prosecution.

4. Summary

For these reasons, we are not persuaded by Petitioner's argument that the Petition presents "substantially new art and arguments." *See* Pet. 62. Instead, we determine that the Petition presents the same or substantially the same art and arguments previously presented to, and considered by, the Examiner.

B. Becton, Dickinson Factors (d), (e), and (f)

Because the "same or substantially the same prior art or arguments previously were presented to the Office" in the case, we now turn to

considering whether Petitioner has demonstrated sufficiently that the Office erred in evaluating those art or arguments. *Becton, Dickinson*, Paper 8 at 24 (considering whether the petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art).

Petitioner alleges that the Examiner erred in allowing the claims because "the Examiner has reconsidered the patentability of certain claimed features at issue since his allowance of the challenged claims," and "the Petition includes new factual information that demonstrate how the minor, allegedly novel features of the claims are obvious in view of the prior art." Pet. 62–64, 66–67. We address each issue, in turn, below.

1. Whether the Examiner has reconsidered the patentability of certain claim limitations

Petitioner contends that the Examiner has reconsidered the patentability of certain claim limitations found in the challenged claims, and thus, "the Board should institute trial and likewise find the challenged claims unpatentable." Pet. 63–64. As evidence for its assertions, Petitioner cites to the Examiner's statements—made during prosecution of subsequent patent applications—about the capability of Murphy's mouse to breed, *id.* at 63 (citing Ex. 1022, 13, Ex. 1023, 6), the ability of chimeric J/C introns to produce functional antibodies, *id.* (citing Ex. 1072, 19), and the routine use of 129Sv-derived ES cell lines for gene-targeting experiments in mice, *id.* at 63 (citing Ex. 1072, 14). Patent Owner disagrees that these statements demonstrate that the Examiner has reconsidered the patentability of the challenged claims. Prelim. Resp. 12–15. Instead, Patent Owner argues, "the statements cited by Petitioner, along with the surrounding portions of the file histories, actually confirm the Examiner's consistent treatment of the art

across the various cases in the entire family." *Id.* at 13. After careful consideration, we determine that Patent Owner has the better position.

Petitioner relies mainly on Office Actions mailed in U.S. Patent Application No. 15/383,101 ("the '101 application") as evidence that the Examiner has reconsidered his views on the patentability of certain claim limitations.[5] But, as Patent Owner points out, the Examiner rejected the claims of the '101 application ultimately because those claims did not require the step of obtaining or using the transgenic mouse. Prelim. Resp. 14; Ex. 1072, 19. Indeed, the Examiner stated that "[s]hould applicant amend the instant claim to recite the step of immunizing the mouse previously allowed with an antigen prior to steps of expressing the humanized antibody from a first cells, [the] instant obviousness rejection may be overcome." Ex. 1072, 20 (emphasis omitted). We agree with Patent Owner, therefore, that the Examiner's statements, if anything, "establish that he understood the '101 application claims to be directed to a different invention than the previously allowed claims." Prelim. Resp. 14–15. Those statements do not translate into the Examiner reconsidering his position on the patentability of the claims at issue here, or misapprehending the teachings of the prior art.

2. Whether the Petition presents new factual evidence

Petitioner contends that the Petition presents "new evidence concerning the relevant state of the art that was not previously considered by

[5] Petitioner also relies on an Office Action rejecting claims of U.S. Patent Application No. 14/516,461 (Ex. 1022) as obvious over Murphy and other references. However, that rejection was overcome resulting in the issuance of U.S. Patent No. 10,064,398 B2—the patent at issue in IPR2019-01580.

the Examiner." *See* Pet. 66–67. Specifically, Petitioner contends that the Petition presents new evidence contradicting "several declarations submitted by Patent Owner" during prosecution that the Examiner relied on "in allowing the challenged claims." *Id.* at 66.

Petitioner first points to a Declaration under 37 C.F.R. § 1.132 executed by Allan Bradley, Ph.D., "contend[ing] that the field was moving away from using 129/129Sv strain mice at the time of invention." Pet. 66 (citing Ex. 1048). Petitioner contends that Dr. DeFranco's Declaration, in contrast, "demonstrate[es] that as of July 2009, the recited 129/129Sv mouse strain sequences were well known in the art, and 129/129Sv mouse strain ES cells were the most commonly used strain of ES cells." *Id.* (citing Ex. 1002 ¶¶ 138–147). Neither Petitioner's arguments, nor Dr. DeFranco's testimony, however, persuades us that the Examiner erred in relying on Dr. Bradley's Declaration.

We find that Dr. DeFranco's testimony that 129/129Sv mouse strain ES cells were well known and commonly used does not contradict the evidence that was already before the Examiner in Dr. Bradley's Declaration. Indeed, Dr. Bradley states in his Declaration that "historically, the vast majority of mouse knockouts had been generated using ES cells derived from the 129 mouse strain." Ex. 1048 ¶ 9. The Examiner found Dr. Bradley's Declaration persuasive because:

> Applicants provide evidence that at the time of the invention, one of skill in the art would have preferred using the C57BL/6 mouse strain . . . to make a transgenic mouse, given that by 2009, the C57BL/6 mouse strain was one of the best characterized inbred strains of mice, was the reference strain for the mouse genome sequence and was being used as a foundation strain for the international mouse knockout program.

Ex. 1058, 6 (citing Ex. 1048 ¶¶ 9–11). Put differently, it appears to us that the Examiner did not misapprehend the historical prevalence of 129/129Sv mouse strain sequences, but was persuaded that the art was moving toward the use of the C57BL/6 mouse strain as a standard strain for generating transgenic mice, as evidenced by the Mouse Genome Sequencing Consortium and the Knockout Mouse Project. *Id.*; *see also* Ex. 1048 ¶¶ 8–10.[6]

Next, Petitioner characterizes another Declaration under 37 C.F.R. § 1.132 executed by Dr. Bradley as "argu[ing] that the claimed mice had 'significant structural differences' from the prior art because of their chimeric J/C intron." Pet. 66 (quoting Ex. 1050 ¶ 5). Citing Dr. DeFranco's Declaration, Petitioner contends that "the Examiner was not provided with the wealth of evidence that chimeric J/C introns were well known and utilized in the immunoglobulin field, and, in particular, in constructs used for expressing antibodies in mouse cells." *Id.* (citing Ex. 1002 ¶¶ 122–128). But Petitioner fails to point us to evidence in the prosecution history that the Examiner was unaware that chimeric J/C introns were well known and/or utilized in constructs for expressing antibodies.

In any event, Dr. Bradley testified that the claimed subject matter was not obvious over Tanamachi, in part, because the mouse component of Tanamachi's chimeric DNA junction was C57B1/6 DNA, whereas "the instant claims require the DNA between said chimeric DNA junction and the

[6] Dr. DeFranco also appears to allege that Dr. Bradley withheld "contemporaneous statements as of July 2009 that directly contradict the assertions he made in his declaration." Ex. 1002 ¶¶ 141–142. But, again, Dr. Bradley did not assert that that 129/129Sv mouse strain sequences were not well known or commonly used historically. Ex. 1048 ¶ 9.

enhancer to comprise mouse 129 strain DNA." Ex. 1050 ¶ 5. For these reasons, upon consideration of Dr. DeFranco's Declaration and the relevant Office Actions, we find that Petitioner does not demonstrate a material error in the Examiner's treatment of Dr. Bradley's Declarations.

Finally, Petitioner asserts that Dr. DeFranco's Declaration is new evidence that "was not previously before the Office and warrants serious consideration." Pet. 67. But the fact that the Declaration of Petitioner's expert was not before the Examiner during prosecution does not itself demonstrate that the Examiner erred. As explained above, the prosecution history reveals that the Examiner considered substantially the same arguments and art advanced in the Petition and Dr. DeFranco's supporting Declaration. To the extent Petitioner argues that its evidence demonstrates that the Examiner erred, we have addressed it above and disagree.

C. Weighing the Factors

Weighing each of these factors, we conclude that, on the record presented, the circumstances of this case warrant exercise of our discretion to deny institution based on § 325(d). The Petition's only ground is premised on the same references, substantially the same secondary references, and presents arguments concerning those references that are substantially the same as those the Examiner considered and the applicants overcame during examination. Petitioner has not demonstrated that the Examiner materially erred in considering the prior art and arguments.

IV. CONCLUSION

Upon consideration of the Petition, the Preliminary Response, the Reply, the Sur-Reply, and the evidence before us, we exercise discretion to deny institution of a trial under 35 U.S.C. § 325(d).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is denied, and no *inter partes* review is instituted.

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