

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMGEN INC.,
Petitioner,

v.

BRISTOL-MYERS SQUIBB COMPANY
Patent Owner.

Case No. IPR2025-00602
Patent No. 10,174,113

**PETITIONER'S REQUEST FOR DIRECTOR REVIEW OF DECISION
DENYING INSTITUTION OF *INTER PARTES* REVIEW**

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I. INTRODUCTION

The Interim Director’s decision discretionarily denying institution of IPR2025-00602 (“Decision”) overlooked that the purported point of novelty in the claimed invention has repeatedly been deemed ***not*** inventive in parallel proceedings Patent Owner (PO) has pursued in Europe, including a counterpart to the challenged ’113 Patent itself. The Discretionary Denial Opposition makes this plain. DD Opp. (Paper No. 8), 3-4, 8-10, 21-22, 29, and 38.

PO’s lack of settled expectations is further corroborated by PO’s August 18, 2025 disclaimer of analogous U.S. claims in U.S. Patent No. 11,332,529 (“’529 Patent”) reciting the same purported point of novelty as to “flat” dosing following referral of IPR2025-00603 to a merits panel.¹ ***The disclaimer constitutes changed circumstances highlighting PO’s lack of settled expectations in these dosage cases*** and the agency’s misapprehension of the significant public policy issues at play here.

Simply put, PO has now abandoned similar anti-PD-1 flat dosage claims in ***both Europe and the United States*** when faced with explanations regarding their obviousness. Yet the ’113 Patent remains in force despite reflecting a glaring “material error” in the agency’s earlier work allowing BMS to unduly extend its

¹ IPR2025-00603 survived discretion and was referred to the panel because it was not in force as long as this patent. Paper 9, 2-3.

market exclusivity on the drug Opdivo® by another eight years based on a known dosage regimen. PO could not possibly have six years of “settled expectations” concerning the patentability of the challenged patent after having abandoned related claims in Europe in 2021, less than three years after the challenged patent issued. Shielding such material errors from correction in the United States will contribute to biosimilars being delayed in coming to market domestically to the detriment of U.S. cancer patients and other healthcare consumers. Far from Petitioner “not provid[ing] persuasive reasoning why an *inter partes* review is an appropriate use of Board resources,” there could not possibly be a more compelling use of an executive agency’s resources but to align with its Chief Executive to advance the critical goal of bringing biosimilars to market in a timely manner—especially here, where the error is plain that the ’113 Patent should never have issued. *Lowering Drug Prices by Once Again Putting Americans First*, Executive Order No. 14273, 90 Fed. Reg. 16441 (Apr. 15, 2025).

The agency’s Decision to deny this IPR as a matter of discretion overlooks or misapprehends: the discontinuity in expectations resulting from previous surrender of counterpart flat dosage claims; the material error in the agency’s earlier work as corroborated by PO’s recent disclaimer of the ’529 Patent’s anti-PD-1 flat dosage claims; the changed circumstance of PO’s most recent exhibition of its pattern of strategic retreat gamesmanship (in which PO seeks to resurrect the ’529 claims); and

the expressed intent of the President’s Executive Order on biosimilars (validating the settled expectations of both PO and the American public). The Decision should be reversed and the Petition grounds referred to a merits panel.

II. THE DISCRETIONARY DENIAL DECISION CREDITS YEARS OF TERM AFTER PO WITHDREW COUNTERPART FLAT DOSING CLAIMS AND THE EPO LATER CONFIRMED THE ELEMENTARY ARITHMETIC UNDERLYING THE PETITION

A. The Decision’s “Settled Expectations” Analysis Overlooks the Impact of and Material Error Evidenced By PO’s European Activity Concerning the Purported Flat Dosing Point of Novelty.

The composition-of-matter patent covering Opdivo® expires in 2028, at which point BMS will have recouped nearly \$10 billion/year for its investment. DD Opp., 12-13. The ’113 Patent is a follow-on patent claiming obvious dosing regimens for Opdivo® (all of which were disclosed in the prior art) to unduly extend BMS’s market exclusivity. The Director’s decision cited alleged “settled expectations” in the validity of the ’113 Patent based on the “six” years the ’113 Patent has been in force and concluded that “the Office is disinclined to disturb” them. Decision, 3. But less than three years after the ’113 patent issued (in October 2021) following PO’s reliance on flat dosing of anti-PD-1 antibodies as the purported point of novelty, PO had already abandoned counterpart flat dosage claims in Europe. To the extent PO *ever* had settled expectations in the distinction between flat dosing and weight-based dosing as a point of novelty, those expectations were unsettled by the EPO’s repeated determinations that flat dosing was not inventive.

The Decision reasons that “Petitioner does not provide persuasive reasoning why an *inter partes* review is an appropriate use of Board resources” and states that the Decision is “based on a holistic assessment of all the evidence and arguments presented.” Decision, 2-3. But the Decision neither discusses nor even mentions the arguments or the evidence that Petitioner provided as to the fate of similar patent claims in Europe directed to flat dosing of anti-PD-1 antibodies to treat melanoma.

As the Petition explains, such flat dosing—administering a fixed dose for all patients—is the only difference between the challenged claims and the prior art. *E.g.*, Petition, 1-3. Indeed, it was PO’s basis for overcoming an anticipation rejection during prosecution. *E.g.*, Petition, 8; EX1002, 68 (“Wolchok does not disclose administering a flat dose of an anti-PD-1 antibody”)

As the Petition further explains, the 240 mg anti-PD-1 antibody flat dose recited in independent claim 1 merely reflects taking the 3 mg/kg nivolumab dose disclosed in the prior art (e.g., NCT-505 and Postow) and multiplying it by the 80 kg average weight of melanoma patients in immunotherapy trials (such as are disclosed in both NCT-505 and Postow). Petition, 3, 23-25. The EPO has already discussed such simple arithmetic—including the 80 kg average patient weight—when concluding that PO’s flat dosage claims were unpatentable. The Decision therefore fails to explain how PO can have “settled expectations” in U.S. patent claims that *it knows it could not secure* in a different jurisdiction.

For example, in counterpart European Patent Application No. 16725959.7, PO pursued claims directed to treating melanoma using anti-PD-1 and anti-CTLA4 antibodies, wherein the anti-PD-1 antibody was administered at a flat dose. EX1050. In an October 2018 first Examination Report, the EPO’s Examining Division (“ED”) noted that the claims were not inventive because “[n]o particular effect has been shown to be associated with” flat dosing. EX1059 at 4. This rejection for lack of inventive step was maintained in a later report emphasizing that “[w]ithout a technical effect associated with the claimed difference(s), the solution represents an arbitrary solution to the problem posed, thereby not involving an inventive step.” EX1051 at 2. After failing to overcome this rejection, PO withdrew the application in October 2021—less than three years after the ’113 Patent issued. EX1053.

Further, European Patent Application No. 16724512.5—filed by PO on the same day as the ’113 Patent and naming the same inventor—granted on March 10, 2021 as European Patent No. EP3288980B1 with claims corresponding to the anti-PD-1 antibody flat dose monotherapy step PO added when prosecuting the ’113 Patent to overcome the anticipation rejection. *See* Petition, 8. The European patent covered a composition comprising nivolumab for use in treating melanoma, wherein the nivolumab is administered as a 480 mg flat dose once every four weeks. EX1054.

After grant, five Notices of Opposition were filed against this patent. Opponents included extensive art and declaration evidence supporting the

obviousness of flat dosing of nivolumab. EX1055, EX1056, EX1057. In the Grounds for the Decision revoking the European patent, dated March 13, 2024, the Opposition Division (OD) noted that a monthly flat dose of 480 mg of nivolumab for treatment of melanoma was not inventive based on disclosure in the prior art of 3 mg/kg every two weeks (corresponding to 240 mg based on an average body weight of 80 kg) and based on the known half-life of nivolumab. EX1058, 25-27 (§§ 19.4.3-6).² The OD noted in particular that the prior art “regimen of 3 mg/kg q2w was shown to be effective for treating melanoma in the samples” and “*can be translated (taking an average weight of 80 kg) as a flat dose of 240 mg q2w.*” *Id.*, 25 (§ 19.4.3). The OD further noted that “the skilled person would self-evidently choose the most convenient mode of administration that remains effective” and that “[i]t is within the normal tasks of the person skilled in the art to verify whether a proposed regimen stands a chance of working,” which the skilled person would have been able to do in this instance due to general knowledge about the pharmacokinetic data for nivolumab. *Id.*, 26 (§ 19.4.6). That case is currently under appeal.

The extensive examination in these corresponding European cases related to flat dosing of nivolumab—including the simple arithmetic based on average patient

² The OD likewise concluded that “a double dose” (i.e., 480 mg) at a “double interval” (every four weeks) was not inventive. *Id.* (noting “elimination half-life”).

body weight—was not before the US Examiner during prosecution of the ’113 patent. It stands in contrast to the U.S. prosecution history, which does not reflect any knowledge and understanding in the art related to flat dosing of nivolumab.

That the flat dosing claims of EP Application Nos. 16725959.7 and 16724512.5 have been flatly rejected and, in the case of the former, ***withdrawn by PO***, demonstrates that PO could not possibly have “settled expectations” in the validity of the ’113 Patent. The only expectations that PO could have is that the claims are unpatentable and that the USPTO clearly erred in allowing them. For the agency to decide that correcting a clear error in issuing an invalid patent is not an “efficient use of its resources” is an affront to the USPTO’s very mission. Instead, *inter partes* review proceedings provide a post-issuance opportunity to challenge issued patents granted in error. The Director’s recent decisions recognize and give due weight to the importance of correcting such errors, including in patents much older than the ’113.

For example, in *Anthony Inc. v. ControlTec LLC*, IPR2025-00559 and IPR2025-00636, the Director rejected discretionary denial requests as to patents “in force for approximately eighteen and seventeen years.” IPR2025-00559, Paper No. 12, 2 (July 16, 2025). Despite this length of time, the Director determined that review was an “appropriate use of Office resources” because the petitioner had identified an apparent “material error by the Office” in “overlooking [prior art] teaching.” *Id.*

Similarly, in *Xencor, Inc. v. Merus N.V.*, IPR2025-00604, the Director rejected a discretionary denial request concerning a patent for producing antibodies even though it had been “in force for approximately nine years” and thus (in the Director’s view) “creat[ed] strong settled expectations for” the patentee. Paper No. 12, 2 (July 17, 2025). Despite those ostensible expectations, the Director concluded that review was appropriate given evidence that the Office had “materially erred during prosecution” in overlooking prior art contradicting the stated reasons for allowance. *Id.*, 2-3 (July 17, 2025). *See also Activision Blizzard v. Milestone Entertainment*, IPR2025-00708 (Aug. 14, 2025) (rejecting DD request as to a patent “issued almost twelve years ago,” as claims omitted limitations cited by Office as basis for allowing parent); *Skullcandy, Inc. v. Earin AB*, IPR2025-00690, Paper 9, 2 (July 31, 2025) (rejecting DD request as to a patent “issued nine years ago” despite “strong settled expectations,” as petitioner “appear[ed] to show a material error by the Office”).

Here, by contrast, the Decision overlooks the material error of the Office in issuing the challenged claims even though there is no indication that the Examiner—who did not have access to the later prosecution histories of the related European cases—considered the advantages of flat dosing, which as explained in the petition were known. *See* DD Opp. VI.B; *see also CSPC Pharmaceutical Group Ltd. v. Ipsen Biopharm Ltd.*, IPR2025-00505, Paper 11, 3 (July 16, 2025) (rejecting DD request, citing petitioner’s “persuasive evidence that the Office erred” in overlooking

“specific teachings in” a clinical study protocol).

The result of allowing such error to stand is a U.S. patent that enables BMS to unduly extend its market exclusivity *while no such flat dosage claims exist in Europe*. Because the Decision misapprehended and overlooked the significance of this countervailing evidence and PO’s unreasonable reliance on expectations since *2021*, the Director should reverse the Decision and refer the Petition to the panel.

B. Patent Owner’s Recent Disclaimer of Analogous Flat Dosing Claims Corroborates PO’s Lack of Settled Expectations and Also Constitutes a Changed Circumstance Highlighting PO’s Ongoing Strategy To Avoid Scrutiny of its Obvious Follow-On Claims.

PO’s August 18, 2025 disclaimer of the ’529 Patent after the Director referred IPR2025-00603 to the merits panel tracks the above-discussed European activity and further confirms that PO could not have reasonably had any settled expectations in the ’113 Patent after having relied during prosecution on the 240 mg anti-PD-1 antibody flat dosing as the purported point of novelty.

Following rejection of the ’113 claims as anticipated by Wolchok, PO amended the independent claims by adding the requirement of administering “a flat dose of the anti-PD-1 antibody of about 240 mg every two weeks or about 480 mg every four weeks.” EX1002, 68. PO argued that “*Wolchok does not disclose administering a flat dose of an anti-PD-1 antibody*, let alone a flat dose of about 240 mg every two weeks or about 480 mg every four weeks.” EX1002, 77. PO did not identify any other claim element purportedly missing from Wolchok, which

expressly discloses the claimed 1 mg/kg weight-based dosing of the anti-PD-1 antibody along with the anti-CTLA-4 antibody. *See* EX1002, 433

PO subsequently broadened the new claim element by removing the “two week” and “four week” requirements. *Id.*, 33-34. As issued, the ’113 patent’s independent claims differ from the Wolchok prior art only in that they require a 240 mg or 480 mg flat dose of an anti-PD-1 antibody following the co-administration of anti-PD-1 and anti-CTLA-4 antibodies (which Wolchok expressly discloses).

The ’529 Patent includes dependent claims with such flat dosing requirements. Yet PO included them in its August 18, 2025 disclaimer following Amgen’s explanation in IPR2025-00603 why such claims are not patentable:

’529 Patent Claims (Disclaimed)	’113 Patent – Claim Element Added to Overcome Anticipation Rejection
Claim 12: The method of claim 11, wherein the administration of the anti-PD-1 antibody and the anti-CTLA-4 antibody is <i>followed by an anti-PD-1 antibody monotherapy</i> .	<i>followed by b) a dose of the anti-PD-1 antibody,</i>
Claim 16: The method of claim 12, wherein the anti-PD-1 antibody monotherapy is administered at a <i>flat dose of about 240 mg</i> once about every 2 weeks.	<i>wherein the dose in (b) is a flat dose of about 240 mg or about 480 mg</i>

As the table reflects, the ’113 Patent’s flat dosing claim element is even broader than that in the disclaimed ’529 Patent claims because it does not specify any frequency.

PO's disclaimer of the '529 Patent thus further confirms the European activity and refutes any suggestion that PO had any reasonable settled expectations after having relied on the 240 mg flat dosage to secure allowance in the United States.

It is immaterial that the '113 Patent concerns melanoma treatment whereas the '529 Patent concerns colorectal cancer treatment. Petitioner's IPR requests relied on the *same* prior art (e.g., "NCT-109" and "Wang"). *See, e.g.*, '113 Petition, 21-24. Yet the Interim Director discretionarily denied IPR2025-00602 while identifying no reason aside from the fact that the '113 Patent had been in force since 2019. Decision, 2-3; *cf. Tanklogix, LLC v. Sitepro, Inc.*, IPR2025-00650, Paper 10 (July 31, 2025) (referring IPRs filed the same day as IPR2025-00602 and concluding that a patent issued in 2019 had "*not* been in force for a significant amount of time").

PO's recent disclaimer of the '529 Patent is also a highly relevant changed circumstance for the further reason that PO now seeks denial of the relevant petition without adverse judgment despite simultaneously pursuing brand new continuation claims that are indistinct (indeed broader) than those purportedly disclaimed in the '529 Patent. That is the subject of separate briefing in IPR2025-00603 (Paper 11).

PO's willingness to abandon the '529 Patent evidences a strategic pattern that the USPTO should not facilitate. Much like its abandonment of the European counterpart to the '113 Patent discussed in § II.A., *supra*—this is just another instance in an ongoing and overt pattern of behavior to avoid merits consideration

of unquestionably obvious dosing claims by sacrificing them when challenged and by pursuing indistinct *or broader* claims in different applications and/or patents. The USPTO should not be manipulated to enable such gamesmanship. This newest, blatant evidence of this shell game strategy—the disclaimer of the ’529 Patent—was brought to the attention of Petitioner and this Board early last week and is being separately pursued in the ’529 IPR to prevent PO from resurrecting its allegedly disclaimed claims—in addition to the ’113 Patent follow-on claims—in a pending continuation application. This change in circumstance demonstrates a pattern of behavior that undermines the public confidence in the USPTO and warrants the Director’s vacating of the Decision and referral of the Petition to the merits panel.

C. The Decision’s “Settled Expectations” Analysis Overlooks Evidence That PO Expected A Challenge to the ’113 Patent.

As previously discussed in the DD Opposition, the regulatory and BPCIA litigation framework underlying development of a biosimilar for Opdivo® create expectations refuting the standard assumption that the expectations of the PO grow in step with the time that passes since issuance. DD Opp. 11-12, 19-21.

Most notably, Petitioner pointed out that *PO itself has argued* in prior litigation that where a competitor initiated an IPR too early (i.e., prior to having an approved product threatened by the challenged claims), it did not have standing to appeal an adverse decision. *Momenta Pharms, Inc. v. Bristol-Myers Squibb Co.*, 915 F.3d 764, 766 (Fed. Cir. 2019). Not only does this contradict PO’s argument that

Petitioner filed the instant IPR too late, it in fact demonstrates that PO *did not have any “settled expectations”* in the ongoing validity of its ’113 Patent.

Because PO knows full well that initiation of an IPR challenge against a patent prior to having an approved product allegedly leaves a challenger without standing to appeal, and because PO was aware of Amgen’s biosimilar launch timeline (DD Br. 8) with approval being years away, PO would not have expected any earlier challenge by Amgen to its ’113 Patent.

D. The Decision Erroneously Overlooks the Public’s Interest in the Swift Advancement of Biosimilars.

In addition to ignoring clear error, the Decision erroneously overemphasizes PO’s “settled expectations” in a suspect patent without any consideration of the interests and expectations of the public (and Amgen) in not having invalid patents keeping competitors from coming to the market. As discussed in the DD Opposition (and overlooked by the Decision), a key aspect of the ability of biosimilar developers to bring critical products to market is the ability to challenge mis-granted patents at around the time such biosimilar developers become aware of the technical feasibility of their biosimilar and based on their entry into the process for application for regulatory approval. DD Opp. 6-7, 19-21. The retroactive narrowing of this opportunity based on the years since a challenged patent issued is a factor that is largely irrelevant in the context of biosimilar development.

As detailed in Petitioner's DD Opposition, Amgen plays a significant role in the biosimilar market and, in particular, the development and commercialization of an affordable alternative to Opdivo®. DD Opp. 7. The Opposition explains that IPRs provide biosimilar developers like Amgen with the ability to identify erroneously granted patents and challenge their patentability prior to launch on a predictable timeline before an expert panel. And, as in this case, a successful challenge to obvious patent claims can help to prevent the issuance of similarly unpatentable patents. DD Opp. 3, 6-7, 19-21. In addition, rendering unpatentable a method of treatment patent, like the '113 Patent, before aBLA approval helps to inform the biosimilar applicant on the swiftest path to obtain regulatory approval of an indication or dosing regimen that may be relevant to the patent or to omit that indication/dosing regimen from a carved-out label to reduce patent risk. DD Opp. 6-7. In short, the continued availability of IPR proceedings to challenge mistakenly granted patents in advance of possible BPCIA proceedings comports with the public's interest in the accelerated approval of biosimilars.

All of this evidence was presented in the Opposition but was overlooked, or at the very least, misapprehended as such evidence clearly dwarfs any error-generated expectations PO has in claims it knows to be unpatentable. In view of the applicability of this critical public interest factor, the Decision should be reversed and the Petition referred to the merits panel.

E. Discretionary Denial Pursuant to Retroactive Application of the Interim Memo’s “Settled Expectations” Factor is Unconstitutional.

Reversal of the Decision denying institution is also necessary because the Decision is based on the Acting Director’s March 26, 2025 “Interim Processes for PTAB Workload Management” memorandum, which itself is unconstitutional as retroactively applied here by PO to petitions filed on February 28, 2025 in reliance on previous policies. The only factor the Decision cites as favoring discretionary denial is PO’s purported “settled expectations” given the length of time the ’113 Patent has been in force. Decision, 3. Yet the March 26, 2025 memorandum was the first time the Office had suggested that the “[s]ettled expectations of the parties, such as the length of time the claims have been in force” could be a factor weighing in favor of discretionary denial. Applying this newly introduced factor to deny Petitioner’s statutory right to pursue IPR exceeded the Director’s powers and ignored notice-and-comment rulemaking processes. Such a denial violated at least Petitioner’s due process rights under the Fifth Amendment by retroactively applying the new factors of the March Memo in contravention of statutory authority.

III. CONCLUSION

For the above reasons, the Decision denying institution should be reversed.

Date: August 25, 2025

Respectfully submitted,

/Scott A. McKeown/

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Counsel for Petitioner Amgen Inc.

CERTIFICATE OF SERVICE UNDER 37 C.F.R. § 42.6 (e)(4)

I certify that on August 25, 2025, a copy of the foregoing document, including any exhibits filed therewith, is being served via electronic mail, as previously consented to by Patent Owner, upon the following:

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