

# Reexamining Negative Limitations After Novartis Patent Ruling

By **Jonathan Fitzgerald and Jaime Choi** (September 26, 2022)

Pharmaceutical patents often use negative limitations in their claims directed to drugs or therapies, to patentably distinguish the claims over earlier drugs or therapies. For example, a claim might use exclusionary language such as "without," "excluding" or "absent" to incorporate a negative limitation, distinguishing the claims over what was previously known.

Every claim limitation, whether negative or positive, must meet the written description requirement to be valid and thus enforceable. Typically, the relevant inquiry is whether there is sufficient description in the patent's specification to support the limitation.

This inquiry intuitively makes sense for a positive limitation, such as a limitation that specifies the drug used in a therapy or the dosage. The question is simply whether there is sufficient written support in the specification for using the specific drug or dosage.

In contrast, for a negative limitation, it is less intuitive how to analyze whether the written description requirement is met. What kind of written support in the disclosure is necessary to show that an element is absent in the drug or therapy? Because the negative limitation excludes the element, is any written support of the element even necessary?

In *Novartis Pharmaceuticals Corp. v. Accord Healthcare Inc.*,<sup>[1]</sup> the Federal Circuit set forth standards of review to examine negative limitations, and it applied these standards to invalidate claims in a patent owned by Novartis<sup>[2]</sup> based on its conclusion that the negative limitations in the claims failed to meet the written description requirement.

Subsequent to this decision, the Federal Circuit denied Novartis' petition requesting an en banc rehearing of the case. Pending the outcome of a potential appeal to the U.S. Supreme Court, the Federal Circuit's decision in *Novartis*, and its denial of Novartis' petition, has created exacting standards that must be met in order for negative limitations to satisfy the written description requirement.

This article discusses the Federal Circuit's standards of review for negative limitations and its application of those standards to the negative limitation at issue in *Novartis*, and it considers the dissent's contention that the majority opinion heightened the standard of review for negative limitations.

The article also compares the Federal Circuit's standard as applied in this case to the guidelines that the European Patent Office applies to similar disclaimers during prosecution of European patents. We conclude with the impact that the *Novartis* decision will have on practitioners who prepare pharmaceutical patent applications as well as the impact of this decision on litigating pharmaceutical patents.

## The Negative Limitation at Issue in the Case

The issue in *Novartis* was whether a negative limitation had sufficient written support to



Jonathan Fitzgerald



Jaime Choi

satisfy the written description requirement. Claim 1, which is representative, includes the negative limitation at the end: "absent an immediately preceding loading dose regimen":

1. A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

The U.S. District Court for the District of Delaware determined that the specification disclosed starting with a daily dose, and that this "plainly implies there is no loading dose." As explained below, the Federal Circuit disagreed.

### **The Federal Circuit's Standard of Review in Novartis for Analyzing Negative Limitations**

To determine if the negative limitation was supported, the Federal Circuit referred to the standard of whether "the specification describes a reason to exclude the relevant [element]."

According to the court, examples of "reasons to exclude" include (1) a statement in the specification describing the disadvantage(s) of using the element, or (2) the specification distinguishing between the element and alternatives to it. What these examples have in common is disclosure of the excluded element. Thus, according to the court, silence regarding the excluded element is generally not sufficient to support a claim in which the element is expressly excluded.

The Federal Circuit characterized "the specification describing a reason to exclude" as an example standard, suggesting that other standards could be used to determine if a negative limitation is supported.

In this, the court stated that the reason to exclude does not necessarily have to come from the specification, if there is evidence that silence with regard to an element means that the element is necessarily excluded. For example, in a particular field, the absence of mention of an element may necessarily mean that the element is excluded. Otherwise, it seems that the reason to exclude must derive from disclosure in the specification.

The Federal Circuit emphasized that expert testimony is no substitute for the specification's disclosure. Specifically, the court indicated that expert testimony discussing the possibility that an element would be excluded is insufficient to show that the negative limitation meets the written description requirement. According to the court, allowing expert testimony to substitute for disclosure in the specification would eviscerate the written description requirement because it would no longer require disclosure in the specification.

### **The Federal Circuit's Analysis of the Loading Dose Limitation**

The specification did not disclose a "loading dose." The Federal Circuit concluded that because of this lack of the disclosure, the negative limitation was not adequately supported, and therefore did not meet the written description requirement.

In analyzing the negative limitation, the Federal Circuit found that there was no evidence to show that a skilled artisan would conclude that silence with respect to the loading dose would mean that it is necessarily excluded. In this, the court cited expert testimony stating

that loading doses are sometimes provided to patients with multiple sclerosis. One expert stated that he "could envision the possibility of starting with a loading dose."

The court also found there was "intrinsic" evidence that a skilled artisan would not conclude that reciting a daily dosing regimen, without mentioning a loading dose, would necessarily exclude a loading dose.

Presumably, the intrinsic evidence that the court was referencing was from the prosecution history, in which Novartis added the negative loading dose limitation and argued that it distinguished the claims over the prior art, stating that the negative limitation made clear "that the [daily dosage] cannot immediately follow a loading dose regimen." The court concluded that if a daily dosage on its own necessarily excluded a loading dose, then it would not have been necessary to add the negative limitation.

Additionally, the Federal Circuit was unpersuaded by expert testimony stating that a person of skill would presume that the specification's lack of reference to loading dose means that a loading dose is not present in the treatment.

According to the testimony, this presumption was based on the belief that the specification is complete, i.e., that it has all the information a person of skill needs to carry out the claims. Thus, silence in the specification regarding a loading dose would teach a person of skill that the loading dose is excluded from the treatment.

But the court disagreed, finding that there is no presumption that the disclosure is complete, so it is improper to presume that the absence of an element means that the element is necessarily excluded. Further, it is possible that the court viewed this and other expert testimony with suspicion, based on its conclusion that expert testimony is no substitute for disclosure in the specification.

For these reasons and others, the Federal Circuit concluded that the specification's silence regarding a loading dose did not provide written support for the negative limitation of "absent an immediately preceding loading dose regimen," and found the patent invalid.

### **A Possible Heightened Standard for Satisfying Written Description for Negative Limitations**

The majority opinion stated that their decision does not create a heightened standard for negative claim limitations. Rather, they are just applying the same standard to both positive and negative limitations, namely whether the disclosure reasonably conveys that the inventor(s) had possession of claimed subject matter at the time of filing.

The dissent disputes this position, arguing that the majority applied a heightened standard to negative limitations by requiring not only a "reason to exclude" but also that the negative limitation is "necessarily excluded."

To support this position, the dissent described what it believed was ample evidence in the specification to support the absence of a loading dose. This evidence included description of multiple dosing regimens that lacked a loading dose, and descriptions of daily doses that lacked a loading dose.

This evidence, according to the dissent, supported the reasonable inference made by the district court that there was support for dosing regimens lacking a loading dose. In addition, the dissent pointed to the expert testimony that indicated that silence regarding a loading

dose suggests that the loading dose is absent.

For the dissent, this evidence was sufficient to show that the inventors possessed the negative loading dose limitation, and showing possession is the typical standard for showing that a claim limitation meets the written description requirement. Notably, this evidence that the dissent cites does not rise to the level of showing that the loading dose is "necessarily excluded" as the majority apparently required. However, meeting the "necessarily excluded" standard is not the typical written description standard, and, according to the dissent, should not be applied to negative limitations.

As noted above, the majority opinion seems to implicitly, if not explicitly, require a showing of evidence of a "reason to exclude," and that the showing of evidence typically, but not always, requires some kind of express disclosure in the specification. For reasons described above, the dissent argued that the majority opinion also required an express showing of evidence that the negative limitation is "necessarily excluded."

The dissent also took issue with the majority opinion's position that adding the negative loading dose limitation during prosecution showed evidence that this negative limitation was not implicit in the claims. The dissent pointed out that, to secure an allowance, applicants often add limitations in claims to make something explicit that is already implicit in the claims. Thus, the dissent believed that the majority opinion was reading too much into the prosecution history.

### **Comparing Novartis on Negative Limitations to European Patent Office Guidelines on Disclaimers**

Those who are familiar with pharmaceutical patent prosecution under European patent law may be wondering whether claims with the types of negative limitations used in Europe may now be more vulnerable to invalidity challenges in view of Novartis.

More specifically, the European Patent Office guidelines for examination allow some subject matter to be excluded via a negative limitation called a "disclaimer." The EPO guidelines provide that this may be done if a feature's absence may be deduced from the application, as filed, and cite a 1991 German case[3] in which the negative limitation "without blurring device" was not expressly disclosed in the original application. The court there found the absence of the blurring device to be implicit, because the claimed device functioned in a way that the blurring device must have been missing.

Notably, the EPO examination guidelines in this regard are not that different from the U.S. Patent and Trademark Office's Manual of Patent Examining Procedure. Indeed, as pointed out by the Novartis dissent, the MPEP does not require the specification to provide literal basis for a negative limitation, and provides that implicit disclosure can support claim limitations. So, at least under the current USPTO examination guidelines and Novartis, disclaimers — or negative limitations — that find implicit written support in Europe also may find such support in the U.S.

Similar to the EPO guidelines, Novartis allows for the possibility that negative limitations can be implicitly supported. However, the Novartis court seemingly only provided a narrow path in which implicit support would be sufficient to support a negative limitation, as the only example it provided is when the absence of mention of the element means that the element is necessarily excluded. In addition, the court emphasized that the hallmark of the written description requirement is disclosure.

## Impact on Practitioners

For practitioners that prepare pharmaceutical patents, because the path to implicitly supporting negative limitations seems narrow, relying on implicit support for negative limitations may be risky. Thus, it may be beneficial to provide explicit support in the specification for negative limitations such that the specification discloses a "reason to exclude" the element.

As the court pointed out in *Novartis*, potential examples of reasons to exclude include describing disadvantages of using the element and providing comparisons of the element to its alternatives. Further, there are likely other ways that the specification can support a reason to exclude that are not described in the *Novartis* decision.

Whether the dissent is correct that the majority opinion applied heightened standard of "necessarily excluded" to negative limitations is an arguable point. What is clear is that the *Novartis* court required evidence supporting a reason to exclude in which the disclaimed element is, typically, expressly disclosed in some form in the specification.

If the Federal Circuit continues to apply this standard (and potentially the standard of "necessarily excluded" described by the dissent), pharmaceutical patent claims that contain negative limitations but do not provide express written support for excluding the element (and potentially for necessarily excluding the element) could be at higher risk for invalidity challenges under the written description requirement.

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*Jonathan B. (J.B.) Fitzgerald, Ph.D., is counsel and Jaime D. Choi, Ph.D., is a partner at Snell & Wilmer LLP.*

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[1] *Novartis Pharmaceuticals Corp. v. HEC Pharm Co., LTD.*, No. 2021-1070, 2022 WL 2204163 (Fed. Cir. June 21, 2022).

[2] U.S. Pat. No. 9,187,405.

[3] T 0278/88 (<https://www.epo.org/law-practice/case-law-appeals/recent/t880278du1.html>).