Keywords: **Method Claims, Limiting Preamble, Reasonable Expectation of Success, Written Description**

General: **Preambles can be limiting when they state an intended purpose for methods of using a compound.**

Eli Lilly and Company, v. Teva Pharmaceuticals International GMBH.
United States Court of Appeals for the Federal Circuit
Nos. 2020-1876, 2020-1877, and 2020-1878
Decided August 16, 2021

I. Facts

Eli Lilly and Company ("Lilly") appeals from a decision of the Patent Trial and Appeal Board ("Board") holding that claims of three patents U.S. Patent No. 8,586,045 ("the '045 patent"), U.S. Patent No. 9,884,907 ("the '907 patent"), and U.S. Patent No. 9,884,908 ("the '908 patent") of Teva Pharmaceuticals International GMBH ("Teva") are not unpatentable as obvious. The three patents generally relate to methods of using a humanized anti-CGRP antagonist antibody, hereinafter the large compound, to treat vascular headaches, including migranes, in an individual.

At the time of challenging the patents, it was uncertain whether migrane treatments must cross a blood-brain barrier ("BBB"). Moreover, the large compound was known to have difficulty crossing the BBB. This raised uncertainty and unpredictability of the effectiveness of using the large compound for treating migranes.

The claims at issue are directed to methods of using the large compound to bind with a mediator protein (i.e., CGRP), known to exacerbate the pain symptoms of migranes, to prevent the mediator protein's binding with receptors to treat migranes. A portion of representative claim 1 of patent '907 directed to methods of treating migranes including the step of administering the large compound recites:

> 1. A method for treating headache in an individual, comprising:
> administering to the individual an effective amount of a humanized monoclonal anti-Calcitonin Gene-Related Peptide (CGRP) antagonist antibody.

Lilly challenged some of the claims of the ‘045, ‘907, and ‘908 patents, in an *inter partes* review, as obvious over three references: Olesen (“first reference”), Tan (“second reference”), and Queen (“third reference”). The first reference describes using a small molecule (i.e., BIBN), that can cross the BBB more easily as compared to the large compound for treating migranes. The small molecule blocks a receptor of the mediator protein, as opposed to binding with the mediator protein, to prevent the protein’s binding with the receptors. The second reference describes using a non-humanized version of the large compound with rats to prevent binding of different mediators with their respective (and different) receptors. The second reference also described reducing blood flow of rats using such methods. Reduced blood flow was known to exacerbate migrane symptoms in humans. The third reference is related to a method of humanizing monoclonal antibodies, such as the large compound.

The Board issued a combined final written decision in the three IPRs. For issuing the final written decision, the Board (I) construed the claims, including (A) the preambles and (B) the term “effective amount,” (II) analyzed the asserted prior art based on the claim construction, and (III) concluded that Lilly failed to prove that the challenged claims in the three patents would have been obvious over the references.

(I) (A). The Board determined that the preamble claim language is a statement of intended purpose to the extent of requiring performing the method for the intentional purpose of treating a headache. The Board discussed that based on such limiting construction of the preambles, Lilly’s burden to demonstrate reasonable expectation of success in combining the teachings of the references involves achieving a particular result (e.g., treating migranes in humans) as the intended purpose of performing the challenged method. The Board explained that “what is required is not proof that the recited method would *actually* bring about the recited result, but rather proof that a person of ordinary skill in the art would have had a reasonable expectation that performing the recited method would bring about the recited result.”

(I) (B). The Board construed the term “effective amount” based on the written description of the patent as “an amount sufficient to effect beneficial or desired result.” The results, based on the intended purpose construed from the preamble, are related to treating migranes in humans (e.g., reducing severity, duration, or frequency of headaches).

(II). The Board found that the asserted prior art teaches each and every element of the challenged claims. The Board also found that a skilled artisan would have been motivated to combine the teachings of the prior art to treat migranes in humans. However, the Board found that the mechanisms and, therefore, treatment of migranes was uncertain at the time. Moreover, the Board found that the existing unpredictability and uncertainty regarding whether the large compound had to cross the BBB to be effective for treating migranes counsels against reasonable expectation of success. Accordingly, the Board found no reasonable expectation of success to treat migranes by administering the effective amount of the large compound based on the asserted prior art.

(III) The Board found that Lilly failed to prove that a skilled artisan would have had a reasonable expectation of success as to any of the challenged claims. Lilly appealed from the Board’s decision to the Federal circuit raising the following issues.

II. Issue

I. The Board erred by reading a result into the construction of (A) the preambles and (B) the term "effective amount."

II. The Board erred by applying too high a standard when weighing the evidence to determine whether a skilled artisan would have had a reasonable expectation of success.

III. Discussion

I. Regarding the construction of the preambles, Lilly argued that a preamble contains only a statement of purpose and cannot be limiting. Lilly argued that the preambles should be attributed no weight and therefore are irrelevant to the obviousness analysis. Teva responded that the Board construed the preambles of the challenged claims as limiting correctly, in particular, because the preambles are central to the invention, they provide antecedent basis for the later claim limitation "individual," and they give meaning to administering an "effective amount" to the individual. The Federal Circuit agreed with Teva.

The Federal Circuit provided that whether to treat a preamble as a claim limitation is determined on the facts of each case in light of the claim as a whole and the invention described in the patent. Moreover, the Federal Circuit explained that while there is no rule for determining whether a preamble is limiting, the Federal Circuit has generally construed statements of intended purpose in methods of using a composition for a specific purpose as limiting. The Federal Circuit also explained that method claims are different from composition and apparatus claims because claimed structure allows the composition or apparatus to function identically whether or not used for a stated intended purpose. Method claims are directed to what a method "does" rather than what the method "is," where what the method does is usually recited in the preamble.

In this case, the Federal Circuit explained that the preambles limit the scope of the claims because these claims would not read on, for example, the performance of the same method step to treat other conditions. The preambles are not merely statements of effect but rather statements of the intentional purpose for which the methods must be performed. For example, the treatment of headaches, including migranes, is central to the inventions of the challenged patents, which is reflected in the extensive discussions of such treatment in every section of the written description of the patent.

Regarding the term "effective amount," Lilly argued that the Board's errors in imposing required results based on the construction of preambles compounded to the erroneous construction of the term "effective amount." The Federal Circuit provided that Lilly is incorrect when it argues that the methods would be performed in the same way regardless of the preamble. The Federal Circuit explained that the preambles of the challenged claims provide the only metric for determining whether the administered amount is an "effective amount" when practicing the claim. Accordingly, this case is not like cases where the administration of a specified amount is the same regardless of the purpose. The Federal Circuit added that without an individual experiencing a migrane, there would be no effective amount to treat the nonexistent symptoms. In addition to giving life and meaning to the method step of each claim, the preambles also provide antecedent basis for at least one later claim term (i.e., the individual).

As such, the Federal Circuit found no error in the Board's conclusion that the preambles are limiting.

II. The Federal Circuit also agreed with the Board's decision that a skilled artisan would have not had a reasonable expectation of success based on the provied prior art. The Federal Circuit explained that a party seeking to invalidate a patent based on obviousness must demonstrate by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so. That is, a finding by the Board that a patent challenger has demonstrated a motivation to combine the references does not necessarily imply that the challenger has also met its burden of showing a reasonable expectation of success in achieving a claimed method of treatment. Accordingly, Lilly must not only prove that a skilled artisan would be motivated to combine the asserted prior art, but also that the skilled artisan would have reasonably expected success in administering the large compound for treating migranes.

The Federal Circuit found no error in the Board's assessment of reasonable expectation of success when combining the asserted prior art based on sufficient uncertainty and unpredictability suggesting against obviousness. The decision was, at least, based on (1) uncertainty regarding whether migraine treatment must cross the BBB to be effective, (2) the large compound having difficulty crossing the BBB, (3) the use of the small molecule for treatment of migranes in the first reference not being analogous to the challenged claims, and (4) an unresolved dispute regarding whether the non-humanized version of the large compound can reach an effective area for treating migranes in humans in the second reference.

IV. Conclusion

The Federal Circuit affirmed the Board's final written decision upholding the patentability of the claims of the challenged patents.