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SYMPOSIUM

Patenting Carboxyformin in the United States: How Does It Work and What Does It Mean?

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Abstract

Carboxyformin, a new biguanide, shows promise as a treatment for type 2 diabetes mellitus (attributes assumed for the purpose of this article). But is a carboxyformin-based therapeutic formulation patentable? And if the formulation is patentable, what protection is afforded by the patent? This article examines the patent prosecution process, beginning with the initial discovery and continuing through the issuance of the patent. The article also briefly discusses issues of patent infringement and considers whether the inventor is able to practice his invention and whether he is able to keep others from the unauthorized use of his invention.

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Introduction

Congratulations! After years of research, you and your fellow diabetes researchers have formulated and tested a carboxyformin-based therapeutic, a new biguanide, for the treatment of type 2 diabetes mellitus. The great news is, unlike other oral medications indicated for the treatment of type 2 diabetes, carboxyformin does not cause gastrointestinal distress or lactic acidosis. (Carboxyformin, shown in **Figure 1**, is an unknown, hypothetical molecule; the attributes stated herein are assumed for the purposes of this article.)

So now what? What do you do first? You have a celebratory beer (or favorite beverage of choice), of course! Then what do you do? Do you tell all your friends about your invention? No. Do you race to put together a publication detailing the synthesis and characterizations of the invention? No. Do you call your technology transfer office and/or your patent attorney? Yes.

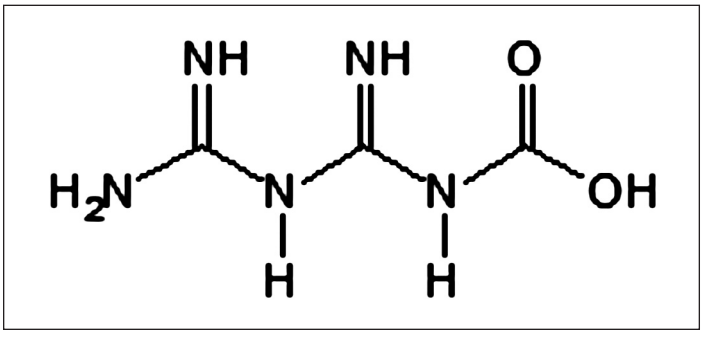

Figure 1. Carboxyformin.

Do You Have a Patentable Invention?

Your first meeting with the patent attorney will be to discuss the intricacies of the invention so that he can perform an assessment to evaluate whether your invention is patentable in the United States. To make this determination, the patent attorney will analyze the prior art, i.e., the world's patent and nonpatent literature in

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existence before the filing date of your invention. There are four statutory criteria for patentability, and the patent attorney's assessment will focus on those criteria to determine whether your invention (1) falls within a statutory class (is a process, machine, article of manufacture, composition of matter, or any improvement thereof); (2) is useful; (3) is novel (i.e., has not been invented before); and (4) is nonobvious (i.e., the differences between the subject matter of the patent application and the prior art are sufficiently different that the invention would not have been obvious to a "person having ordinary skill in the art"). This assessment will also determine whether a patent filing for your invention is barred by any statutory provisions, the details of which are beyond the scope of this article, but which reward the early filing of patent applications on inventions in either provisional or regular utility application form.

In a typical case, the patent attorney will perform the assessment within a few weeks and return a report to you detailing his findings. The report will most likely identify the chemical structure of carboxyformin, and in its discussion of prior art, the report will most likely note that it is closely related to metformin, the well-known molecule shown in **Figure 2**. The report will also likely discuss the side effects of metformin, including a patient's propensity to gastrointestinal distress and/or lactic acidosis while on a metformin regimen.

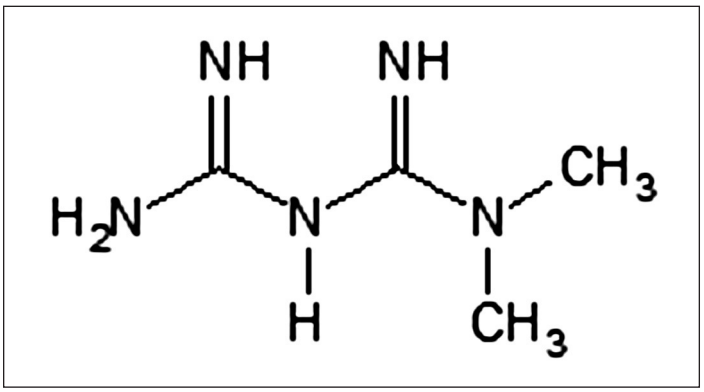


Figure 2. Metformin.

Also included in the report will be a discussion of the development of metformin as a therapeutic agent. The report will note that metformin was first synthesized in the 1920s and that its blood-glucose-lowering potential was first noticed in the same decade. Also included in the report will be a discussion of its development as a pharmaceutical, Glucophage, beginning in the 1950s. The report will likely discuss the history of Glucophage® in the United States and will note that Bristol-Myers Squibb was the first pharmaceutical company to obtain approval from the U.S. Food and Drug Administration for the use of metformin in diabetes therapy. To be complete, the report will also likely include a discussion of the current formulations containing metformin, including, Fortamet®, Glumetza®, Riomet®, ACTOplus met®, Avandamet®, Glucovance®, Janumet®, Jentadueto®, Kombiglyze™, Metaglip®, and PrandiMet®. The report may also include a discussion of other biguanides, including phenformin, buformin, and proguanil.

The patent attorney will advise you that your invention meets the statutory requirements for novelty because he found no metformin derivatives identical to carboxyformin (assumed true for the purposes of this article). Importantly, the patent attorney will also review the report to determine if a carboxyformin-based therapeutic is rendered obvious by any of the art he uncovered. His analysis will involve a three-pronged inquiry to determine (1) if the scope and content of the prior art is related to your invention, (2) whether a patentable distinction can be made between your invention and the prior art, and (3) whether a person having ordinary skill in the art would view your invention as an obvious improvement over the prior art at the time the invention was made.

The patent attorney will also consider secondary considerations when deciding whether a carboxyformin-based therapeutic is rendered obvious by the art he uncovered. Secondary considerations are items of evidence that tend to demonstrate that the invention is not obvious. Secondary considerations may include[1–3]

- Long-felt, but unsatisfied, need for the invention;
- Commercial success of the invention causally related to the invention itself;
- Failure of others to conceive of and execute the invention.
- Copying of the patentee's invention by competitors;

- Teaching by those skilled in the art away from the technical direction pursued by the patentee; and
- The unexpectedness, to those skilled in the art, of the results of the invention.

For the purposes of this article, we will also assume that the invention is nonobvious in that the substitution of a carboxylic acid group is often not considered as "obvious" over a methyl alkyl group. The substitution of a hydrogen atom for a methyl group is a slightly more difficult determination, but since the analysis is not typically performed on an atom-by-atom basis, the overall differences should be sufficient.

You, or your company, instruct the patent attorney to file a patent application. He does so forthwith, and over the next few years, he prosecutes the patent application before the United States Patent Office. During the prosecution period, the patent attorney will consider references cited by the patent examiner and may amend, or edit, the claims of the patent application to overcome the cited references. Also during the prosecution period, the patent attorney may cancel or add claims to the patent application to overcome references cited by the patent examiner. After a period of years, the patent application issues as a utility patent. However, an important question remains: now that you have a utility patent covering a carboxyformin-based therapeutic, will you be able to use it?

Practicing Your Invention in the Art

While your patent attorney successfully obtained a patent protecting a carboxyformin-based therapeutic, are you able to use it commercially to treat type 2 diabetes? Sadly, the answer to this question is more likely "maybe" than "yes."

The initial patentability analysis focused on novelty and obviousness of your invention and whether patentable differences existed between your invention and the prior art. To answer this new question, the analysis switches to a determination of whether any blocking patents exist that might prevent you from commercializing your invention. For this analysis, you and your patent attorney will consider the claims of the relevant patents, not the teachings of the specification of the patents.

Claims are the numbered sentences at the end of a patent document. They define the legal scope of a patent's coverage, similar to the way a fence defines the edge of a yard. A product may infringe the claims of one or more patents through literal infringement or through the doctrine of equivalents. Your patent attorney will begin his analysis by analyzing the claims of the blocking patent and then comparing them to your invention to ensure you do not make, use, or sell a product protected by the blocking patent. The patent attorney's analysis will be further informed by all parts of the patent i.e., the specification or written description showing how to make and use the invention of the patent, the drawings of the patent, and the file wrapper or prosecution history of the patent. This is because, although the claims define the legal scope of the patent's coverage, the remaining parts of the patent may be used to interpret the meaning of the claims.

Literal infringement is found when the product or process accused of infringement meets, i.e., matches, each and every element of at least one claim of the patent.[4] Literal infringement is often found when an accused product or process is an improvement of a claimed product or process. This is because literal infringement can be found even if the accused product incorporates additional elements. Remember, the relevant question now is not "are there patentable differences," but "does the accused device meet or match each and every element of the claim."

United States Patent No. 3,174,901[5] (the '901 patent) is a patent covering the treatment of type 2 diabetes using metformin and its nontoxic acid addition salts. Assuming, for the sake of example, that the patent is still in force (the '901 patent has already expired and you cannot infringe the claims of an expired patent), and assuming claim 1 merely covered the use of a metformin-based therapeutic in the treatment of type 2 diabetes, your carboxyformin-based therapeutic does not literally infringe the claim. Why? Because you substituted a hydrogen and a carboxyl group for the two methyl groups, your compound, or product, does not meet each and every element of the claim. For easy reference, a side-by-side comparison of the relevant molecules is shown in **Figure 3.** This change is sufficient to avoid literal infringement, because there is no one-to-one match between the claim and your composition as illustrated in **Figure 3**.

But is this change sufficient to avoid the doctrine of equivalents? The doctrine of equivalents teaches that an accused product or process infringes a claim if it performs substantially the same function in substantially the same way to obtain the same result ("the way/function/result test").[6] A patentee wishing to prove infringement under the doctrine of equivalents must prove an accused product meets all three prongs of the test. Proof that the prongs of the test are met may be made in any form: expert testimony, testimony of others versed in the art, treatises and texts, and disclosures in the prior art. Each of these pieces of proof, or evidence, will be judged for its credibility, persuasiveness, and weight. If the proof tends to show the doctrine of equivalents is applicable, the fact finders will also consider mitigating factors such as estoppel, i.e., the scope the patent owner surrendered during patent prosecution, and whether the claims according to the proposed construction are invalid in view of the prior art.

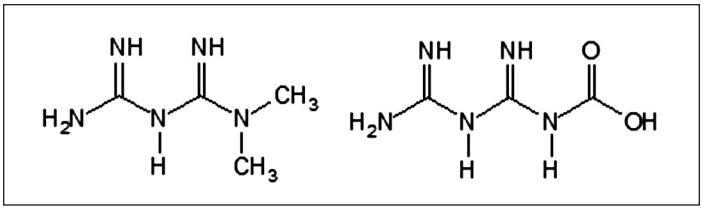


Figure 3. A side-by-side comparison of metformin and carboxyformin.

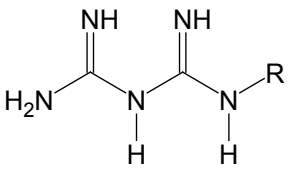
For this article, we assumed the carboxyformin-based therapeutic is also used to treat type 2 diabetes, and we will assume that it performs substantially the same function as metformin to obtain the same result, the lowering of blood glucose. But does it do so in substantially the same way as metformin? For the purposes of this article, we will assume carboxyformin causes a distinct biochemical reaction and does not treat type 2 diabetes in substantially the same way, negating the doctrine of equivalents. Thus, in the universe created for this article, your carboxyformin-based therapeutic does not literally infringe claim 1 of the '901 patent directed toward the method of treating type 2 diabetes with metformin, and it does not infringe the claim under the doctrine of equivalents. Your carboxyformin-based therapeutic may be freely used to treat type 2 diabetes.

Preventing Others from Practicing Your Invention

Now that you have patented a carboxyformin-based therapeutic and know you are able to manufacture and sell it as a therapeutic for the treatment of type 2 diabetes, are you able to keep others from doing the same? The question typically arises when you notice a competitor selling a derivative of your product, and the answer lies again in the precise wording used in the claims.

What if your competitor is manufacturing and selling an ester derivative of carboxyformin of the type shown in **Figure 4** for the treatment of type 2 diabetes? Does your patent prohibit your competitor from this activity? The answer is determined by the scope of your claims as written by you and your patent attorney. The initial analysis will involve the following comparison between the claims as written and the potentially infringing product. First he will check for literal infringement, and if there is no direct infringement, he will check for infringement under the doctrine of equivalents.

Assume for the sake of argument your patent attorney formulated your claim 1 to read, "A method of treating type 2 diabetes that comprises administering a biguanide having the following formula:



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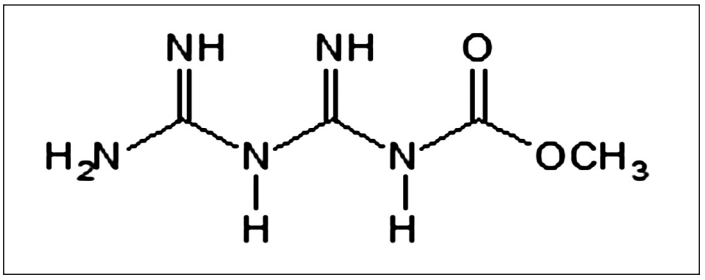

Figure 4. An ester derivative of carboxyformin.

wherein R is selected from the group consisting of C_{1-3} carboxylate groups and C_{1-4} carboxylic acid groups."

Similar to chemistry, the "R" convention for naming portions of formulas in patent documents indicates not an atom, but rather a group of possible substitutions and is a shorthand notation often employed in chemical claims. In this claim, R can be any of the two named groups and be covered by the protection of claim 1.

In this instance, your competitor's product literally infringes claim 1 of your patent because it meets the literal wording of the claimed elements of claim 1, the "methyl ester" falling within the more generic class of "$C_{1–3}$ carboxylate groups" in claim 1. Thus the product falls within the scope of coverage obtained by the patent attorney, and its use is not permitted in light of your blocking patent. However, since patent enforcement is not self-executing, to stop the manufacture and sale of the competing product, you may have to sue your competitor for patent infringement, a discussion for another day.

Conclusion

It is important that research scientists have familiarity with patent prosecution and with the benefits afforded by patent protection. A patent attorney will evaluate your invention to ensure that it meets the statutory requirements for patent protection, i.e., that the invention falls within a statutory class and is useful, novel, and nonobvious. After the patent attorney obtains patent protection for your invention, the patent attorney will evaluate similar patents to ensure that you do not literally infringe another patented invention and that you do not infringe another patented invention under the doctrine of equivalents. Finally, the patent attorney will evaluate your competitors to ensure that their activities do not infringe the patent protection for your invention literally or under the doctrine of equivalents. For the purposes of explanation, we used the framework outlined in the article to analyze a carboxyformin-based therapeutic. We saw that it met the statutory requirements, that it did not infringe a related patent, and that a competitor's product infringed the claims directed to its use. The authors encourage you to meet with a patent attorney when you invent a new product or process so that he may perform similar types of analyses directed to your invention.

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