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GILEAD'S REJECTED PATENT APPLICATION HIGHLIGHTS SECTION 3(D) UNCERTAINTIES

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Nearly two years after the Novartis decision, questions about India's Section 3(d) remain

The patent office's written decision points to some unanswered questions surrounding Section 3(d) of the Patents Act. The provision states that where an applicant seeks to patent a new form of a known substance, the application must show that the new form provides enhanced efficacy over the prior art form.



The explanatory notes to [Section 3\(d\)](#) states that "salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy".

The patent controller last week [rejected Gilead's application](#) (India patent application no 6087/DELNP/2005) for its Solvaldi hepatitis C drug, [finding that Gilead failed to establish](#) that there was enhanced efficacy. Gilead has already announced that it will appeal the decision.

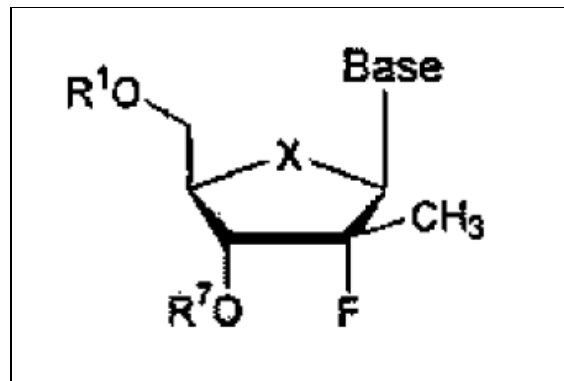
K&S Partners represented Gilead in this matter.

When does Section 3(d) apply?

One question applicants are struggling with is what exactly constitutes a new form of a known substance.

In the patent office's written decision, it found that Gilead's molecule was in fact novel and non-obvious. The grounds for rejection laid instead on Section 3(d).

Gilead argued that Section 3(d) did not apply to the claimed molecule. It said that Section 3(d) is supposed to raise the bar for patentability to avoid alterations to the form of known substances in order to extend the market exclusivity of the known substance. The claimed molecule in Gilead's application was not a derivative of the prior art molecule. Applying Section 3(d) in this situation, Gilead argued, would "create a higher bar for new substances by deeming all new compounds to be merely derivatives of known compounds".



The claimed molecule

The patent controller found that the claimed molecule is "structurally and functionally similar" to a molecule in the prior art, a compound XI (actually a genus that covers several compounds), and thus the Section 3(d) requirements must be met. It found that Gilead's claimed molecule was a stereoisomer of

compound XI, triggering the Section 3(d) requirements. Stereoisomers are isomers that have the same molecular formula but differ only in the 3-D spatial orientation of their component atoms. As noted in the explanation notes to Section 3(d), isomers are considered a new form of a known substance.

"[Compound] XI as disclosed [*sic*] in [patent] D1 is the closest prior art as being structurally closed to the presently claimed compound and therefore is the same compound to D1 in the eyes of the section 3(d)," the controller noted.

Pankaj Soni of Remfry & Sagar said that the patent office's use of Section 3(d) here is concerning, because Gilead's application does not implicate the key rationale behind the provision.

"Compound XI from the prior art and the claimed compound are stereoisomers and this technically brings this application within the purview of Section 3(d), but I think this is a very simplified way to look at it," Soni said. "If you look at the purpose of Section 3(d), it is to prevent evergreening of drug patents. But that's not what's happening here; Gilead does not hold a patent covering compound XI that it is trying to extend."

However, Mohan Dewan of RK Dewan and Co said that the patent controller was correct in finding that Section 3(d) applied and that the office was bound by the plain language of the law. Instead, he said that Gilead's mistake was making focusing on arguments based on law rather than on science.

"The Sovaldi application is a story of how a good molecule can be destroyed by bad handling"

"The test for enhanced efficacy was the test that the controller was required to apply under the law," he said. "Gilead argued that its molecule was a new substance and thus didn't need to establish clinical efficacy, which is a legal argument. They did not make a scientific argument supporting this."

The lack of clarity about the applicability of Section 3(d) may also lie with the patent controller's written decision. Meenakshi Khurana of Khurana and Khurana said that though the decision held that the claimed molecule and compound XI are similar substances with only minor variations, the patent controller could have clarified the issue by clearly stating that Section 3(d) applied because Gilead's molecule was a stereoisomer of compound XI and thus falls explicitly within the provision.

Proving enhanced efficacy

The patent office's holding also highlighted the difficulty applicants face in establishing enhanced efficacy to clear the Section 3(d) hurdle.

Gilead had presented evidence demonstrating lower toxicity in the claimed molecule. It compared the claimed compound to four other compounds but did not do so in comparison to compound XI, the prior art molecule that the patent office said triggered Section 3(d) analysis.

"It appears that the data provided by Gilead does not cover what we believe is the closest stereoisomer [2'-fluoro (up), 2'-methyl (down)] of compound XI," explained Jitesh Kumar of Remfry and Sagar. "Providing this data, if possible or available, may have helped the applicant in strengthening its efficacy argument to overcome Section 3(d)."

However, even this may not have saved the application, because toxicity evidence alone, even if presented in comparison to compound XI, may not be enough to show enhanced efficacy.

"The Supreme Court precedent in the *Novartis* case clearly lays down that the efficacy in Section 3(d) is the 'therapeutic efficacy', thus cytotoxicity data is not likely to be considered as showing enhanced therapeutic efficacy," Khurana said.

In the *Novartis* case, the Supreme Court held that while enhanced bioavailability, the extent to which a drug reaches its intended site of action, is one aspect showing enhanced efficacy, that alone is not enough.

Dewan said that it appeared as if the applicants were perhaps too confident in their argument that Section 3(d) was not applicable.

"What Gilead should have said was that even if Section 3(d) did apply, it would not stop the drug from being patented because the molecule would show enhanced efficacy," he said. "Instead of spending more money on lawyers making legal

arguments, it should have spent the money on more chemists to run a battery of tests showing the activity of the claimed molecule and the prior art molecule."

"The Sovaldi application is a story of how a good molecule can be destroyed by bad handling," he added.

OPPOSITION HANDLING STILL UNCLEAR

In addition to the Section 3(d) issues, Gilead's patent application also highlighted some uncertainties concerning the handling of pre-grant oppositions. Generic manufacturer Natco as well as the non-profit Initiative for Medicines Access and Knowledge both filed oppositions to the application. However, Soni pointed out that the patent controller's office has been inconsistent in how it handles oppositions. He said that while some examiners will notify the applicant that an opposition has been filed and give the applicant a chance to respond, others will handle the patent application first, to see if the invention is patentable first, before looking at whether the points raised in the opposition would affect the application. Soni pointed out that not only are many rights holders concerned with having a consistent practice, but also there are worries that the examiners are looking at pre-grant oppositions and allowing the arguments made within to influence their thinking without giving the applicant a chance to respond.

So where's that finish line?

Furthermore, even though more tests may have strengthened Gilead's application, the exact threshold for establishing enhanced efficacy is still unclear.

"The challenge is how to cross that gap, and the *Novartis* decision doesn't clarify that. Thus the applicants are at a loss of how to demonstrate enhanced efficacy," Soni explained.

Soni said that he is unaware of any pharmaceutical companies that have submitted clinical trial data to show enhanced efficacy. However, Kumar suggested that expert affidavits may be a way to meet the criteria.

"Most of the data that is provided with patent applications is *in vitro* data (data from a test tube) but to show efficacy you need *in vivo* data (data from the body)," he said. "One method we have used is to have an expert give an opinion on the *in vitro* data and the basis on which it can show efficacy."

However, there is still no definitive ruling on what is enough to show enhanced efficacy, though the practitioners who spoke with Managing IP said that they hope that Gilead's appeal will raise this issue and clarify the law.

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