

## **Patent Opposition against Indian Application for Tenofovir Disoproxil Fumarate (TDF)**

On 9 May 2006, The Indian Network for People Living with HIV/AIDS (INP+) and the Delhi Network of Positive People, supported by public interest intellectual property lawyers, filed a pre-grant opposition at the Delhi Patent Office against Gilead's patent application for TDF.

### **Gilead's claimed invention**

The application opposed claims an invention for 'discovering' and preparing the fumaric acid salt (and its crystalline form) of Tenofovir Disoproxil ("TD"), the ester derivative of the already known Tenofovir molecule.<sup>1</sup> Gilead claims in its patent application that by adding the fumaric acid salt to the known TD, it provides "excellent bioavailability" as well as providing "better chemical stability for storage purposes".

### **Legal Grounds for Opposition**

Under s25(1) of the Indian Patents (Amendment) Act ("Act"), any person may legitimately file an opposition to the grant of a patent application based on a number of grounds available. These include, but are not limited to, proving that the claimed invention had already been published; that the invention claimed does not involve any inventive step and would have been obvious to a person working in the relevant field; or that the claimed invention simply does not meet the definition of an invention under the Act. With respect to the last ground, it is important to note that India has adopted a unique provision that states: "new forms of a known substance which do not result in the enhancement of the known efficacy of that substance" are not inventions and, therefore, are not patentable. For this purpose, "salts" of a known substance shall be considered to be the same substance unless they differ significantly in properties with regard to efficacy.

### **The Arguments**

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<sup>1</sup> Tenofovir, and its antiviral properties, were discovered by a Czech Academic Institute in 1985 and was patented at the same time. The Czech Institute subsequently gave an exclusive licence on the invention to Gilead. However, until around 1995 it appears academic public institutions conducted all further studies on Tenofovir until Gilead developed and patented TD. The patent on Tenofovir itself should have expired this year, on 25 April 2006.

Taking the above available grounds, strong arguments, backed by credible publications and evidence, have been submitted. The opposition shows why Gilead's patent application for claiming the fumaric acid salt for TD does not warrant an invention under Indian Law. The main grounds of the opposition rest on two particular points:

1. A number of publications, which pre-date Gilead's application for TDF (24 July 1998), teach that fumaric acid is a suitable pharmaceutically acceptable salt to use for phosphonate nucleotide analogues and their esters, like TD, in order to achieve better bioavailability and stability. In particular an earlier Japanese patent (1995) discloses this practice. There are also a number of science journals, which direct how to go about salt selection for basic drugs for optimisation purposes and which specifically mention fumaric acid.
2. The unique provision in the Act, which states that patents should not be granted for known substances (including the salts of the known substance) that do not show improved efficacy, should block Gilead's application. As it is simply claiming the salt of TD and the specification filed fails to show any therapeutic efficacy, the application fails to overcome this hurdle. It should be stressed that according to legal practitioners (and as recently stated in the Gleevec decision) increased/better bioavailability should not equate to efficacy.

In addition to the above arguments put forward, the opposition also points to a number of procedural flaws in Gilead's application, which should be rejected if a strict interpretation of the Act is applied. Moreover, Gilead's patent specification, which details the claimed invention, is riddled with misrepresentations as to the claimed advantages of the invention, in particular as to why the fumaric acid salt performs better than other salts. The fact that Gilead only demonstrates a comparison against only one other salt, citrate (which would obviously have been known not to work alongside a soluble drug like TD) shows a "manipulation" of evidence to obtain a patent.

### **Importance of TDF to HIV/AIDS**

TDF is clearly emerging as an important option for patients starting AIDS treatment for the first time, and those who have been on antiretroviral treatment therapy (ART) for some time and require access to newer drugs due to occurrence of toxic effects or as they develop resistance to first-line drug regimens. Because there are fewer known side effects associated with the use of TDF in adults, it is commonly prescribed in the US and Europe, where the

drug is widely available at a priced at approximately USD 5,700 per patient per year.