

# **The Patents Act, 1970**

## **IN THE MATTER OF:**

**A representation under s25(1) of The Patents Act, 1970 as amended by the Patents (Amendment) Act 2005 (“the Act”) and Rule 55 of The Patents Rules, 2003 as amended by the Patents Rules, 2006 (“the Rules”) by the Indian Network for People Living With HIV/AIDS (“INP+”) and the Delhi Network of Positive People (“DNP+”) (“the OPPONENTS”)**

**And**

## **IN THE MATTER OF:**

**Indian Application No PCT/2001/00018/MUM, filed by Abbott Laboratories USA. (“the APPLICANT”)**

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### **STATEMENT OF CASE OF THE OPPONENTS**

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1. The Opponents are community based, non-profit organisations representing the needs of people living with HIV/AIDS (“PLHAs”). The Indian Network for People Living With HIV/AIDS (“INP+”) is registered as Society No. 231/1997 under the Tamil Nadu Societies Registration Act 1975, having its registered address at Flat No.6, Kash Towers, 93 South West Baag Road, T.Nagar, Chennai, 600 017. The Delhi Network of Positive People (“DNP+”) is registered

as Society No. S-52850 under the Societies Registration Act XXI 1860, having its registered address at House No. 136, Village Neb Sarai, New Delhi, 110068.

2. The Opponents represent and provide support for PLHAs at the local, regional and national levels in order to facilitate systemic change in critical areas such as care and support, access to treatments and addressing issues of discrimination facing PLHAs in Indian society. Of particular concern to the Opponents is the impact of the new product patent regime on PLHAs' access to safe, effective and affordable HIV/AIDS treatments.
  
3. The HIV/AIDS epidemic poses one of the greatest challenges to global public health today, but even more so for developing countries, including India. Over 40 million people worldwide are infected with the HIV virus, with an estimated 5.1 million being infected in India. Although medical treatments, such as the patent application in case, can help infected people to manage this lifelong condition, this is only possible if people can afford to access such treatments. In the developing world, including those infected with the virus in India, access to key treatments and, therefore life itself, is only possible if these treatments are priced within the reach of these people. While true innovations for new treatments can help towards offering new hope for HIV sufferers around the world, they also take away that opportunity. Patents granted for 20 years on such treatments allow the "inventor" not only to dictate the prices, which are nearly always beyond the income of most people in the developing world and India, but also determine

who can manufacture them. This reality creates a difficult situation between the patents system and the matter of life and death.

4. As a result, patents on “inventions” such as the one that is the subject of this opposition, should only be granted where they do not harm the public’s needs, including the progress of science and development itself. All too often in the pharmaceutical sector, patents are granted for minor and inconsequential changes to known substances in order that the company, which is the proprietor of the already known patented substance, can extend its monopoly over the same and, therefore, continue to dictate the prices and make unjust profits. Such practice does not fit within the founding philosophy of patents, namely real innovation and development of the art in question for the benefit of the public at large. More significantly, such practices in the face of an epidemic such as HIV can lead to the unnecessary death of millions of people around the world, including within in India, and also stifle further scientific development in the field.
  
5. In view of such practices, the duty on Patent Offices, such as this one, is to ensure that they act as the safety net to ensure that only patents for true innovations are granted. As such, the Patents Act offers this Patent Office the safeguards and tools, such as s3(d), to ensure that frivolous patents that are not true inventions are weeded out not only for the public’s benefit, but also for science and development. However, the failure to do so in matters such as the one in question could lead to the loss of millions of lives tomorrow and in the future to come, which ultimately could easily have been prevented.

6. Taking the above comments into account, the Opponents have learnt that on 3 January 2001, the Applicant filed for a patent titled "Polymorph of a Pharmaceutical" at this Patent Office, which was allotted Application No. PCT/2001/00018/MUM (hereinafter '018). '018 was published for opposition in the Official Journal of the Patent Office on 4 March 2005, a copy of which is attached as **Exhibit 1**, and which is understood to be currently under examination and has not as yet been granted.
7. '018 is an application for a crystalline polymorph of the pharmaceutical compound (2S,3S,5S)-5-(N-(N-(N-methyl-N-992-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane, commonly known by the chemical name Ritonavir or the commercial brand name Norvir®. The field of invention which '018 relates to is the treatment of HIV. Ritonavir, and its combination drug Kaletra® are now emerging as an important option in antiretroviral treatment for people living with HIV/AIDS
8. As noted in paragraph 7 above, the invention claimed within '018 is a polymorph of a known antiviral compound Ritonavir. The Applicant confirms this on page 3, at paragraph 2, by stating that "it has now been unexpectedly discovered that Ritonavir can be prepared as a new crystalline polymorph which is termed crystalline Form II." The Application is for this crystalline form of Ritonavir,

which has been known since at least 1996. In addition, the Application also claims a substantially pure amorphous form of Ritonavir.

9. More specifically, the Applicant's claims within '018 may be summarised as follows:

- a) Claims 1-4 relate to crystalline polymorph forms of (2S,3S,5S)-5-(N-(N-((N-methyl-N-992-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane.
- b) Claims 5-6 relate to substantially pure amorphous forms of (2S,3S,5S)-5-(N-(N-((N-methyl-N-992-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane.
- c) Claim 7-30 relate to processes for the preparation of the compound (2S,3S,5S)-5-(N-(N-((N-methyl-N-992-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane.

This Opposition will focus only on claims 1-6 and will not address the various processes.

10. The Opponents have closely studied the specification and claims made by the Applicant in '018 and believe that the Applicant has failed to meet its burden of showing that the alleged invention described in the Application, which uses well-known methods of recrystallisation, is entitled to a patent under the following grounds of s25(1) of the Act:

- a) s25(1)(e) – that the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step having regard to the matter published as mentioned in clause (b) or having regard to what was used in India before the priority date of the applicant's claim.
- b) s25(1)(f) – that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act, in particular under sections 3(d).
- c) s25(1)(h) – that the applicant has failed to disclose to the Controller the information required by s8 or has furnished the information that in any material particular was false to his knowledge.

Accordingly, as permitted under s25(1) of the Act and Rule 55(1) of the Rules, which allow an opposition to be filed by any person after publication but before the grant of a

patent, the Opponents submit their opposition to '018 on the grounds set out below. Furthermore, as '018 was filed at this Patent Office (Mumbai), the Patent Controller of the said office has the authority to hear and decide on this opposition.

### **GROUND**

The Opponents submit their opposition on the following grounds:

#### **Claims 1-6 of the invention are not patentable under sections 2(j), 2(ja) and 25(1)(e) of the Act**

11. Claims 1-6 of '018 do not qualify under the definition of an invention as provided in sections 2(j) and 2(ja), particularly in reference to the requirement of "inventive step". Section 2(j) sets out that an invention means a new product involving an inventive step. Section 2(ja) further elaborates on the meaning of 'inventive step' as being a "feature of an invention that involves a technical advance compared to existing knowledge and that makes the invention not obvious to a person skilled in the art." Section 25(1)(e) relies on these definitions in sections 2(j) and 2(j)(a) for allowing an opposition when "an invention which is obvious and clearly does not involve any inventive step having regard to matter published as mentioned in s25(1)(b) or having regard to what was used in India before the priority date of the applicant's claim."

12. In '018 the Applicant sets out that Ritonavir is a known substance from US Patent No. 5541206, **Exhibit 2**. The Opponents believe that the claimed invention in '018 of the crystalline or the amorphous form from this known form of Ritonavir, would have been obvious to someone skilled in the art. Crystalline forms contain “different arrangements and/or conformations of the molecules in the crystal lattice” and amorphous forms are those that have “disordered arrangements of molecules that do not possess a distinguishable crystal lattice”, as stated in the *Guidance for Industry, ANDAs: Pharmaceutical Solid Polymorphism, FDA Center for Drug Evaluation and Research (CDER)*, **Exhibit 3**. It is widely known in the pharmaceutical industry that a solid form of a drug may exist in either amorphous or crystalline forms. Obtaining either the amorphous or crystalline forms, therefore, would certainly have been obvious to a person skilled in the art.
13. Moreover, it is well known in the pharmaceutical industry that drugs may exist in various crystal states and the particular state a drug exists in depends on the solvent used. It is well known in the art that crystalline forms of a given compound may be reached using routine experiments. Generally, the process of recrystallisation involves purification and crystallization of a compound. This entails dissolution in solvent(s), filtration and cooling of the heated solution. When cooled, the solubility limit of the compound is exceeded, so the dissolved substance crystallizes out, separating the crystals from the solution. A second routine method of carrying out recrystallisation is the addition of an anti-solvent.

Recrystallisation is also commonly accomplished by dissolving the compound almost to the limit of solubility in a particular solvent and adding seed crystals. This Application obtains Ritonavir crystalline form II using these conventional methods demonstrating that there is a clear lack of an inventive step.

14. Furthermore, a person ordinarily skilled in the art would have found it obvious to utilise solvent mixtures such as ethanol, ethyl acetate or ethyl acetate hexane in the recrystallisation process. These solvents mentioned in this Application are commonly used in the recrystallisation process. Therefore, there can be no inventive step claimed for this recrystallisation process.
15. Furthermore, neither the polymorphic form nor the amorphous form constitute any technical advance. For the Applicant to succeed in obtaining a patent, some technical advance from the existing art must be demonstrated. The Opponents submit the existing art of US Patent No. 5635523 as **Exhibit 4**, US Patent No. 5674882 as **Exhibit 5**, US Patent No. 5541206 previously introduced as **Exhibit 2**, and US Patent No. 5567823 as **Exhibit 6** to show clearly that the Applicant has not made any technical advance over the known art. Therefore '018 claims 1-6 are not inventive.
16. Based on the above points, the Opponents believe that claims 1-6 of '018 do not have any inventive step and fail to meet the criterion of technical advance and non-obviousness. The prior art disclosed demonstrates that it would definitely

have been obvious to a skilled person in the art that another crystalline form could exist and that this would not have required any inventive steps to achieve the desired result. Furthermore, it would also have been evident to a person skilled in the art that the pure amorphous form would exist and that this would not have required any inventive steps to lead to this form. It would simply be a question of routine laboratory work to obtain both the crystalline and amorphous forms.

**Claims 1-6 of the invention are not patentable under sections 25(1)(f) and 3(d) of the Act**

17. In the alternative and without prejudice to the above, the Opponent relies on s3(d) read with sections 2(j), 2(ja) and 25(1)(f). Section 3(d) sets out that a “*mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance*” does not amount to an invention and is not patentable under the Act. The ‘Explanation’ to s3(d) provides further clarification in that “*salts, esters, ethers, polymorphs, metabolites, pure form,....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*”.

18. In this case the Application makes no submission of increased efficacy for either the polymorphic form of claims 1-4 or the amorphous pure form of claims 5-6.

The Opponents seek to emphasize here that term ‘efficacy’ is commonly defined both pharmacologically and therapeutically. Pharmacological efficacy is defined as “the strength of response induced by occupancy of a receptor by an agonist. It describes the way in which agonists vary in the response they produce, even when they occupy the same number of receptors.” Therapeutic efficacy refers to “the ability of a drug to produce an effect, and refers to the maximum such effect.” See **Exhibit 7**, *The Textbook of Pharmaceutical Medicine, Fourth edition 2002, Edited by John P Griffin and John O'Grady*. Chapter 6 *Clinical trials and good clinical practice by Nigel Baber and John Sweatman, page 283*. From these basic definitions, it is evident that efficacy relates to the activity of the drug itself to produce an effect or response in the human body.

19. In the present case, the Applicants not only lack a showing of an increase in efficacy claimed in ‘018 over the original (2S,3S,5S)-5-(N-(N-((N-methyl-N-992-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane, the Applicants make absolutely no claim to a showing of efficacy at all. The present claims are, therefore, mere discoveries that are not inventions and unpatentable.

20. The intent of s3(d) is clearly to show, within the ambit of pharmaceutical inventions and the effect in the human body, what does not constitute an invention. In the present case, both the crystalline and amorphous forms of (2S,3S,5S)-5-(N-(N-((N-methyl-N-992-isopropyl-4-

thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane do not demonstrate any increase in efficacy and should be promptly rejected by the Examiner.

**Claims 1-6 of the invention are not patentable under the sections 25(1)(h) and 8 of the Act.**

21. Section 8(1)(a) and (b) makes it an obligation on the Applicant to keep the Controller informed of an application which is being prosecuted in another country and which is considered to be the same invention, or substantially the same invention, as the patent applied for in India. This obligation requires the Applicant to provide at the of filing its application or within a prescribed period as the Controller may allow, a statement setting out detailed particulars of the application being prosecuted in another country and an undertaking to keep the controller informed of the same up to the date of grant of the said patent in India. Section 8 is read into s25(1)(h) as a strict ground of opposition to the grant of a patent where the Applicant has failed to meet the undertaking as required under the said section. Based on the above, the Opponents question whether the Applicant has provided this Patent Office with the information and particulars of the equivalent foreign applications that the Applicant is currently prosecuting. In particular, according to the Opponents searches, it understands that the Applicant has an identical application to '018 pending in the Slovak Republic under

Application No. SK0100092A5. The Opponents ask whether the Applicant has provided the required information in relation to this Application to this Patent Office. In the event that the Applicant has failed to do so, the Opponents believe that this is a strict ground for refusing '018.

22. Without prejudice to the arguments raised in paragraph 21, should this Patent Office not take the view of the Opponents, the Opponents ask to be kept informed throughout these proceedings of whether the Applicant has provided this Patent Office with the required details of matters relating to the Applicant's corresponding applications in other countries, including the Slovak Republic.

Based on the grounds set out in paragraphs 1-22 above, the Opponent requests that Application No. '018 be refused in its entirety. As permitted under Section 25(1) of the Act and Rule 55(1) of the Rules, the Opponent requests that this Patent Office inform the Opponents immediately of any response filed by the Applicant to this opposition and also grant the Opponents a hearing in the above matter.

Dated 28th day of August 2006

For and behalf of the Indian Network for People Living With HIV/AIDS (INP+)

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For and behalf of the Delhi Network of Positive People (DNP+)

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Our address for service in connection with these proceedings is:-

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To:

The Controller of Patents

The Patent Office, NEW DELHI