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 Delhi Network of Positive People ("DNP+"), and the Indian Network for People Living With HIV/AIDS ("INP+") ("the OPPONENTS")

And

IN THE MATTER OF:

Indian Application No. IN/PCT/2001/01312/MUM, filed by ABBOTT LABORATORIES, INC. ("the APPLICANT")

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 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. 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.

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, especially in developing countries, including India. Over 42 million people worldwide are infected with the HIV virus, with an estimated 5.2 million infected in India. Medical treatments, such as that described in the patent application in this case, can help infected people to manage this lifelong condition—but only if patients can afford access to such treatments. For those infected with the virus in India, access to key treatments, and therefore survival itself, is impossible unless these treatments are priced within reach. While true innovations for new treatments can offer new hope for HIV positive people around the world, that hope can be extinguished just as quickly. Patents granted for 20 years on life-saving medicines allow the patent owner not only to dictate prices, which are nearly always beyond the means of most people in the developing world and India, but also to

determine who can manufacture those medicines. This reality puts the patents system in constant tension with the lives of those suffering from disease in developing countries.

4. As a result, patents should only be granted where they do not contradict the public interest, including in science and development. All too often in the pharmaceutical sector, patents are granted for minor and inconsequential changes to known substances in order that the proprietor of the already known patented substance can extend its monopoly and thereby continue to dictate the prices and extract unjust profits. This practice does not align with 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, in the face of an epidemic such as HIV, this practice can lead to millions of unnecessary deaths around the world, including within in India, while stifling further scientific development in the field.

5. In view of the practices of some patent applicants, it is the duty of Patent Offices, such as this one, to ensure that only patents for true innovations are granted. As such, the Patents Act offers this Patent Office safeguards and tools, such as s3(d), to ensure that frivolous applications are weeded out—not only for the public's benefit, but also to ensure the continued flourishing of science and development. The failure to do so in matters such as the one in question could lead to the unnecessary loss of millions of lives.

6. It is in light of the above concerns that the Opponents file this opposition. The Opponents have learnt that the Applicant filed for a patent titled "Improved Pharmaceutical Formulations" at this Patent Office, which was allotted Application No. IN/PCT/2001/01312/MUM (hereinafter '312). '312 is understood to be currently under examination, and not as yet granted.

7. '312 is an application for compositions of HIV protease-inhibiting compounds comprising:

    a) one or more HIV protease inhibiting compounds;
    b) a long chain fatty acid or mixture of long chain fatty acids;
    c) ethanol;
    d) water;
    e) and optionally a surfactant.

    These compositions are optionally encapsulated into a hard or soft gelatin capsule.

8. An embodiment of the above composition has become most important for the preparation of soft gelatin capsules of the HIV protease inhibiting compound Ritonavir, marketed by the Applicant under the brand name Norvir®, as well as for the preparation of soft gelatin capsules containing a combination of the HIV protease inhibiting compounds Lopinavir and Ritonavir, sold together by the Applicant under the commercial brand name Kaletra®. '312 is, essentially, a formulation of these previously known active ingredients. Lopinavir and Ritonavir have emerged as an important option in antiretroviral treatment for people living with HIV/AIDS starting therapy for the first time,

and also for those who require access to newer drugs as they develop resistance to prior first-line fixed dose combination of antiretroviral drugs. Ritonavir, in particular, is crucial for anti-retroviral therapy, because most other protease-inhibitors must be co-administered with Ritonavir (as a 'booster').

9. The Applicant asserts on page 18 of '312, at lines 15-18, that the claimed composition of known antiviral compounds constitute an invention because the compositions "provide greatly improved solubility for HIV protease inhibiting compounds contained therein when compared to analogous compositions without water."

10. More specifically, the Applicant's claims within '312 may be summarised as follows:

    a) Claim 1 relates to the general form of the composition described in paragraph 7, above.

    b) Claims 2-4 relate to the use of specific HIV protease inhibiting compounds in the composition, including Ritonavir and Lopinavir.

    c) Claim 5 relates to the use of oleic acid as the long chain fatty acid in the composition.

d) Claims 6 relates to the use of Polyoxyl 35 castor oil as the optional surfactant in the composition.

e) Claim 7 relates to the encapsulation of the composition in a soft or hard gelatin capsule.

f) Claims 8 and 9 relate to embodiments of the general composition using percentage ranges of the component elements.

g) Claims 10-16 relate to yet further embodiments of the composition based on variations of those described above (i.e. specification of particular component elements, encapsulation, and/or percentages).

11. The Opponents have closely studied the specification and claims made by the Applicant in '312 and strongly believe that the invention is not patentable under the following grounds of s25(1) of the Act:

a) s25(1)(b)(ii) – that the invention so far as claimed in any claim of the complete specification has been published before the priority date of the claim, elsewhere, in any other document.

b) s25(1)(d) – that the invention so far as claimed in any claim of the complete specification was publicly known or publicly used in India before the priority date of that claim.

c) 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.

d) s25(1)(f) – that the subject of any claim of the complete specification is not an invention within the meaning of the Patent Act, or is not patentable under the Patent Act, in particular under section 3(d) and 3(e).

e) s25(1)(h) – that the Applicant may have failed to disclose to the Controller the information required by s8.

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 '312 on the grounds set out below. As '312 was filed at this Patent Office (Mumbai), the Patent Controller of the said office has the authority to hear and decide on this opposition.

GROUNDS

The Opponents submit their opposition on the following grounds:

Claims 1-16 of the invention are not patentable under sections 25(1)(b)(ii), 25(1)(d) and 2(j): numerous compositions claimed therein are not novel.

12. Section 2(j) clearly defines an 'invention' to mean only a new product. Section 25(1)(b)(ii) clarifies this definition by providing that where the invention claimed has been published before the priority date of the claim in India **or elsewhere**, the alleged invention is not patentable. Section 25(1)(d) provides further support to s2(j) by providing a ground for objection to a patent where the claimed invention was publicly known or publicly used in India before the priority date of the Applicant's claim. For the purpose of defining the above, this Patent Office should recognise that it is established practice in the law of patents that 'publication' can include disclosure in written, oral or any other form, and a publication can be considered 'publicly known' even if only disseminated within the relevant trade sector. Therefore, on the grounds above, the Opponents believe claims 1-16 are not patentable because they fail to meet the required standard of novelty as defined within the Act and are anticipated by prior published disclosures.

13. In order to confirm the prior disclosure of compositions claimed in '312 and set the context for the remainder of this opposition, the Opponents submit the following publications which were published before the priority date for '312, which is 4 June 1999, deriving from the filing date of United States patent application 09/325,826.

14. *The Theory and Practice of Industrial Pharmacy*, published in 1987, and attached as **Exhibit 1**, clearly indicates that the combination of ethanol, water, and a long-chain fatty acid was well known in the art for delivery of medications in soft gelatin capsule form. Specifically, at page 402, the authors indicate that "water and alcohol can be used as cosolvents to aid in the preparation of solutions for capsulation." However, because these ingredients on their own would "migrate into the hydrophilic gelatin capsule and volitize from its surface," they can only constitute a small percentage of the capsule contents and must be combined with other ingredients. (The authors indicate the limit for the fraction of such ingredients would be "about 5%". Other soft gelatin capsules in use at the time provide examples of concentrations up to 10-15%. One example thereof (Cyclosporin A) is documented in **Exhibit 2**.) The authors indicate that "aromatic and aliphatic hydrocarbons" (which include long chain fatty acids) would be common choices to constitute the remaining percentage of the soft gelatin capsule, "as solvents or vehicles for suspension-type formulations." This basic reference work thus clearly discloses the use of ethanol-water-fatty acid mixtures for delivery of pharmaceutical substances and indicates that such combinations would have been well known in the art.

15. Claims 8, 9, 14, and 15 of '312, which claim embodiments of the general composition comprising specific percentages of the constituent elements, are also caught by the aforementioned prior art. The percentages claimed therein are implicit in the prior art. It is well established in patent law that prior art should be read through the eyes of one skilled in the art. So read, Exhibit 1

would most simply be understood to describe the combination of the dosage of a relevant pharmaceutical compound, dissolved in the ethanol/water mixture that provides greatest solubility for said compound, with said mixture constituting the maximal fraction of the total that can be included in the gelatin capsule, and combined with the oily phase to constitute the remaining fraction.

16. Thus, for example, for the standard dosage of Ritonavir (100 mg) in the form of a 1 mL (approx. 1g) soft gelatin capsule, the prior art would have immediately implied:

    a) Ritonavir as approximately 10% of the total;

    b) a water/ethanol mixture titrated to maximise solubility of Ritonavir, in the amount from approximately 5% to approximately 15% of the total; and

    c) aromatic and aliphatic hydrocarbons (such as long chain fatty acids) to constitute the remaining fraction, after any additional needed excipients, surfactants, etc. were added.

    The Opponents understand the Applicant to represent that the utility of claims 8, 9, 14, and 15 arises because the ratio of water and ethanol has been thus titrated to maximize the solubility of Ritonavir or Ritonavir/Lopinavir in combination—i.e. it is the same ratio that would be implied by the reading above. In all other respects, the compositions claimed in claims 8, 9, 14, and 15 also are in accordance with the above described mixture. Hence, the prior art directly anticipates these compositions.

17. WO 95/25504 (hereinafter '504), first published as an application on 28 September 1995, and attached as **Exhibit 3**, constitutes further novelty-destroying prior art. '504 discloses and claims the use of emulsions and microemulsions composed of an oily phase, an aqueous phase, and optionally one or more surfactants for the delivery of HIV protease inhibiting compounds and other insoluble pharmaceutical compounds. '504 specifically discloses the use of water/ethanol mixtures as the aqueous phase in such compositions. In particular:

a) Table 17 of Example 15 (Column 29A), on page 32, discloses a formulation to deliver insoluble pharmaceutical agents consisting of: linoleic acid (a long chain fatty acid), ethanol, Hank buffer (composed primarily of water, along with pH-stabilizing salts), and Pluronic L44 (a surfactant). Formulations B through J of Table 19 on page 33 disclose different compositions of the same elements.

b) Table 18 of Example 15 (Column B), on page 33, discloses a formulation to deliver insoluble pharmaceutical agents consisting of: oleic acid (a long chain fatty acid), ethanol, Hank buffer (composed primarily of water, along with pH stabilizing salts), and Pluronic L44 (a surfactant);

c) Claim 1 of '504 claims stable emulsions of a pharmaceutical agent incorporated into a hydrophobic emulsion of a long chain carboxylic

acid. Claim 2 claims any such preparation where the emulsion is a microemulsion.

d) Claims 3 and 22 of '504 claim the embodiment of the invention where the long chain fatty acid is oleic acid (as in claim 5 of '312)

e) Claims 15 and 34 of '534 claim the embodiment of the invention where the dissolved pharmaceutical agent is an HIV protease inhibitor.

f) Claims 17, 19, and 36 of '534 claim the encapsulation of the claimed formulations in soluble capsules for oral delivery (as in claims 7, 13, and 16 of '312)

18. In addition, the Applicant's own previous patent, United States patent 5,484,801 (hereinafter '801), granted 16 January 1996, attached as **Exhibit 4,** discloses many embodiments of the compositions claimed in '312. Specifically, Column 4 of '801 discloses "a preferred composition of the invention compris[ing] . . . (1) propylene glycol and (2) ethanol." This composition "can also comprise from about 0% to about 25% . . . of water", "one or more pharmaceutically acceptable oils", and "one or more pharmaceutically acceptable surfactants". In other words, '801 discloses any embodiment of the '312 composition that additionally comprises propylene glycol.

19. In light of the above prior art, none of the claims of '312 are patentable. All attempt to claim compositions that were clearly anticipated in the existing art, and should not be rewarded as inventions. Therefore, the claims should be refused.

Claims 1-16 of the invention are not patentable under sections 2(j), 2(ja) and 25(1)(e) of the Act: they do not involve any inventive step.

20. In the alternative and without prejudice to the grounds raised in paragraphs 12-19, claims 1-16 of '312 do not meet the requirements of the definition of an invention as provided in sections 2(j) and 2(ja), and are, therefore, objected to under s25(1)(e). Section 2(j) clearly states that an invention means a new product involving an inventive step. Section 2(ja) qualifies 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) defines the abovementioned sections for the purpose of an opposition as "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."

21. Under the above definitions, claims 1-16 of '312 clearly do not have any inventive merit and, therefore, fail to meet the criteria of a technical advance. The prior art disclosed in **Exhibits 1-4**, even if not novelty-destroying, would certainly have made the claimed compositions and methods in claims 1-16

obvious to a person skilled in the art and would not have required any inventive steps to achieve the same. As a result, these claims do not warrant patent protection.

22. In particular, the only difference between the specific embodiments of the ethanol/water/oleic acid compositions claimed in '312 and the compositions of the same elements described in detail in '504, discussed in detail in paragraph 17 above and attached as **Exhibit 3**, is the relative composition of water and ethanol. It would have been clearly obvious to one skilled in the art to adjust these ratios based on the particular solubility characteristics of Ritonavir and/or Lopinavir.

23. Similarly, the compositions in '312 would have been obvious based on the Applicant's patent application WO 98/22106 (hereinafter '106), first published 28 May 1998, and attached as **Exhibit 5**. '106 is in all respects nearly identical to '312. The only significant difference is that '106 discloses and claims the pharmaceutical compositions in the absence of water. '312 essentially claims the addition of water to these compositions. At page 18 of '312, the Applicant references '106 implicitly when it states: "the compositions of the present invention provide greatly improved solubility for HIV protease inhibiting compounds contained therein when compared to analogous compositions without added water." However, it would have been obvious to one skilled in the art to attempt the addition of a small amount of water to the compositions in '106 in order to change to solubility properties of the mixture or to create an emulsion, and thereby attain this end.

24. In particular, to confirm the obviousness of the aforementioned addition, the Opponents submit the chapter on "Solubilization by Cosolvents" from the volume *Solubility and Solubilization in Aqueous Media*, attached as **Exhibit 6**. Exhibit 6 does not constitute prior art for the purposes of '312, as it was published shortly after the priority date, in November 1999. However, the Exhibit serves as a useful, concise summary of the abundance of relevant prior art that would have been known to one skilled in the art seeking to address the issue of solubilization of Ritonavir or other protease inhibitors. (The Opponents can provide original copies of the relevant pieces of prior art at the request of the Controller.) In particular, Exhibit 6 summarizes the literature regarding the well known phenomenon of downward concavity or parabolic curvature in solubility curves for water-cosolvent mixtures at high cosolvent concentrations. In particular, Figure 6.7 on page 196 summarizes relevant data from the 1984 Ph.D. dissertation of J. T. Rubino, *Solubilization of Some Poorly Soluble Drugs by Cosolvents*, and page 201 describes the results published by J. T. Rubino and E. K. Obeng in "Influence of solute structure on deviations from the log-linear solubility equation in propylene glycol:water mixtures," in the *Journal of Pharmaceutical Science*, 1991. Similarly, page 202 refers to the chapter "Solubilization of Drugs by Cosolvents" by S. H. Yalkowsky and T. J. Roseman in *Techniques of Solubilization of Drugs* from 1991, indicating that "many experimental solubility versus cosolvent composition curves show this type of behavior." All these results indicate that one skilled in the art would expect that the solubility of a water insoluble compound like Ritonavir might be greater in a

composition with a small amount of added water than in a composition with only pure ethanol. The Opponents draw particular attention to the middle frame of Figure 6.7 on page 196 of the Exhibit. This frame excerpts data from Rubino 1984 demonstrating precisely this phenomenon for the experimental substance Benzocaine—the substance was found to be more soluble in an ethanol-water mixture containing 90% ethanol than it was in pure ethanol. Based on this well known and widely documented phenomenon, it would have been obvious for one seeking to improve solubility of a protease inhibitor in the compositions disclosed in '106 to try the addition of a small amount of water thereto.

25. Additionally, early versions of the Applicant's own Norvir® products constitute further prior art from which the present claimed composition would have been obvious to one skilled in the art. As mentioned above, Norvir® is the brand name under which the Applicant has marketed Ritonavir oral solution and capsules since 1996. Thus, when the Applicant first applied for a patent on the 'improved formulation' in '312, it had already been marketing Norvir under earlier formulations for over three years. In particular, Norvir oral solution, approved for marketing in the United States at least since 26 May 1999 comprised Ritonavir dissolved in a solution of ethanol, water, polyoxyl-35 castor oil, and propylene glycol. The Applicant's United States informational label for said product, confirming this formulation, is attached as **Exhibit 7.**

26. Based on this existing formulation, compositions claimed in '312 would have been obvious. As described in paragraph 14 above, it is well known in the art that ethanol and water cannot constitute greater than approximately five to fifteen percent of the total solution in a soft gelatin capsule. *The Theory and Practice of Industrial Pharmacy,* cited above and attached as **Exhibit 1**, clearly describes this well-known problem. As described therein, a common solution to this problem for organic or mixed water-organic solutions is to incorporate them into an oily phase. Hence, for one skilled in the art seeking to formulate Ritonavir or a closely related protease inhibitor (such as Lopinavir) in an improved gelatin capsule, an obvious starting point would be to incorporate the cosolvents in the existing oral solution into an oily phase. Such a step would have led one skilled in the art immediately to the compositions now claimed by the Applicant.

27. The abovementioned prior art thus indicates not just one, but numerous obvious routes by which one skilled in the art would have been led to the compositions claimed in '312. In short, the compositions claimed by the Applicant are no more than the logical result of well known, standard approaches in pharmaceutical formulation. The claimed compositions are clearly obvious and in no way constitute an 'invention'.

Claims 1-16 of the invention are not patentable under sections 25(1)(f) and 3(d) of the Act: they are merely attempts to patent a new form of a known substance without proof of significantly increased efficacy.

28. In the alternative and in support of the grounds raised in paragraphs 11-23 above the Opponents rely 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' for s3(d) provides further clarification in that *"salts, esters, ethers, polymorphs….****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"*.

29. The embodiments of the present invention constitute "new form[s] of . . . known substance[s]"—namely protease inhibitors, which are the active compounds of the claimed solutions. This is confirmed by the Applicant itself in the "Background of the Invention", where the Applicant repeatedly refer to the invention as an "oral dosage form" or an "improved oral dosage form" of HIV protease inhibitors. The Opponents refer the Controller, for example, to page 2 at lines 3-4, and page 14 at lines 16 and 22. In addition, the invention clearly falls with the very specific language of the Explanation to s3(d), which covers "combinations . . . of known substances". Thus, under s3(d), the composition in '312 cannot be patentable if the Applicant has not shown increased efficacy in comparison to known compositions.

30. Specifically, the Opponents advocate that for the purpose of determining whether '312 meets the requirement of s3(d), the Patent Controller must:

a) First, choose an interpretation of 'efficacy' in the context of the Act and the application. The specific term 'efficacy' is used in the Act in contradistinction to the more general terms 'utility' or 'capable of industrial application' and cannot be a mere synonym for those terms. It is clear that s3(d) and its supporting explanation are directed at and particularly relevant to pharmaceutical product patent applications such as '312. 'Efficacy' is a common and well known term of art in the pharmaceutical sciences. Thus, the definition chosen should be standard and in accordance with this usage.

b) Second, following this definition, determine whether the Applicant has evaluated the efficacy of known or obvious forms of the active substance in the present application.

c) Finally, evaluate whether the Applicant has demonstrated that its claimed "invention" has greater efficacy as compared to these known or obvious forms.

31. The Opponents propose as a useful and standard definition for 'efficacy' that provided in Bowman's *Dictionary of Pharmacology* (1986): "the capacity of an agonist to initiate a response once it occupies receptor sites." Another useful and more detailed definition is that provided in the attached **Exhibit 8**, which broadly defines efficacy as "referring to the capacity of a drug to produce an alteration in a target cell/organ after binding to its receptor." Exhibit 8 also states that efficacy is related to 'intrinsic efficacy', which broadly means "the property of a drug that determines the amount of biological effect

produced per unit of drug-receptor complex formed." For a definition of 'intrinsic efficacy' see attached **Exhibit 9**.

32. Using the above stated standard definitions of 'efficacy', the Opponents contend that the Applicant has failed to meet the heightened standard required to claim an invention for claims 1-16. The antiviral activity of the previously known active substances Lopinavir and Ritonavir (and other HIV protease inhibitors) remain the same when administered as part of '312's claimed compositions. In particular, the capacity of the molecules to bind to the HIV protease enzyme and inhibit its activity is in no way improved by the Applicant's claimed invention.

33. In particular, the solubility data provided by the Applicant in Figures 3-7 of '312 does not supply the needed evidence. As an initial matter, the Applicant attempts to claim the compositions in '312 for delivery of numerous protease inhibitors, but the presented solubility evidence only relates to the solubility of Ritonavir. Data for other protease inhibitors, which would be required to support the Applicant's broad claims, are not even mentioned. More importantly, the solubility data that is presented does not prove any increased activity of Ritonavir, Lopinavir, or other protease inhibitors in the claimed form at their biological point of action. It is hence not a demonstration of increased efficacy.

34. Finally, and decisively, optimized formulations of Ritonavir in water/ethanol/oleic acid mixtures have been demonstrated to be bioequivalent to earlier known formulations. It is widely recognized that proof of

bioequivalence between two products constitutes effective proof of equivalent efficacy. For example, the Opponents submit Guideline CPMP/EWP/QWP/1401/98 on "Investigation of Bioavailability and Bioequivalence", published 26 July 2001 by the European Agency for the Evaluation of Medicinal Products (now known as the European Medicines Agency), and attached as **Exhibit 10**. Section 2.6 of the aforementioned Guideline specifies: "A medicinal product is therapeutically equivalent with another product if it contains the same active substance or therapeutic moiety and, clinically, **shows the same efficacy** and safety as that product . . . . [D]emonstration of bioequivalence is generally the most appropriate method of substantiating therapeutic equivalence." Hence, two bioequivalent products have the same efficacy.

35. As mentioned in paragraph 25 above, the Applicant had already been marketing Ritonavir (Norvir®) for several years in other formulations when it first applied for the patent in '312. The Scientific Discussion released by the European Medical Agency in conjunction with its continued oversight of the manufacture and sale of Norvir is attached as **Exhibit 11**. This Discussion analyzes a "soft capsule formulation [of Ritonavir that] has been optimised with respect to the vehicle (co-solvent of ethanol, oleic acid and water)" (see page 1, section entitled "Product development and finished medicinal product"). In other words, the Discussion analyzes an optimized embodiment of the composition claimed in '312. The Discussion further compares this formulation of Ritonavir with respect to earlier known and marketed formulations. The Discussion indicates that "[b]ioequivalence has been

demonstrated between the original hard capsule formulation and the oral solution containing 80 mg/ml of Ritonavir dissolved in a mixed system of water, ethanol, propylene glycol and polyoxyl 35 castor oil. Bioequivalence between the soft capsule and the oral solution has also been demonstrated." Stated simply, the Exhibit thus demonstrates that the optimized form of the composition now claimed by the Applicant, the previously existing and known oral formulation of Ritonavir, and the previously existing and known hard capsule formulation, were all biologically equivalent. The formulation claimed in '312 has therefore been scientifically proven to have no increased efficacy.

36. In light of the above, it is clear that claims 1-16 do not meet the efficacy standard of s3(d). Therefore, these claims are not inventions and not patentable under the Act.

Claims 1-16 of the invention are not patentable under sections 25(1)(f) and 3(e) of the Act: they constitute merely an admixure resulting in an aggregation of the properties of the components thereof.

37. Under s3(e), "a substance obtained by the mere admixture resulting only in the aggregation of the properties of the components thereof" is not an invention within the meaning of the Act, and forms a ground of opposition under 25(1)(f). As already highlighted in paragraphs 25 and 26 of this opposition, the compositions claimed in '312 may be considered an admixture of two known elements:

a) Ritonavir, Lopinavir, or another protease inhibitor dissolved in a cosolvent mixture of water and ethanol, as in the Ritonavir oral solution that existed in 1999;

b) A long chain fatty acid as the oily-phase vehicle for inclusion of the above cosolvent composition in a soft gelatin capsule.

The Applicant makes no attempt to demonstrate any synergistic interaction between these two components of the admixture. To the contrary, the limited data provided by the Applicant suggests no advantage beyond a mere "aggregation of the properties" of these elements, with respect to their solubilizing ability, and with respect to the ability of the fatty acid to act as a vehicle for the aqueous phase in a soft-gel. As a result, the claimed compositions are not patentable under s3(e).

Claims 1-16 of the invention may not be patentable under the sections 25(h) and 8 of the Act: the Applicant may have failed to apprise this patent office of information regarding foreign applications.

38. Section 8(1)(a) and (b) makes it an obligation on the applicant to keep the Controller informed of an application that is being prosecuted in another country and that is the same as the invention applied for in India. This obligation requires the Applicant to provide a statement setting out detailed particulars of the application being prosecuted in the other 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 ground of opposition to the grant of a patent. 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.

39. In particular, as stated above, the priority of the present application is based on United States application 09/325,826. According to United States Patent Office publications, application 09/325,826 has not to date been granted as a patent in the United States. This implies that the application has been refused, has been abandoned by the Applicant, or is still under consideration by the United States patent office. In the latter case, if the United States application is currently being prosecuted by the Applicant, the Opponents question whether the Applicant has informed this Patent Office of its status. If the Applicant has not, its failure to do so is a strict ground to refuse '312 in its entirety.

In conclusion, on the grounds set out above, the Opponents request that Application No. IN/PCT/2001/01312/MUM be refused in its entirety. As permitted under Section 25(1) of the Act and Rule 55(1) of the Rules, the Opponents request that this Patent Office informs 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 this 4th day of August 2006

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

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

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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, MUMBAI