# 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, 2005 ("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. 896/DEL/2002 A (a divisional to Indian Application No. 2174/DEL/1998), filed on 24 July 1998 and divided on 4 September 2002 by GILEAD SCIENCES, INC. ("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, but also 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 24 July 1998, the Applicant filed for a patent titled "A Process for Preparation of Fumarate Salt of 9-[2-(R)-[[bis[isopropoxycarbonyl)oxy]methoxy] phosphinoyl] methoxy]propyl]-Adenine" at this Patent Office, which was allotted Application No. 2174/DEL/1998 (hereinafter '2174). On 4 September 2002, the Applicant, under sections 16(1) and 16(2) of the Act, divided Application No. 2174 /DEL/1998 into 896/DEL/2002 A (hereinafter '896) titled "Nucleotide Analog(ue) Composition", which is the subject of this opposition, and 963/DEL/2002 A. '896 only relates to the product part of the original Application No. 2174, whereas 963/DEL2002 A is believed to claim both the product and process for the alleged invention. '896 was published for opposition in the Official Journal of the Patent Office on 21 January 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. '896 is an application for a composition of a formula which includes 9-[2-(R)-[[bis[(isopropoxycarbonyl)oxy]methoxy]phosphinoyl]methoxy]propyl-adenine fumaric acid(1:1), referred to also as bis(POC)PMPA fumarate (hereinafter "BPPF") or its crystalline form (hereinafter "cBPPF"). The above composition is more commonly known by the generic name of Tenofovir Disoproxil Fumarate, or the commercial brand name Viread®. '896 is, therefore, an oral prodrug of the previously known active antiviral ingredient Tenofovir (hereinafter "PMPA") and its ester derivative Tenofovir Disoproxil (hereinafter "bis(POC)PMPA"). The field of invention which '896 relates to

is the treatment or prophylaxis of one or more viral infections in man, animals, including particularly retroviruses, HIV, SIV and GALV and hepadnaviruses. However, it is in relation to HIV that the claimed invention in '896 has become important as the drug is now emerging as an important option in antiretroviral treatment for people living with HIV/AIDS starting therapy for the first time, and also those who require access to newer drugs as they develop resistance to prior first-line fixed dose combination of antiretroviral drugs.

8. As noted in paragraph 7 above, the invention claimed within '896 is a prodrug of a known antiviral compound and compositions in the art, namely PMPA and bis(POC)PMPA. The Applicant confirms this on page 4, at lines 30-37, of '896 by claiming an "invention" for discovering, preparing and contacting fumaric acid with bis(POC)PMPA in order to achieve an "unexpectedly superior combination of physio-chemical properties compared to the free base and other salts, which are useful for manufacturing and for contributing to excellent bioavailability properties in humans and animals, therefore, allowing efficient delivery of BPPF or PMPA."

9. More specifically, the Applicant's claims within '896 may be summarised as follows:

    a) Claims 1-6 relate to different compositions of bis(isopropyloxycarbonyloxymethyl) PMPA fumarates (BPPF),

wherein claim 3 relates to formula (I) but where the composition is a crystalline solid (cBPPF).

b) Claims 7-8 relate to an intermediate for the preparation of the known intermediate bis(POC)PMPA.

c) Claim 9 relates to a therapeutic method of medical treatment.

d) Claims 10-11 relate to the method of contacting the known intermediate bis(POC)PMPA with fumaric acid as claimed in the composition in claim 1.

e) Claims 12-15 relate to the mixture of known compounds.

f) Claims 16-20 relate to further embodiments of the above claims, in particular claims 2-6.

g) Claims 21-22 amount to omnibus claims

10. The Opponents have closely studied the specification and claims made by the Applicant in '896 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 this Act, or is not patentable under this Act, in particular under sections 3(d), 3(e) and 3(i).

e) s25(1)(g) – that the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed.

f) 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.

g) S25(1)(i) – that in the case of a convention application, the application was not made within twelve months from the date of the first application for protection for the invention made in a convention country by the applicant or a person from whom he derives title.

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 '896 on the grounds set out below. Furthermore, as '896 was filed at this Patent Office (New Delhi), 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 7-8 and 12-15 of the invention are not patentable under sections 25(1)(b)(ii), 25(d) and 2(j)**

11. Section 2(j) clearly defines an 'invention' to mean a new product. Section 25(1)(b)(ii) supports 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 a publication can be taken to include written, oral or any other form and can be considered 'publicly known' even if only disseminated amongst the relevant trade sector. Therefore, based on the grounds above, the Opponents believe claims 7-8 and 12-15 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.

12. As defined by the Applicant's claims, it is clear that the invention claimed in '896 is for the Applicant's discovery, preparation and contacting of fumaric acid with bis(POC)PMPA in order to, in the words of the Applicant on page 4, at lines 30-32, obtain an "unexpectedly superior combination of physio-chemical properties compared to the free base and other salts". The scope of the claimed invention is confirmed by the Applicant in its admission on page 7, at lines 1-2, that "PMPA and bis(POC)PMPA are known to be useful in the treatment of prophylaxis of one or more viral infections, including particularly retroviruses HIV…..". The Applicant further admits on page 7, at lines 7-9, that "the prior art describes the antiviral specificity of PMPA and the invention compounds share this specificity".

13. In order to confirm the prior disclosure of PMPA and bis(POC)PMPA and set the context for the remainder of this opposition, the Opponents submit the following publications which were published before the priority date for '896, 25 July 1997:

EP 0206459 (hereinafter '459), first published as an application on 30 December 1986, attached as **Exhibit 2**, and claiming a priority date of 25 April 1985 from Czech Patent No. 3017-85, discloses the compounds 9-(phosphonylmethoxy-alkyl) adenines of the general formula as shown in claim 1 on page 20. The compounds disclosed in '459, in particular page 8 of '459, show an active ingredient of an antiviral medication and which can be converted into compounds with antiviral effect. Example 2 on page 11 and Table 1 on page 19 clearly define the active antiviral compound of Tenofovir, (PMPA). The '459 patent has subsequently been followed by a series of publications in scientific journals which describe the antiviral specificity of PMPA and which all pre-date the priority claim for '896. These include, but are not limited to: J.Balzarini et al, *Differential Antiherpesvirus and Antiretrovirus Effects of the (S) and (R) Enantiomers of Acyclic Nucleoside Phosphonates: Potent and Selective In Vitro and In Vivo Antiretrovirus Activities of (R)-9-(2-Phosphonomethoxypropyl)-2,6-Diaminopurine*, Antimicrobial Agents and Chemotherapy, February 1993, Vol 37, No.2, pages 332-338 (in particular see page 335, left hand column, paragraph 3), attached as **Exhibit 3** and Che-Chung Tsai et al, *Prevention of SIV Infection in Macaques by of (R)-9-(2-Phosphonylmethoxypropyl) adenine,* Science, Vol. 270, No. 5239, 17 November 1995, pages 1197-1199 (in particular see page 1199), attached as **Exhibit 4**.

14. With respect to the prior disclosure of bis(POC)PMPA, which claims to be a chemically stable candidate exhibiting an oral bioavailability of 30% and

useful for the treatment of HIV infections, the following relevant state of the art was disclosed prior to 25 July 1997, N. Bischofberger et al, *Bis(POC)PMPA, an orally bioavailable prodrug of the antiretroviral agent PMPA*, 4th Conference of Retroviruses and Opportunistic Infections, Washington DC, January 22-26, 1997, Abstract No. 214, attached as **Exhibit 5**.

15. In light of the above prior art, claims 7-8 and 12-15 are not patentable given that they consist merely of a mixture of materials which have already been disclosed and, therefore, should not be rewarded as inventions. For example, the subject matter of claim 8, PMPA, has already been disclosed in the prior art attached herein. In particular, **Exhibit 2** discloses on pages 14 and 15, in 5 and 6, the compound (2-hydroxypropyl)adenine. **Exhibit 2** also discloses analogous compounds on page 19 in Table 1 (No.2), and claim 2 of the said patent. **Exhibit 5** further supports this contention. Claims 7 and 12-15 amount to nothing more than a manipulation of materials which are clearly known substances in the art. As a result, claims 7-8 and 12-15 do not amount to a new product and, therefore, should be refused.

**Claims 1-8 and 10-22 of the invention are not patentable under sections 2(j), 2(ja) and 25(1)(e) of the Act**

16. In the alternative and without prejudice to the grounds raised in paragraphs 11-15, claims 1-8 and 10-22 of '896 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."

17. Under the above definitions and as discussed in paragraph 15 above, claims 7-8 and 12-15 of '896 clearly do not have any inventive merit and, therefore, fail to meet the criteria of a technical advance. The prior art disclosed in **Exhibits 2** and **5**, even if not novelty destroying, would certainly have made the claimed compositions and methods in claims 7-8 and 12-15 obvious to a skilled person 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.

18. With respect to claims 1-6, 10-11 and 16-22, the Applicant cannot claim any technical advance or inventive step. It is obvious from prior published art and common general practice within the pharmaceutical industry that the formation of pharmaceutically acceptable salts of compounds and their crystalline form, such as the preparation of fumaric acid salts for phosphonate nucleotide esters like bis(POC)PMPA in '896, will achieve the "unexpected advantages" claimed by the Applicant.

19. The Opponents point this Patent Office to the earlier patent EP 0632048 A1 (hereinafter '048), which was first published as an application on 4 January 1995, attached as **Exhibit 6**. '048 discloses the formation of pharmaceutically acceptable fumaric acid salts of phosphonate-nucleotide esters, such as for compound 345, otherwise known as 9-(2-phosphonylmethoxy)ethyl adenine ("PMEA"), as shown on page 26 of '048. '048 specifically mentions on page 4, at lines 40-47 that, "Phosphonate-nucleotide ester derivatives of the present invention represented by the above general formula (I) can form acceptable salts thereof. Examples of such salts include, for example, in the presence of acidic groups, metal salts such as lithium, sodium……**fumarate**…." In light of this disclosure, there can be no doubt that '048 spells out the same advantages which the Applicant is claiming in '896. As a result, the Opponents strongly believe that the skilled person would consider the invention claimed by the Applicant as being a normal design option and a mere routine exercise for optimisation of an existing compound like PMPA or composition like bis(POC)PMPA.

20. The Opponents refer to two further prior art publications which clearly support **Exhibit 6** and the reasoning that the claimed invention in '896 would have been obvious to a skilled person in the pharmaceutical field: Philip L. Gould, *Salt Selection for basic drugs*, International Journal of Pharmaceutics, 33, 1986, pages 201-217, attached as **Exhibit 7** and Morris et al*, An integrated approach to the selection of optimal salt form for a new drug*

*candidate*, International Journal of Pharmaceutics, 105, 1994, pages 209-217, attached as **Exhibit 8**.

21. On page 202, reading from the penultimate paragraph of the left hand column of **Exhibit 7**, Gould discusses the relative acid/base strengths of resultant salts and their stability and clearly states that "It would seem sensible that any acid relating to normal metabolism, or present in food and drink (as is known to be case with fumaric acid) can be regarded as a suitable candidate for preparing salts." The author goes on to list in Table 1 on page 202, right hand column, the FDA-Approved Commercially Marketed Salts, which lists fumarate. On page 209, right hand column, the author then provides a table which provides examples of the solubility of some salts which are tested as well as describing in the final paragraph under the heading "Salt Solubility and Salt Stability" how low solubility and low hygroscopicity can contribute significantly to the stability of a salt form. Morris et al in **Exhibit 8** offers further evidence of how to go about achieving a systematic, expeditious approach to finding the optimal salt for any given new drug candidate, including the determination of solubility and stability of salts, which can be completed within a short period of 4-6 weeks (see in particular pages 213 and 217).

22. Taking into account the above prior art, it would have been well known to a skilled person in the art that bis(POC)PMPA qualifies as a basic drug due to the presence of the amino group and that it is already soluble in water. The relevant skilled person would have also been aware from the prior art that

fumaric acid is a high melting solid, has low hygroscopicity and is less soluble in water when compared to citric acid, which is known to be a highly soluble salt. Taking this common knowledge into account, it would have been obvious for the Applicant to select a salt like fumaric acid, with its low solubility and low hygroscopicity, in order to complement the active ingredient of bis(POC)PMPA and achieve the "unexpected stability/advantages" and bioavailability claimed in '896. More importantly, it would have been obvious to the Applicant that BPPF/cBPPF, when compared with bis(POC)PMPA citrate, would naturally demonstrate the "unexpected stability/advantages" of BPPF/cBPPF as shown in Example 3 on page 28 of '896. This is because any skilled person would have known that adding a highly soluble salt like citrate with an already soluble active ingredient like bis(POC)PMPA would not be the sensible selection in order to obtain the desired stability. Therefore, by doing so, the Applicant has effectively manipulated the "unexpected stability/advantages" in '896 by comparing BPPF/cBPPF against a salt like citrate, which it knew would show less stability. This fact is further compounded by the Applicant's omission of examples from the specification comparing BPPF/cBPPF with other less soluble salts, despite claiming on page 4 at lines 30-31 that "cBPPF has an unexpectedly superior combination of physio-chemical properties compared to the **free base** and other **salts**". Since the bis(POC)PMPA base is a low melting solid which is not suitable for the purpose of manufacturing and creating formulations, it would have been obvious to have converted it into a salt, such as fumarate, which has a high melting point.

23. Despite the obvious nature of the claimed invention, the Applicant, nevertheless, attempts to make a distinction between BPPF and cBPPF in order to strengthen its claims for an invention, in particular claim 3. The Applicant suggests on page 5, at lines 3-5, that it has also obtained BPPF in a crystalline form, which has an "unexpectedly superior combination of physico-chemical properties compared to the free base and other salts." The Opponents believe this Patent Office should not be misled by the Applicant's unfounded assertions and that no distinction should be made between BPPF and cBPPF. Aside from the fact that the Applicant fails to even demonstrate in '896 how cBPPF is unexpectedly more superior to BPPF and uses the terms interchangeably without any consistency or accuracy in relation to demonstrating the claimed advantages, the methods used to obtain a crystalline form of a salt like fumarate is common general knowledge within the pharmaceutical industry. Indeed, the Applicant's discussion on pages 5 and 6 of the methods used to do so confirm this. Moreover, the practice of obtaining the crystalline form of a salt through X-Ray Diffraction analysis is nothing but a specific method for a chemist to study the properties of a substance in the solid state to understand the nature of the crystalline form. As such, the findings claimed in '896 and in particular claim 3, are simply mere discoveries using available modern technology and should not for one instance be mistaken as an "invention".

**Claims 1-8 and 10-22 of the invention are not patentable under sections 25(f) and 3(d) of the Act**

24. 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"*.

25. Based on a plain reading of s3(d), it is fair to say that the key issue in point for determining whether the new form of a known substance (including its salts) can be deemed patentable is to provide an interpretation of 'efficacy' in the context of the Act and the application in question. As a useful starting point, it is appropriate to state that s3(d), and its supporting explanation, is directed at and particularly relevant to pharmaceutical product patent applications such as '896. On this basis, it would seem logical that 'efficacy' should be interpreted according to a standard and uniform definition as used in the pharmaceutical industry and field of pharmacology. Therefore, taking the above rationale approach, the Opponents believe that for the purpose of determining whether '896 meets the requirement of efficacy one needs to look at: (1) how the pharmaceutical industry commonly defines or uses the

term “efficacy” in relation to pharmaceutical products; (2) the known activity of the existing substances in question, in this case PMPA, bis(POC)PMPA and fumaric acid (with respect to the claimed fumaric acid salt, as it is by definition to be considered the same substance for the purpose of s3(d), the Act requires the further consideration as to whether it differs significantly in properties with regard to efficacy); and (3) how the claimed “unexpected advantages” in ‘896, namely the alleged improvement in the stability of the product for storage at elevated temperature and relative humidity and oral bioavailability, sit in relation to points (1) and (2).

26. The Opponents believe a sensible starting point for the first point in question is to provide a standard and commonly used pharmacological definition for ‘efficacy’. A useful and standard definition for ‘efficacy’ is provided in Bowman’s ‘Dictionary of Pharmacology’ (1986) as being “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 9**, 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 9** 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 10**. In addition to the above definitions, it must be noted that efficacy is also a term that is used to refer to the ‘clinical efficacy’ of a drug, being the efficacy and safety of a drug to treat the claimed indications in real patients.

27. Taking the above standard definitions of efficacy it is then a question of determining whether the alleged improvements or "unexpected advantages" claimed in '896 amount to efficacy over the known substances. As already proved by the Opponents in **Exhibits 2-5** and as admitted by the Applicant on page 7, at lines 1-10, PMPA and bis(POC)PMPA were both known for their antiviral qualities prior to the priority date of '896. Likewise, the Opponents have already proved in **Exhibits 6-8** that fumaric acid and fumarate salts of phosphonate nucleotide esters such as bis(POC)PMPA are known to achieve the "advantages" claimed by the Applicant in '896. Moreover, as salts of a known substance are to be considered the same substance under s3(d), the claimed invention in '896 for a composition of formula (I) with the added fumaric acid salt is nothing more than a new form of known substances. Therefore, the Applicant cannot claim that these substances or their qualities are not known. The next question then is whether the alleged improvement or "unexpected advantages" claimed in '896 amount to an enhancement of the known efficacy of the existing substances in question.

28. Using the standard definitions of 'efficacy' as provided in paragraph 26 above and **Exhibits 9** and **10**, the Opponents contend that the Applicant has failed to meet the standard required to claim an invention for claims 1-8 and 10-22. This is clearly obvious by the fact that the previously known active substances PMPA and bis(POC)PMPA, and their known antiviral activity, still remain the same when administered as BPPF or cBPPF to a patient. To put it another way, the efficacy of the known compound and composition remain the same. Viewed in light of the standard definition of 'efficacy'

provided herein, BPPF and cBPPF are simply new forms of known substances but which fail to meet the normative standards of 'efficacy'. This fact is further compounded by the Applicant's failure to provide any evidence or working examples that the claimed compositions in the said claims come anywhere close to the standard definition of 'efficacy'.

29. If anything, as mentioned on page 5, at lines 1-2 of '896, the Applicant can only point to an "excellent" oral bioavailability of >30%-40% of PMPA for the claimed compositions, but even then has failed to demonstrate this by way of working examples and comparisons with the known substances. Therefore, such statements technically amount to just hearsay. More significantly, in light of the standard definition of 'efficacy', bioavailability and efficacy are obviously not interchangeable terms as they are two entirely different tests and properties within the field of pharmacology. Bioavailability is commonly used to describe the rate and extent of absorption of a drug from a product, but which does not affect the efficacy of the active substance in terms of occupying the receptor sites. To substantiate its reasoning, the Opponents point to the recent decision of the Chennai Patent Office in *Cancer Patients A.J Association, India v Novartis AG* (25 January 2006), attached as **Exhibit 11,** which serves as a precedent for this Patent Office. On page 4, paragraph 3 of that decision, the Assistant Controller clearly held that an increase of (>30%) bioavailability between the free base and the beta-crystal form of imatinib mesylate (which was the subject matter of the patent application), including the difference in their solubility in water, did not amount to an improvement in efficacy. Therefore, it can be conclusively stated that aside

from the deficiencies in '896 for proving "excellent bioavailability", the Applicant can not point to bioavailability as meeting the requirement of showing an 'efficacy' for the purpose of s3(d).

30. With respect to the claimed "unexpected advantages" in '896, the Applicant only attempts to demonstrate such advantages in relation to the purpose of benefiting the manufacture of the claimed product and for storage purposes. In Example 3 on page 27, continued on page 28, the Applicant claims that "the solid state chemical stability of cBPPF and bis(POC)PMPA was compared by analysing each compound after storage under different conditions. The results shown by the Applicant indicate that BPPF powder was "unexpectedly more stable to storage at elevated temperature and relative humidity." However, as the wording of the specification clearly states, such results are only useful for showing that BPPF was unexpectedly more "stable to storage", which is a factor that is only useful for manufacturing and storage, and not improving 'efficacy' as understood by the common usage of the term in pharmacology and the pharmaceutical field. Furthermore, the Applicant has failed to show in any examples how cBPPF is "unexpectedly more advantageous" than BPPF, despite claiming the same, let alone attempting to show that it is more superior in 'efficacy'.

31. Without admitting the same, even if s3(d) could be interpreted so generously so as to allow inventions in relation stability of a product for storage purposes, the Opponents contend that the claims in '896, in particular Example 3 provided on pages 27 and 28, are flawed and technically amount

to deceiving this Patent Office in order to show an "unexpected improvement". The Opponents point to the fact that on page 4, at lines 30-32, the Applicant states that "cBPPF has an unexpectedly superior combination of physio-chemical properties compared to the free base and **other salts**". However, other than Example 3 which compares BPPF (and not cBPPF) and bis(POC)PMPA citrate salt, the Applicant fails to provide any working examples of a comparison of BPPF/cBPPF with these "other salts" or the "free base" mentioned on page 4. As already mentioned in paragraph 22 of this opposition, it would have been known in the field that citrate salt is not a suitably stable salt for bis(POC)PMPA, given the latter's existing solubility. Therefore, in view of this common knowledge the Applicant's claims of an "unexpected advantage" would not stand up to scrutiny if tests were conducted against other less soluble salts, as the Applicant has obviously adopted a less stable salt in order to bolster its claims for an invention. To that end, the Applicant has simply manipulated its results and findings to support the invention claimed in '896.

32. However, the matter does not end there. The Applicant has then proceeded to claim an "unexpected advantage" relating to the stability and storage of BPPF at an elevated temperature and relative humidity of 40°C and 75%. However, according to the Opponents research, under generally accepted international guidelines the normal storage conditions to establish stability of a product is 25 ± 2 °C at 60 ± 5% relative humidity. This standard is otherwise known in the industry as 'real time stability', which is used to reflect the general and real time conditions under which the product will be stored and transported.

As a result, if the tests shown in Example 3 were conducted under 'real time stability' guidelines, as is the norm, the Opponents believe that bis(POC)PMPA citrate salt would also show better stability and, therefore, the claimed "unexpected advantages" by the Applicant would not be so unexpected so as to be able to claim an invention.

33. In light of the above, it is plain to see that claims 1-8 and 10-22 fail to meet or provide the necessary examples or evidence for the standard required to even meet the alleged improvements and "unexpected advantages" claimed, let alone the much higher standard of 'efficacy' required under s3(d). Therefore, the said claims are not inventions and not patentable under the Act.

**Claims 7 and 8 of the invention are not patentable under sections 25(f) and 3(e) of the Act.**

34. 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. As already highlighted in paragraph 12 of this representation, claims 7 and 8 consist merely of a mixture of materials that are already disclosed in the art, see **Exhibits 2 and 5**. As a result, the claimed compositions are nothing more than an "aggregation of the properties" of the components thereof and fail to provide any additional properties to those already known.

**Claim 9 of the invention is not patentable under sections 25(f) and 3(i) of the Act.**

35. Under s3(i), “any process for the medicinal, surgical, curative, prophylactic [diagnostic, therapeutic] or other treatment of human beings” shall not be considered an invention. Claim 9 amounts to nothing more than a therapeutic method, claiming the process of oral administration of a therapeutically effective quantity of a composition to a patient and as such is caught by s3(i) and does not amount to an invention.

**Claims 1-8 and 10-22 of the invention are not patentable under the sections 10(4)(a) and 25(g) of the Act.**

36. Section 10(4)(a) requires that “every complete specification shall fully and particularly describe the invention and its operation or use and the method by which it is to be performed.” Section 10(4)(a) is incorporated as one of the grounds of opposition against the grant of a patent under s25(1), namely, s25(1)(g), whereby a patent may be opposed if “the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed.” In light of these grounds, the Opponents contend that the Applicant has failed to fully describe the invention clearly by omitting key information from ‘896, which if available, would negate the invention claimed.

37. As already noted in paragraphs 22, 30, 31 and 32 above, the Applicant on page 4, lines 30-32, states that “cBPPF has an unexpectedly superior combination of physio-chemical properties compared to the free base and other salts.” However, other than demonstrating in Example 3 on pages 27-28

a comparison between the solid state chemical stability of BPPF and bis(POC)PMPA citrate salt, the specification fails to provide any other examples of how cBPPF/BPPF compared to the free base and other salts as mentioned on page 4 of the specification. The Opponents believe this is a key omission as it would be obviously known that adding a highly soluble salt like citrate with an already soluble active ingredient like bis(POC)PMPA would not achieve the desired stability and would only serve to make the composition BPPF and cBPPF look like it has "unexpected advantages". Therefore, the Opponents believe the claimed invention should have also demonstrated its "unexpected stability" against other salts that are known to be more stable than citrate salt. As a result the specification has not been sufficiently or clearly described so as to warrant an invention, but leaves open a number of questions as to its validity.

38. On page 4, at lines 32-35, of '896 the Applicant also makes the claim that because of the excellent solid state stability and good aqueous solubility and stability of cBPPF, these properties are useful for contributing to excellent bioavailability properties in humans and animals. Apart from mentioning on page 5, at lines 1-2, and page 7, lines 26-29, the oral bioavailability achieved, the specification fails to demonstrate or provide suitable comparisons with known substances of how the claimed properties achieve the claimed "excellent bioavailabilty", not to mention a significant difference in efficacy as required for s3(d).

39. In view of the above, the Opponents believe that the Applicant has deliberately omitted complete and detailed examples of the claimed invention, because such information would be damaging to its claims and would lead this Patent Office to reject '896.

**Claims 1-22 of the invention are not patentable under the sections 25(h) and 8 of the Act.**

40. 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 as the invention applied for in India. This obligation requires the Applicant to provide, 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 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.

41. In particular, the Opponents are aware that the Applicant has applied to patent the same invention claimed in '896 in Brazil, under Brazilian Application No. PI9811045-4, titled "Analogue Nucleotide Composition and Synthesis Process" and which claims priority from U.S Application Nos. 08/900,752

and 60/053,777, both dated 25 July 1997. More importantly, the Opponents understand that Brazilian Application No. PI9811045-4 is the subject of a 'third party observation process' in Brazil. The Opponents seriously doubt whether the Applicant has informed this Patent Office of the status of its Brazilian application and the pending observation process. As a result, the Applicant's failure to do so is a strict ground to refuse '896 in its entirety.

42. In the event that this Patent Office does 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 its corresponding application in Brazil. The Opponents believe such matters are relevant to proceedings here, albeit, of course, the laws are different. Moreover, the Opponents also request this Patent Office exercise its discretion under s8(2) and require the Applicant to furnish details of the processing of the abovementioned Brazilian application.

**Claims 1-22 of the invention are not patentable under the sections 25(1)(i) and 7 of the Act.**

43. Section 7(2) states that "where the application is made by virtue of an assignment of the right to apply for a patent for the invention, there shall be furnished with the application proof of the right to make the application." Section 25(1)(i) provides that where an application is not made by the applicant within 12 months of the first application in the case of a convention application, then it can be opposed on such grounds.

44. For the purpose of s7(2), Form 1, which accompanies an application, provides a section where the original inventors can declare that they are the true and first inventors for the claimed invention in the convention country and that the relevant applicant(s) applying for the application are their assignee. For the purpose of '896 it is clear that the Applicant, Gilead Sciences, Inc., is the assignee. Therefore, as is required under s7(2), the Applicant is required to obtain proof that an assignment has taken place between the original inventors and itself and that it has the right to make the application.

45. According to the copy of Form 1 accompanying '896 and which has been made available by this Patent Office to the Opponents, it appears that the relevant declaration section where the original inventors give the Applicant the right to make the application herein has not been signed. Attached as **Exhibit 12** is a copy of the said page. The Opponents realise that '896 is a divisional to the original application '2174 and that an 'assignment' and declaration from the original inventors may have been made for that particular application. However, even though '896 is deemed under the Act to have been filed on the same date as '2174, legally it exists and proceeds as a separate **substantive** application, as defined in s16(3). Indeed, this is confirmed by the need to file a separate Form 1 for the said application. As a result, the accompanying Form 1 for '896 should also have been executed by the original inventors of the claimed invention as proof that the Applicant could make the said application.

46. Therefore, if the above facts are true, the application for '896 has failed to comply with s7(2) and is not a valid application. As a result, strictly speaking, '896 has not been filed within 12 months of the first application in a convention country, being 25 July 1997, and should be refused on this basis.

Based on the grounds set out in paragraphs 11-46 above, the Opponent requests that Application No. 896/DEL/2002 A 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 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 9 day of May 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:-

Indian Network for People Living With HIV/AIDS (INP+) / Delhi Network of Positive People (DNP+)

c/o No. 4, 3rd Cross

Vasanthanagar

Bangalore, 5600-52

To:

The Controller of Patents

The Patent Office, NEW DELHI