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+") ("the OPPONENT")

And

IN THE MATTER OF:

Indian Application No. '872/CAL/98 A, filed on 14 May 1997 by Glaxo Group ("the APPLICANT)

STATEMENT OF CASE OF THE OPPONENT

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1. The Opponent is a community-based organisation dedicated to meeting 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.

2. Amongst their various mandates, the Opponent works to ensure that medicines in India are accessible and affordable for PLHAs. The particular class of medication available for Human Immunodeficiency Virus (HIV) is

known as anti-retrovirals (ARVs). In the early 1980s, when HIV first emerged as a deadly virus, there was no known treatment for the infection. Today, PLHAs can live long, healthy, productive lives, due to the development of ARVs that inhibit the proliferation of the retrovirus in the human body. This is largely due to the development of medicines, most of which were invented in the 1980s, known as nucleoside reverse transcriptase inhibitors and non-nucleoside reverse transcriptase inhibitors. By the early 1990s, another type of ARV was launched, known as protease inhibitors. All of these drugs are attributed to saving the lives of PLHAs globally.

3. The current class of ARVs essentially comprise these old drugs. However, by making only neglible improvements, pharmaceutical companies claim these new versions of ARVs as so-called "inventions". While these drugs may be patentable under legislations in other countries due to their liberal standards of patenting, in India, section 3(d) requires the rejection of patents that do not show a significant difference in efficacy over existing substances. Indeed on reviewing over 100-plus applications in the patent 'mailbox' for HIV medications, the Opponent has found that virtually none are for actual inventions or new chemical entities, and barely any are able to meet the efficacy requirement of Section 3(d).

4. In light of the above, the Opponent has learnt that on 14 May 1997, the Applicant, Glaxo Group Limited, filed a patent application titled 'A Novel Salt' which was allocated Application No. 872/CAL/98 A ('872), herein attached as **Exhibit 1.** This application was published for opposition in the

Official Patent Office Journal on 18 March 2005, and is believed to be under examination and has not as yet been granted.

5. '872 is an application which relates to the hemisulfate salt of the compound (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, referred to by its generic name Abacavir Sulfate or the commercial brand name Ziagen®.

6. A brief history of Abacavir Sulfate traces the drug back to 1980's and the development of carbocyclic nucleoside analogs containing antiviral properties. In particular, an important development transpired in the invention of carbovir or carbovir triphosphate, which required a 'vehicle' to alleviate solubility concerns to allow carbovir to be introduced into the human body. Such a 'vehicle' was patented in 1990 through Abacavir, a compound which is cleaved in vivo into the previously known active moiety carbovir triphosphate. Subsequently in 1994, a salt of Abacavir was also filed for as a patent, known as Abacavir Succinate. Three years later, a patent application was submitted in India for Abacavir Sulfate, which is the subject of application '872 and this opposition.

7. The field of invention of '872 is the treatment of HIV. As discussed above, the invention claimed within '872 is based on a known compound, Abacavir. The Applicant confirms that Abacavir is a known compound on page 1, at lines 10-15, of '872 by stating that (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol was disclosed

in European Patent Specification Number 0434450, published on 26 June 1991 Bulletin 91/26, which, incidentally, also describes on page 4 in lines 45-50 "pharmaceutically acceptable acid addition salts…for example organic carboxylic acids…organic sulfonic acids…inorganic acids such as hydrochloric, sulfuric, phosphoric and sulfate methanesulphonate sulfamic acids."

8. On page 2, at lines 10-15 of '872, the Applicant alleges that "the advantages of the hemisulfate salt of the compound over the disclosed hydrochloride salts and succinate salt renders the hemisulfate salt particularly suitable and advantageous to prepare on a large scale, and in particular for use in the preparation of pharmaceutical formulations." The Applicant further claims an 'invention' for the precursor salts it uses to make the hemisulfate salt via "salt conversion", which it claims enriches the optical purity over that of the precursor salt, and which reduces or eliminates the need for "any further preparative or purification steps to enhance the optical purity of the hemisulfate salt product."

9. The Applicant's specific claims within '872 are set out below:

    a) Claim 1 relates to the hemisulfate salt of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a solvate of the compound.

    b) Claim 2 relates to the hydrate form of the hemisulfate salt of (1S, 4R)-

cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol.

c) Claim 3 relates to the method of treatment of the hemisulfate salt of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol.

d) Claims 4-6 relates to the uses of the hemisulfate salt of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol.

e) Claims 7-14 deal with processes relating to the other claims.

f) Claim 15-18 are for pharmaceutical formulations of the hemisulfate salt of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol.

g) Claims 19-21 claim additional salts of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, particularly the dicarboxylate salts including glutarate, hemisuberate, adipate, fumarate, hemisecabate and pimelate, and the separate salts glutarate, monosulfate, benzoate and salicylate.

h) Claims 22 and 23 relate to the pharmaceutical compound (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-

methanol and the formulation, as set out in the examples.

10. For the purpose of this Opposition, the Opponent is only concerned with claims 1-6 and 15-23 of '872. Accordingly, claims 7-14, which deal only with processes, do not form part of this Opposition.

11. The Opponent firmly believes that the claims made by the Applicant in '872 are 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) and 3(i).

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 Opponent submits their opposition to '872 on the grounds set out below. Furthermore, as '872 was filed at this Patent Office (Calcutta), the Patent Controller of this office has the authority to hear and decide on this opposition.

GROUNDS

The Opponent submits their opposition on the following grounds:

Claims 1, 4-6, 15-18, 21, 22-23 of the invention are not patentable under sections 25(1)(b)(ii) and 2(j)

12. An invention, as defined by s2(j), is a "new product". This requirement of "newness" is reaffirmed in s25(1)(b)(ii), which disallows patenting in cases where the invention claimed has been published in India or elsewhere before the priority date of the claim. The Opponent contends that claims 1, 4-6, 15-18, 21, 22-23 are not patentable because they are not "new" and stand anticipated by prior publication.

13. As defined by claims 1, 4-6, 15-18, 21, 22-23, the invention claimed in '872 is for the Applicant's selection of a salt in order to, as stated by the Applicant

on page 1, lines 15-25, meet the "need for the compound to be prepared in a form suitable for ease of isolation in large scale manufacture, and for the ease of formulating into an acceptable product for administration to humans." In particular, the Applicant states that the free base of Abacavir "produces an amorphous solid which traps solvents and is, therefore, unsuitable for large scale purification, or for formulation, without additional purification procedures." The succinate salt of Abacavir, according to the Applicant, "agglomerates to form a "lumpy" mass which will not easily pour and is thus unsuitable for use in commercial tableting machines, such that an extra processing step of high energy milling is required to give a uniform particle size." Therefore, in essence, the invention claimed in '872 is for the hemisulfate salt, which the Applicant claims is suitable for ease of large-scale manufacture.

14. The alleged 'invention' is not new and stands anticipated by prior publication. In order to confirm the prior disclosure, the Opponent relies upon EP 0434450 (hereinafter '450), attached herein as **Exhibit 2**, which was first published as an application on 26 June 1991, Bulletin 91/26, and which pre dates the priority date of 17 May 1997 for '872.

'450 discloses the compound (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as shown in claims 1-3 on page 27. The compounds disclosed in '450, in particular page 4, show a compound that can be converted to an active metabolite demonstrating antiviral activity. This clearly discloses the compound Abacavir.

In particular, '450 claims "pharmaceutically acceptable salts, esters and salts of esters of the (1S, 4R) enantiomeric compounds" in claim 4 on page 27. On page 4 of '450, in lines 45-50, the Applicant specifically names "basic salts with the appropriate acid…such as sulfuric". This constitutes a specific disclosure of the acid-salts of sulfuric acid, which naturally includes the salts sulfate, hemisulfate as claimed in claim 1 of '872, and monosulfate, as claimed in claim 21 of '872.

Indeed, on page 3 of '872, the Applicant itself explicitly sets out that the hemisulfate salt means the base compound plus sulfuric acid. "Hemisulfate" by definition is nothing more than two molecules of the base or active compound forming a salt by the addition of one molecule of sulfuric acid. This disclosure, therefore, includes both the hemisulfate and monosulfate salts.

15. Under the basic criteria of novelty, the hemisulfate and monosulfate salts of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol are unpatentable. Selecting an acid-salt from a list cannot under any circumstances be considered novel. Therefore, all claims relating to the hemisulfate and monosulfate salts should be rejected for specifically being disclosed in '450 as demonstrated above.

Claims 1, 4-6, 15-18, 22-23 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 12-15, claims 1, 4-6, 15-18, 22-23 of '872 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 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."

17. Based on these definitions, the Opponent believes that claims 1, 4-6, 15-18, 22-23 of '872 do not have any inventive step and fail to meet the criterion of technical advance and non-obviousness. Without admitting the same, even if the hemisulfate salt is considered to be novel, the prior art disclosed in **Exhibit 2** demonstrates that it would definitely have been obvious to a skilled person in the art to develop the salt form and that this would not have required any inventive steps to achieve the desired result. As a result, these claims should not be granted as they fail to meet basic standards of inventive step.

18. With reference to claims 1, 4-6, 15-18, 22-23, the Applicant in '450, page 4,

lines 45-50, discloses "pharmaceutically acceptable acid addition salts… inorganic acids such as hydrochloric, sulfuric…" To a person skilled in the art, page 4, lines 45-50 of '450 clearly signposted and made it obvious that sulfuric acid was an appropriate acid to use in the formation of acid addition salts.

19. The Opponent also seeks to emphasize that utilisation of the sulfate salt alone does not amount to a technical advance. To achieve the so-called advantage of aiding the tabletting process, there are many other salts that obviously could have provided the same benefit. Such salts could have been manipulated through various methods, including wet granulation or the addition of excipients, rendering these salts suitable for ease of manufacture. Simply selecting the sulfate salt from the list in'450 does not constitute a technical advance and would have been obvious to a person skilled in the art.

20. The Opponent presents two prior art publications which further support the contention of obviousness: Philip L. Gould, *Salt Selection for basic drugs*, International Journal of Pharmaceutics, 33, 1986, pages 201-17, attached as **Exhibit 3** 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 4**.

21. In **Exhibit 3**, Gould lists in Table 1 on page 202, right hand column, the FDA-Approved Commercially Marketed Salts. This list includes sulfate and several other salts. This publication demonstrates that it would have been

evident to someone skilled in the art to select salts from this list for product development, as it clearly sets out salts that were capable of production for pharmaceutical use, particularly those with suitable properties for clinical administration such as free flow characteristics and crystallinity. Since sulphuric acid salts were specifically recommended in '450, and known in the pharmaceutical industry's standard practice at the time, it is beyond doubt that someone skilled in the art would have found the development of a sulfate obvious.

22. Salt selection is a common procedure in the pharmaceutical industry to determine optimal salts for drug candidates. In 1992, in **Exhibit 4**, Morris et al demonstrated that finding the optimal salt is a process that can be executed in a matter of 4-6 weeks. A systematic, tiered approach can allow expeditious finding of optimal salt forms of a compound. In this case, the Applicant specifically mentioned sulfuric acid as recommended for acid addition salt formation, thereby rendering it obvious to select this salt during the drug development process. It is, therefore, indisputable that the Applicant is attempting to obtain a patent on a salt that was clearly described in '450, and which a person skilled in the art would have found obvious to make.

23. Therefore, the Applicant cannot claim any technical advance or inventive step for claims 1, 4-6, 15-18, 22-23. It is obvious from prior published art and common practice in the pharmaceutical industry that the formation of pharmaceutically acceptable salts of compounds, such as the preparation of the sulfate salt in '872, will achieve the "advantages" claimed by the

Applicant. A person skilled in the art would, therefore, find the so-called "invention" an obvious selection in the drug development process.

Claims 19-23 of the invention are not patentable under sections 2(j), 2(ja) and 25(1)(e) of the Act

24. Section 25(1)(e) relies on the definitions in sections 2(j) and 2(j)(a), as already defined in paragraph 16 above, 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."

25. With respect to claims 19-23, the Opponent contends that compared to the existing knowledge, there is no new product that involves a technical advance and which would not have been obvious to a person skilled in the art. For these claims, on page 2, at line 25 onwards, the Applicant asserts that "where the hemisulfate salt is prepared by a 'salt exchange' process, that is to say by conversion of a precursor salt of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, particularly the glutarate or succinate salt, an enrichment in optical purity over that of the precursor salt is achievable. Thus, the need for any further preparative or purification steps to enhance the optical purity of the hemisulfate salt product may be reduced or eliminated." Notwithstanding the fact that the hemisulfate salt is not an invention, the Applicant's assertion that the preparative route and starting compounds for making the hemisulfate salt reduces or eliminates

steps to enhance the optical purity of the hemisulfate salt, is not only unsubstantiated but also misleading. To substantiate its assertion, the Opponent refers this Patent Office to WO 96/06844 (hereinafter '844), first published as an application on 7 March 1996, attached as **Exhibit 5** and Exhibit 2.

26. In '844, the Applicant claimed a succinate salt of the compound (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol. The Applicant explicitly states on page 3 of **Exhibit 5** that "optional washing or recrystallisation may be used to increase the purity of the product, if required. The compound of the invention being in a crystalline form provides a means for large scale manufacture by rapid and efficient filtration." Therefore, in '844, Applicants have already set out that extra steps of recrystallisation and washing may increase the purity of the product. Therefore, there is no inventive step in '872 that constitutes a technical advance over this, that would not have been obvious to a person skilled in the art.

27. Furthermore, the Applicant's contention that using the salt conversion process results in advantages in purity is unsubstantiated by data. There is no direct comparison of recovered optically pure hemisulfates prepared by direct conversion versus the pre-formed salt method of conversion. The Applicant has proffered no evidence of actual production yield of the optically pure hemisulfate in percentage terms. As a result, claims 19-23 of '872 lack the ability to claim that there exists any technical advance or advantage.

28. The Applicant is misleading the Examiner by stating that "the need for any further preparative or purification steps to enhance the optical purity of the hemisulfate salt product may be reduced or eliminated" by using the salts in claims 19-21 as precursors in the conversion process. In fact, the Applicant has failed to demonstrate with actual data that the hemisulfate, if recrystallised again, would not achieve the same results of enhanced purity. Without providing any demonstration of this assertion, it is misleading to suggest that the need for 'additional' purification steps have been eliminated. To prove an attainment of an "advantage", the Applicant needed to show a comparison of the recrystallised sulfuric acid addition salt yield versus the salt conversion yield. In the absence of such data, the Applicant is making misleading statements in order to claim an invention.

29. In claims 19-21, the Applicant claims a wide range of salts: "dicarboxylate salt…selected from the group consisting of glutarate, hemisuberate, adipate, fumarate, hemmisebacate and pimelate…the glutarate salt…the monosulfate, benzoate, salicylate salt of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol." In addition to the grounds set out above, the following disclosures clearly demonstrate that a person skilled in the art would have found these salts obvious. In '450, page 4, lines 45-50, the Applicant discloses "pharmaceutically acceptable acid addition salts…for example organic carboxylic acids such as…succinic." Since glutaric acid is a known homolog of succinic acid, it would have been evident to a person skilled in the art that glutaric acid would have been an appropriate acid to

utilise for salt selection purposes. Furthermore, the Applicant in '450, page 4, lines 45-50, discloses "pharmaceutically acceptable acid addition salts…for example organic carboxylic acids." From this disclosure it would be clearly obvious to a person skilled in the art that benzoic and salicylic acid would be logical choices for drug design purposes.

30. The Opponent also refers to **Exhibit 3** and the table on FDA-Approved Commercially-Marketed Salts. In this table, benzoate, salicylate, succinate and fumarate are all listed. This demonstrates that to a person skilled in the art, selecting these salts would have been obvious and a standard practice in the pharmaceutical industry for drug development. Furthermore, as set out in **Exhibit 4**, the salt selection process can be a simple procedure taking 4-6 weeks, which can hardly be considered a technical advance.

31. In light of these facts, it is clear that Applicant's claim that is not a technical advance. Accordingly, the Opponent requests that claims 19-21 be rejected.

Claims 1, 4-6, 15-18, 22-23 of the invention are not patentable under sections 25(f) and 3(d) of the Act

32. In the alternative, 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….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"*.

33. The Opponent has demonstrated through **Exhibit 2** and as admitted by the Applicant in'450, that Abacavir was already recognised for its conversion to carbovir triphosphate (containing antiviral properties) before the priority date of '872. Under s3(d), salts are considered to be the same substance as the main compound. Therefore, the claimed invention in '872 for Abacavir with the added sulfuric acid salt is simply a new form of known substance, which under the Act means it is not an invention and not patentable.

34. Section 3(d) does, however, contain the caveat 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**"*. The Opponent contends that claims 1, 4-6, 15-23 fail to meet the efficacy requirement as absolutely no evidence is submitted to show that the claims differ significantly in properties with regard to efficacy.

35. The Opponent seeks 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 6**, *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 the term "efficacy" as adopted within s3(d) relates to the field of pharmaceuticals and the activity of the drug itself to produce an effect or response in the human body.

36. The claimed benefit of the hemisulfate salt in '872 is the removal of an extra step in the manufacturing process, which the Applicant is describing when asserting that the hemisulfate salt is "particularly suitable and advantageous to prepare on a large scale". In light of the intended meaning of efficacy under s3(d), the Applicant's invention of claiming and advantage of preparation on a large scale, fails to meet this standard and should accordingly be rejected.

37. Having established that the Applicant's claim does not amount to 'efficacy', as required under s3(d), the Applicant's claimed 'advantages' relating to the sulfate salt, which provides for ease of manufacturing and formulation, is misleading. These so-called advantages are not unique to the sulfate salt. The Applicant could have used tablet formation techniques commonly used in the industry, such as adding an excipient, in order to convert the succinate salt in

‘844 to a tablet. Furthermore, an ‘advantage’ in manufacturing should not be confused with the s3(d) requirement of ‘efficacy’. Therefore, no enhancement in efficacy can be demonstrated over the known compound Abacavir Succinate.

38. Claims 19-21 of the invention are also not patentable under sections 25(f) and 3(d) of the Act, as no enhancement of efficacy is demonstrated. As defined earlier, efficacy is commonly referred to as either pharmacological or therapeutic, but ultimately must demonstrate a response or effect in the human body. Here, the Applicant has asserted “where the hemisulfate salt is prepared by a ‘salt exchange process’…by conversion of a precursor salt… particularly the glutarate or succinate salt, an enrichment in optical purity over that of the precursor salt is achievable…thus, the need for any further preparative or purification steps to enhance the optical purity of the hemisulfate salt product may be reduced or eliminated.” These alleged “advantages” clearly do not amount to pharmacological or therapeutic efficacy.

39. Notwithstanding the above, three additional points must be raised here. Firstly, elimination of steps in the manufacturing process does not constitute efficacy, particularly since repeat recrystallisation always leads to enriched optical purity. Thus this so-called “advantage” is merely a manufacturing benefit, not efficacy under Section 3(d). Secondly, the Applicant has not and cannot demonstrate an increase in efficacy between using the hemisulfate salt alone or using the input succinate salt. As the table on page 19 of ‘872 shows,

the percentage difference in ratio of enantiomers of the input succinate salt versus the product hemisulfate salt is 99.5: 0.5 versus 99.9:0.1; 99.0:1.0 versus 99.7:0.3; 98.0:2.0 versus 99.5:0.5; 96.0:4.0 versus 99.0:1.0. The Applicant cannot and has not proven that any significant difference in efficacy occurs between these results, particularly since these measurements are determined by optical criteria and no data has been submitted to demonstrate a difference in biological activity. Without a showing of difference in vivo, the baseline for efficacy has not been reached. Thirdly, the Applicant has made no showing of why the "unwanted" (1R, 4S) isomer is indeed "unwanted". In fact, no explanation is offered and no is data submitted to substantiate this point. Absent such an explanation, any advantage or claim for efficacy is nullified.

40. The Applicant on page 2 of '872 has shown that the enrichment in optical purity of hemisulfate via conversion is over that of the precursor salt, not over the recrystallised hemisulfate. Notwithstanding that this is not efficacy, to achieve even a demonstration of increased advantage, the Applicant needed to show a comparison of the recrystallised sulfuric acid addition salt yield versus the salt conversion yield. Without such data, and by only offering the precursor salt itself as the marker for comparison, the Applicant is making misleading statements and has not met the efficacy standard under s3(d).

41. The Opponent further submits that the Applicant will not be able to show that percentage yield will be greater for the hemisulfate via conversion than any other known acid-salt. Without providing comparative data, the Applicant has

not proven an increase in efficacy. The Applicant must be able to demonstrate that Abacavir Hemisulfate, prepared through a "salt conversion" process, results in increased optical purity and other therapeutic advantages. In this case, the Applicant has not made a basic showing for s3(d) to be met.

42. In light of the above, it is plain to see that claims 1, 4-6, 15-23 fail to meet the standards required under Section 3(d) and, therefore, should not be patentable.

Claim 2 of the invention is not patentable under sections 25(f) and 3(d) of the Act

43. Claim 2 is also not patentable under Section 3(d). As set out above, s3(d) excludes from the definition of invention "the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance." Claim 2 of '872 claims the hydrate form of (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol. The hydrate form is not an invention within the meaning of the Act as it is, at best, merely the discovery of a new form of a known substance, and at worst, not even a new form given that it is merely the compound with the addition of water. This is not an invention as it refers to the crystallisation of a compound and the form in which the molecules arrange in a specific arrangement, within the crystal lattice. Without prejudice to the above, if the hydrate form is the new form of the compound, the Applicant has still failed to provide any evidence to demonstrate any enhancement of the known efficacy. Claim 2 of '872 should be rejected outright for these reasons.

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

44. 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 3 is merely a method of treatment for administering an effective amount of the compound and should be rejected outright.

Based on the grounds set out above, the Opponent requests that Application No. '872/CAL/1998 A be refused in its entirety. Based on s25(1) of the Act and Rule 55(1) of the Rules, the Opponent requests that this Patent Office informs the Opponent immediately of any response filed by the Applicant to this opposition. The Opponent also requests a hearing in the matter of Application No.'872/CAL/1998 A.

Dated _____

For and behalf of the Indian Network of Positive People (INP+)

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

To:

The Controller of Patents

The Patent Office, Calcutta