

Before the Controller of Patents, Kolkata

**In the matter of Section 25(1) of the Patents Act,
1970;**

AND

In the matter of the Patents Rules, 2003

AND

**In the matter of Patent Application No.
3658/KOLNP/2009 filed by Pharmasett
Laboratories on 20 October 2009 titled
“Nucleoside Phosphoramidate Prodrugs”**

AND

**In the matter of representation by way of
opposition by Sankalp Rehabilitation Trust,
Hepatitis Coalition of Nagaland (HepCon) and
network of PLHIV living in the Asia Pacific
region APN+ (Opponents)**

STATEMENT OF FACTS AND EVIDENCE

INTRODUCTION

1. The Opponents are community based, non-profit organizations representing the needs of people living with Hepatitis-C and HIV/AIDS. Sankalp Rehabilitation Trust is a community-based organisation, registered under the Bombay Public Trusts Act, 1950 bearing registration No. E15459 having its office at SS Bengali Municipal School, First floor, Thakurdwar road, Charni road east, Mumbai- 400 002. The Opponent provides care, treatment and rehabilitation services for injecting drug users. The Opponent has over a thousand beneficiaries who are injecting drug users and who need treatment for Hepatitis C. Injecting drug users are particularly vulnerable to infection with HIV and Hepatitis-C. With

respect to health status, HIV as well as Hepatitis-C are a major cause of concern amongst drug users. A survey carried out as part of the sentinel survey in 2003 revealed that 79% of 250 drug user-patients of the Applicant tested positive for Hepatitis C. In July 2011, 41 of 95 of the Applicant's drug user patients tested positive for Hepatitis C. Out of these, only two who are also co-infected with HIV are on treatment that is being provided free of cost by an international aid agency.

2. HepCoN is a non-profit organisation with its office at Red Cross Building Complex, Raj Bhavan Road, Kohima Nagaland 797001. Spearheaded by Nagaland Users Network, the coalition has been active in addressing the issue of HCV in Nagaland, ever since its formation in August 2013 at Kohima. The organisation also has numerous beneficiaries who are injecting drug users. They have been working at different levels from spreading awareness among the community members, advocating with key stakeholders including the State Government, providing information and referral services to patients in need of information's or treatment relating to Hepatitis C.
3. HepCoN has been active in 11 district headquarters of Nagaland in order to impart basic information on HCV to persons most vulnerable to HCV. In the past 10 months, about 594 people have been reached out to. Since formation, as a part of its activities, the coalition has been a part of regional, national and Asian regional efforts relating to Hepatitis C. The coalition now aims to take its campaign to the next level in order to capacitate the district partners on treatment aspect.
4. APN+ is the network of PLHIV living in the Asia Pacific region, registered as a foundation under the Thailand laws with registration number Kor Tor 1575, address at 75/12 Ocean Tower II, 15th Floor, Soi Sukhumvit 19, Klong Toey Nua, Wattana, Bangkok, Thailand-10110. The foundation has come to about two hundred fifty thousand persons living with Hepatitis C. The network was established in 1994 at a meeting in Kuala Lumpur by 42 PLHIV from eight countries in response to the need

for a collective voice for PLWHA in the region; to better link regional PLHIV with the Global Network of PLHIV (GNP+) and positive networks throughout the world, and to support regional responses to widespread stigma and discrimination and better access to treatment and care. APN+ established the IDU Working Group of APN+ in 2008 to address specific issues that affect the lives of HIV positive drug users in the Asia Pacific region. The group currently works towards remedying non availability of Hepatitis C prevention, testing and treatment services, lack of knowledge about HIV and Hepatitis co-infection among positive drug users, lack of available data on Hepatitis co-infection and insufficient community engagement to inform research, non availability of Oral Substitution Therapy (OST), clean syringes and other harm reduction services among positive people.

5. Often the high cost of medicines is exacerbated by patent protection. It is well known that product patent on a medicine allows the patent holder to exclude other pharmaceutical companies from manufacturing the medicine for a period of twenty years and thereby allows it to set monopolistic prices for the medicine. The opponents are therefore concerned about the impact of product patent on access to safe, effective and affordable treatment for Hepatitis C. It is established that grant of patents to routine modification to already known drugs to overcome known problems will place life-saving drugs out of the reach of thousands of patients who require it. The high costs of patented medicines also impact the ability of government to procure these medicines for the national treatment programme.

II. ACCESS TO MEDICINES AND STRICT INTERPRETATION OF PATENTABILITY STANDARDS

6. The present application pertains to nucleoside phosphoramidates for the treatment of viral diseases, particularly Hepatitis C. These compounds are inhibitors of RNA-dependent RNA viral replication and are useful as inhibitors of the virus.

7. HCV NS5B polymerase is required for the synthesis of a double-stranded RNA from a single-stranded viral RNA that serves as a template in the replication cycle of HCV. Therefore, NS5B polymerase is considered to be an essential component in the HCV replication complex. A number of effective targets for drug development against HCV therapeutics includes NS5B polymerase.
8. Nucleoside inhibitors of NS5B polymerase can act either as a non- natural substrate that results in chain termination or as a competitive inhibitor which competes with nucleotide binding to the polymerase. To function as a chain terminator the nucleoside analog must be taken up by the cell and converted *in vivo* to a triphosphate to compete for the polymerase nucleotide binding site.
9. Nucleoside phosphoramidate prodrugs have been shown to be precursors of the active nucleotide triphosphate and to inhibit viral replication when administered to viral infected whole cells.
10. Present application claims allegedly novel phosphoramidate prodrugs of nucleoside derivatives for the treatment of viral infections mainly HCV.
11. The most effective way to lower the cost of these essential medicines is to promote competition. However, in order for there to be any effective generic competition, it is imperative that patents not be granted in India for uninventive, incremental improvements or to inventions that do not meet the strict patentability standards set by India.
12. Although India was constrained by its WTO obligations to introduce product patent protection for pharmaceutical products through the Patents (Amendment) Act of 2005, India retains full sovereignty in determining the standards that must be met with respect to patentability. India is under no obligation to follow the perilous path that many developed nations have taken in setting low standards for novelty and inventive step that result in patent protection for incremental innovations, all too often at the cost of public health. This has been recognised by the Hon'ble Supreme Court of India too in *Novartis AG v. Union of India and others*, (2013) 6 SCC 1.

13. Cognisant of public health concerns and the Doha Declaration on the TRIPS Agreement and Public Health (2001), Parliament introduced certain provisions, while passing the Patents (Amendment) Act, 2005 to amend the Patents Act, 1970 (hereinafter referred to as the “Patents Act”), to ensure that patents are granted only for genuine inventions and to prevent “evergreening”, i.e. creation or extension of monopolies through patent terms by obtaining patents for minor or routine modifications. Indian Parliament also set a higher standard of inventive step.
14. The Patents Act should be interpreted by the Hon’ble Patent Controller in light of all the relevant circumstances surrounding the Amending Act. The Hon’ble Madras High Court, in *Novartis AG v. Union of India and Others*, (2007) 4 MLJ 1153, while upholding Section 3(d) against a constitutional challenge, stated: “We have borne in mind the object which the Amending Act wanted to achieve namely, ***to prevent evergreening; to provide easy access to the citizens of this country to life saving drugs and to discharge their Constitutional obligation of providing good health care to its citizens.***” [see para 19] (emphasis added). As such, the Opponent submits that the Hon’ble Patent Controller, while considering the present pre-grant opposition and while interpreting the provisions of the Patents Act, must bear in mind the intent of Parliament in enacting the Patents (Amendment) Act, i.e. to ensure India’s compliance with its obligations under the Agreement on Trade Related Aspects of Intellectual Property Rights while ensuring that patent protection does not come in the way of India’s fundamental duty to provide good health care to its citizens.
15. The Opponents firmly believe that a proper application of the patentability standards set out in Section 3(d) of the Patents Act, as well as those embodied in Section 2(1)(j) and Section 2(1)(ja) of the Patents Act, in a manner that fully carries out the objectives of the Amending Act, will result in the rejection of the present application. The Opponents, therefore, humbly request that the Hon’ble Patent Controller scrutinise the present application with special care, as its decision will determine

whether millions of people will have affordable access to lifesaving treatment.

III. BACKGROUND OF ALLEGED INVENTION

16. 3658/KOLNP/2009 titled 'Nucleoside Phosphoramidate Prodrugs' filed in India on 20 October 2009 is the national phase of WO 2008/121634, filed on March 26, 2008 and published on 9 October 2008. WO/121634 claims priority from three US provisional applications: US 60/909,315 dated 30 March 2007, US 60/982,309 dated 24 October 2007 and US 12/053,015 dated March 2008.

III.A. Nucleoside phosphoramidates were known

17. Admittedly, as of the earliest priority date, nucleoside phosphoramidates and their prodrugs were known substances.
18. At the time of the alleged invention, as will be explained below, the following were well known to persons skilled in the art:
 - (i) The Applicant in the present Specification admits that HCV NS5B polymerase is required for the synthesis of a double stranded RNA from a single stranded RNA that serves as a template in the replication cycle of HCV.[As admitted on page 3, para 2, *placitum* 15 of the Present Specification]
 - (ii) The applicant also admits that Inhibitors of HCV NS5B as potential therapies for HCV infection were known at [As admitted on page 6, para 4, *placitum* 18 of the Present Specification]
 - (iii) The fact that nucleoside inhibitors of NS5B polymerase can be taken up by cells and act as a chain terminator or as a competitive inhibitor which competes with the nucleotide binding to the polymerase was known and has been admitted in the present specification. It was also known that to function as a chain terminator the nucleoside analogue must be taken up by the cell

and converted *in vivo* to a tri phosphate. [As admitted on page 6, para 5, *placitum* 29 of the Present Specification]

- (iv) Nucleoside phosphoramidate prodrugs have been known to be precursors of the active nucleoside triphosphate and to inhibit viral replication when administered to viral infected whole cells. [As admitted by the Applicant on page 7, para 2, *placitum* 13 of the Present Specification]

IV. SUMMARY OF CLAIMS

19. The claims of the present application can be summarised as follows:

- (i) Claim 1 relates to (S)-2-{[2R,3R,4R,5R]-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-yl-methoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester or a stereoisomer thereof, popularly known as sofosbuvir.
- (ii) Claim 2 is dependent on claim 1 and relates to a composition comprising the compound claimed in claim 1 and a pharmaceutical medium.
- (iii) Claims 3-5 relate to a method of treatment for HCV and other viruses with an effective amount of compound claimed in claim 1 and a pharmaceutically effective medium.
- (iv) Claim 6 relates to a process for preparing compound claimed in claim 1.
- (v) Claim 7 is a product by process claim relating to the compound or a stereoisomer thereof claimed in claim 1 obtained by a process as claimed in claim 6.
- (vi) Claim 8 is an independent claim claiming a diastereomer of the compound claimed in claim 1.
- (vii) Claim 9 is dependent on claim 8 and relates to the compound claimed in claim 8 and a pharmaceutically acceptable medium.

- (viii) Claim 10-12 relate to a method of treatment for HCV and other viruses with an effective amount of compound claimed in claim 8 and a pharmaceutically acceptable medium.
- (ix) Claim 13 relates to a process for preparing the compound claimed in claim 8.
- (x) Claim 14 relates to a product by process claim relating to the compound claimed in claim 8 with the process claimed in claim 13.

V. SUMMARY OF GROUNDS OF OPPOSITION

- 20. The Opponent brings this opposition under the following grounds, amongst others, each of which are without prejudice to one another:
- 21. Claims 1-3 & 8-10 the present application are not new, are anticipated and lack novelty, and therefore fail under Section 2(1)(j) of the Patents Act. Therefore, the Opponent brings this opposition under Section 25(1)(b)—that the invention so far as claimed in any claim of the complete specification has been published before the priority date in India or elsewhere in any document;
- 22. Claims 1 to 14 of the present application lack inventive step, and therefore fail under Sections 2(1)(j) and 2(1)(ja) of the Patents Act. Therefore, the Opponent brings this opposition under Section 25(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 before the priority date in India or elsewhere in any document;
- 23. Claims 1-3 and 8-10 of the present application do not satisfy the test of Section 3(d) of the Patents Act in as much as the subject matter does not exhibit enhanced therapeutic efficacy. Further, Claims 3 to 5 and 9 to 12 are drawn to a method of treatment or relate to excluded subject matter under Section 3(i) of the Patents Act. Therefore, the Opponent brings this

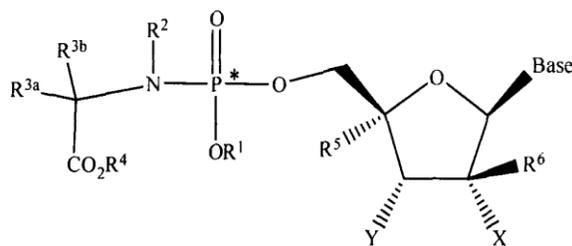
- opposition under Section 25(1)(f)—that the subject of any claim of the complete specification is not an invention within the meaning of this Act.
24. The complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed. Therefore, the Opponent brings this opposition under Section 25(1)(g) of the Act—that that complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed; and
25. The Patent Applicant has failed to comply with the requirements of Section 8 of the Patents Act. Therefore, the Opponent brings this opposition under Section 25(1)(h) of the Act—that the Patent Applicant has failed to disclose the Controller information required by Section 8 or has furnished information which in any material particular was false to his knowledge.

VI. DETAILED GROUNDS

VI.A. Claim 1-3 & 8-10 are not new, lack novelty, are anticipated by prior publication and, therefore, should be rejected under Section 25(1)(b)(ii) of the Patents Act.

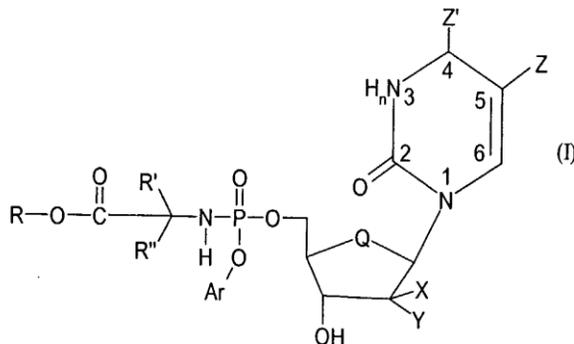
26. Section 2(1)(j) of the Patents Act defines an “invention” as “a *new* product or process involving an inventive step and capable of industrial application” (emphasis added). Section 25 (1)(b)(ii) provides a ground for opposition if the alleged invention, in so far as claimed in any claim of the complete specification, is not new, having been published before the priority date of the claim in India or elsewhere, in any other document. Thus, if a publication, published prior to the priority date of a patent application, discloses the claimed invention, then the claims of the patent application are not new, lack novelty, are anticipated by prior publication and must be rejected.
27. “Newness” or novelty is to be determined by comparing the claims of a patent application to the disclosures in the prior art, read in light of the general knowledge available to a person skilled in the art.

28. Without prejudice to other grounds raised herein, Claims 1 of the present application are not new, lack novelty and are anticipated by prior publication on account of the enabling disclosures of WO 2005/012327 published on 10 Feb 2005, (hereinafter referred to as the “‘327 Application”) a copy of which is hereto annexed and marked as “Exhibit A”.
29. The general formula of the alleged invention as disclosed in the Present application compared with the ‘327 application is reproduced below:



I

30. The first aspect of the ‘327 Application discloses a compound of the following formula [disclosed at internal page 3 of the specification]:



wherein:

R is selected from the group comprising alkyl, aryl and alkylaryl;

R' and R'' are, independently, selected from the group comprising H, alkyl and alkylaryl, or R' and R'' together form an alkylene chain so as to provide, together with the C atom to which they are attached, a cyclic system;

Q is selected from the group comprising -O- and -CH₂;

X and Y are independently selected from the group comprising H, F, Cl, Br, I, OH and methyl (-CH₃);

Ar is a monocyclic aromatic ring moiety or a fused bicyclic aromatic ring moiety, either of which ring moieties is carbocyclic or heterocyclic and is optionally substituted;

Z is selected from the group comprising H, alkyl and halogen; and n is 0 or 1, wherein

when n is 0, Z' is -NH₂ and a double bond exists between position 3 and position 4, and

when n is 1, Z' is =O;

or a pharmaceutically acceptable derivative or metabolite of a compound of formula I;

with the proviso that when n is 1, X and Y are both H, R is methyl (-CH₃), one of R' and R'' is H and one of R' and R'' is methyl (-CH₃), then Ar is not phenyl (-C₆H₅).

In this formula, the compound sofosbuvir is covered, since, R can be alkyl, R' and R'' can be -H and methyl respectively,

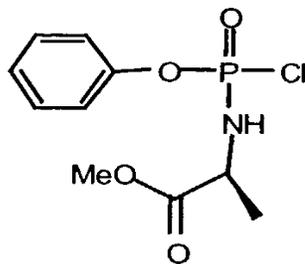
Q can be -O-

X and Y can be methyl and F

Ar can be an unsubstituted phenyl (C₆H₅) group:

N can be 1, Z' can be 0.

31. Further, on internal page 73, *placitum 5*, the '327 Application exemplifies the process involving synthesis of phosphoramidate esters containing alanine as the amino acid, and unsubstituted phenyl is clearly exemplified by the preparation and use of the following prodrug moiety into the base compound:

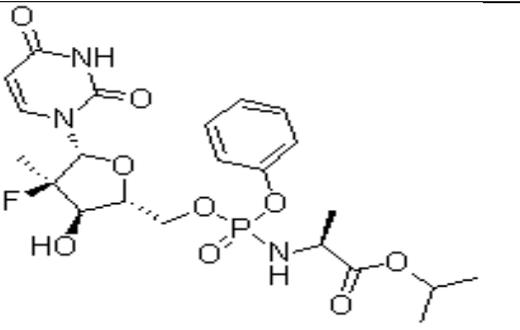
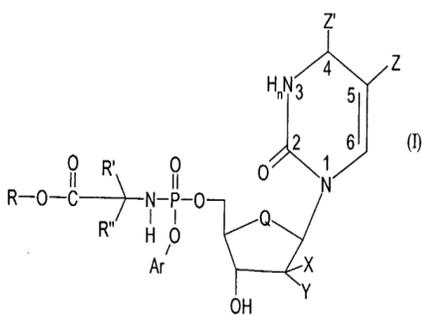


32. A comparison of the disclosures made in the Present application and the '327 Application is presented in a table below and clearly shows that '327 has disclosed the compound claimed in present specification:

Structure of compound in Claim 1	Formula disclosed in '327 Application
<p>Compound of choice in claim 1- (S)-2-{{[2R,3R,4R,5R]-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester</p>	<p>R =alkyl, aryl and alkylaryl; R' and R'' are, independently, selected from the group comprising H, alkyl and alkylaryl, or R' and R'' together form an alkylene chain so as to provide, together with the C atom to which they are attached, a cyclic system; Q is selected from a group comprising -O- and -CH₂ X & Y are independently selected from the group comprising H, F, Cl, Br, I, OH and CH₃: Ar is a monocyclic aromatic ring moiety or a fused bicyclic aromatic ring moiety, either of which ring moieties is carbocyclic or heterocyclic and is optionally substituted;</p>

	<p>Z is selected from the group comprising H, alkyl and halogen; and N is 0 or 1, Wherein when n is 0, Z' is NH₂ and a double bond exists between position 3 and position 4 and when n is 1, Z' is =O...</p>
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33. Claim 8 pertains to the stereoisomer of the compound claimed in claim 1. The said stereoisomer is also disclosed as is evident in the following comparison with the compound disclosed in '327 Application.

Structure of compound in Claim 8	Formula disclosed in '327 Application
	
<p>Compound of choice in claim 8- dihydropyrimidin-1 (2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl) methoxy)(phenoxy)phosphoryl)amino)propanoate</p>	<p>R =alkyl, aryl and alkylaryl; R' and R'' are, independently, selected from the group comprising H, alkyl and alkylaryl, or R' and R'' together form an alkylene chain so as to provide, together with the C atom to which they are attached, a cyclic system; Q is selected from a group comprising -O- and -CH₂ X & Y are independently selected from the group comprising H, F, Cl, Br, I, OH and CH₃; Ar is a monocyclic aromatic ring moiety or a fused bicyclic aromatic ring moiety, either of which ring moieties is carbocyclic or heterocyclic and is optionally substituted;</p>

	<p>Z is selected from the group comprising H, alkyl and halogen; and N is 0 or 1, Wherein when n is 0, Z' is NH₂ and a double bond exists between position 3 and position 4 and when n is 1, Z' is =O...</p>
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34. Therefore, in light of the disclosures made in the '327 Application which match all features in the structure of the Present Application showing that the compound claimed in claim 1 & 8 are not novel.
35. Therefore, Claim 1 & 8 of the present application are not new, lack novelty and are anticipated by the enabling disclosures of the '327 Application. Claims 2-5 which relate to a composition involving the claimed compound, method of treatment involving the claimed compound, too cannot be considered new.

VI.B. Claims 1 to 14 are obvious, do not involve a technical advance and lack inventive step as defined under Section 2(1)(ja) and are, therefore, should be rejected under Section 25(1)(e) of the Patents Act.

36. Section 2(1)(j) defines an "invention" as "a new product or process involving an *inventive step* and capable of industrial application". (emphasis added). Therefore, all alleged inventions, in order to qualify for a patent, must satisfy the criteria of inventive step. Section 2(1)(ja) of the Patents Act defines an inventive step as "a feature of an invention that involves technical advance as compared to the existing knowledge ... and that makes the invention not obvious to a person skilled in the art".
37. Sub-sections (j) and (ja) of Section 2(1) of the Patents Act thus require a Patent Applicant to show that the feature of the alleged invention involves a technical advance and that it is not obvious to a person skilled in the art. These requirements are laid down to ensure that patents, which result in a monopoly, are granted only to genuine inventions.

38. Section 25(1)(e) of the Patents Act provides a ground for opposition if the alleged invention is obvious and does not involve an inventive step having regard to matter published, as described in Section 25(1)(b) of the Patents Act. Section 25(1)(b) sets out that such published matter includes matter published in India or elsewhere in any document before the priority date of the alleged invention.
39. According to the Complete Specification, the alleged invention essentially relates to a Nucleoside phosphoramidate prodrugs. These are found to be effective in the treatment of HCV.
40. The present specification claims 1- (S)-2- {[2R, 3R, 4R, 5R)-5-(2, 4-Dioxo-3, 4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydrofuran-2-yl methoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester. The said compound is a nucleoside derivative which, for the sake of convenience, can be broken down into the following structural entities:

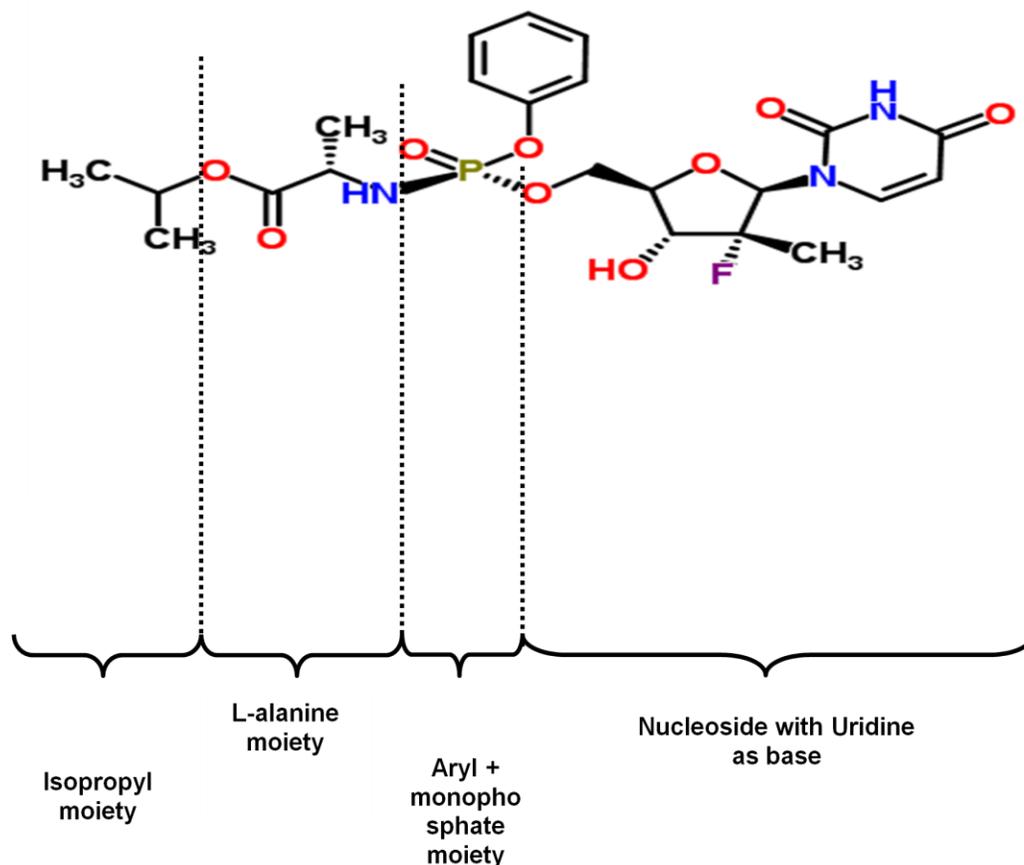
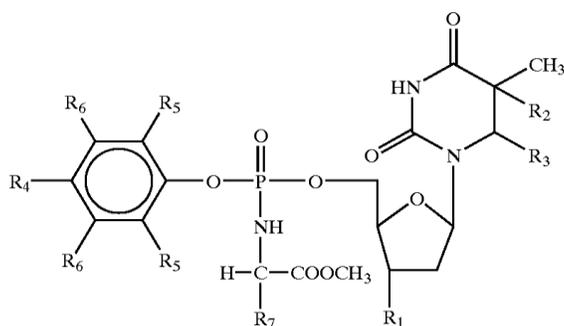


Figure 1: Structural components of sofosbuvir

41. Nucleoside analogue drugs which are long known for their application in competitive inhibition/ chain termination and resultant antiviral effect, have been used in the treatment of cancers and HIV. AZT (INN name-zidovudine), the first revolutionary breakthrough drug approved for treatment of HIV was first synthesized back in 1964.
42. Due to poor oral bioavailability due to their high polarity and low intestinal permeability, nucleoside analogue prodrugs were employed to facilitate drug delivery. A class of prodrugs is aryl phosphoramidate

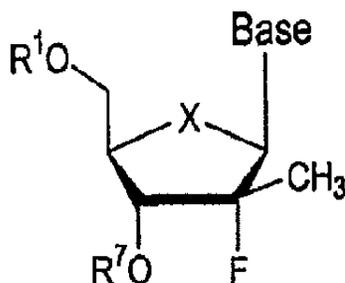
prodrugs which have been employed successfully Derivatives of AZT phosphomonoester amidate, for instance, were known for their efficacy in treatment of HIV as early as in the 1990s. US Patent US6482805 B2, titled ‘AZT derivatives exhibiting spermicidal and anti-viral activity’, published on Nov 19, 2002, discloses an AZT derivative of the following structure:



43. Substitutions on Aryl phosphoramidate prodrugs of nucleosides have been a subject of experimentation amidst scientists for both HIV and HCV. Motivation for application of these nucleoside prodrugs for treatment of *inter alia* Hepatitis C was also well grounded in the prior art. As will be explained in further detail below, the advantages associated with phosphoramidate prodrugs with above structural entities (Figure 1) to overcome the disadvantages of the kinase dependent phosphorylation in the cell for treatment of HCV were well known to a person skilled in the art.
44. Without prejudice to what is stated above under the ground of novelty, it is submitted that in light of the disclosures and teachings made by the ‘327 Application, the subject matter of the present application is rendered obvious.
45. In addition to that, US Patent WO 2005/003147 hereinafter the ‘147 Application published on 13 January 2005 a copy of which is hereto annexed and marked as “**Exhibit B**” at internal page 16, *placitum* 3-8 of the ‘147 specification discloses (2’R)-2’deoxy-2’-fluoro-2’-C-methyl nucleoside (β -D or β -L), or its pharmaceutically acceptable salt or prodrug thereof, and the use of such compounds for the treatment of Hepatitis C

etc. It is further stated that 2' substitutions on the β -D or β -L nucleosides impart greater specificity for hepatitis C virus as well as exhibiting lower toxicity. The reason for this specificity is the presence of a 2'-fluoro substitution on the ribose ring. [See *placitum* 16-28, internal page 16 of exhibit A]

46. Further, claim 6 of the '147 application discloses a (2'R)-2'-deoxy-2'fluoro-2'-C-methyl nucleoside (β -D or β -L) or its pharmaceutically acceptable salt or prodrug thereof of structure:



Wherein the base is a purine or a pyrimidine base;

X can be O,

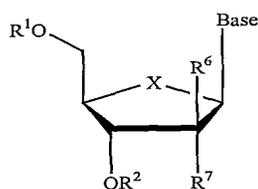
R¹ and R⁷ can be H, phosphate, including monophosphate, diphosphate, diphosphate, triphosphate or a stabilised phosphate prodrug.

The term "pharmaceutically acceptable salt or prodrug" has been described any pharmaceutically acceptable form (such as an ester, phosphate ester, salt of an ester or a related group) of a compound which, upon administration to a patient, provides the active compound. ...Typical examples of prodrugs include compounds that have biologically labile protecting groups on a functional moiety of the active compound. Prodrugs include compounds that can be oxidised, reduced, animated, deaminated, hydroxylated, hydrolyzed, dehydrolyzed, alkylated, dealkylated, acylated, phosphorylated, dephosphorylated to produce the active compound.

47. These prodrugs can include 5'-triphosphatetriphosphoric acid ester derivatives of the 5'-hydroxyl group of a nucleoside compound of the

present invention having the following general structural formula.[See internal page 42-43 of the '147 Application]

48. Further, "Any of the nucleosides of the claimed invention can be administered as a nucleotide prodrug to increase the activity, bioavailability, stability or otherwise alter the properties of the nucleoside"[See internal pages 45-48 of the '147 Application]. Pharmaceutical compositions based on β -D or β -L compound or its pharmaceutically acceptable salt of prodrug can be prepared in a therapeutically effective amount for treating a flaviviridae infection, including HCV. The '147 Application, therefore, teaches 2' substitution on the nucleoside tetrahydrofuran ring, biologically labile protecting moieties, and its delivery *in vivo* through a stabilised phosphate pro-drug and compositions involving the same.
49. WO 01/92282 A2 titled 'Methods and compositions for treating flaviviruses and pestiviruses', published on 6 December 2001, hereinafter '282 Application' a copy of which is attached herein and marked at '**Exhibit C**' also discloses fluorination at the 2' position in nucleoside analogs which can be delivered through stabilised phosphate prodrugs.
50. Embodiment XI of the '282 Patent discloses the compound of the following formula disclosed on internal page :



(XI)

Wherein:

Base is a purine or pyrimidine base as defined herein;

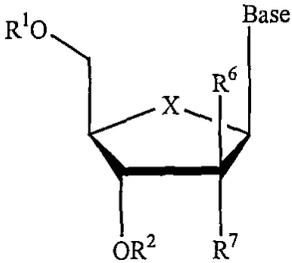
R¹, R² and R³ are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilised phosphate prodrug); acyl (including lower acyl); alkyl; alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and

benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an aminoacid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 , R^2 and R^3 is independently H or phosphate;

R^6 is hydrogen, hydroxyl, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(loweralkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2 , NH_2 , -NH(lower alkyl), -NH(acyl), -N(lower alkyl)₂, -N(acyl)₂

R^7 is hydrogen, OR^3 , hydroxyl, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(loweralkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2 , NH_2 , -NH(lower alkyl), -NH(acyl), -N(lower alkyl)₂, -N(acyl)₂; and

X is O, S, SO_2 or CH_2 which when substituted leads to the impugned compound claimed in claim 1 of the present application. A comparison of the structures of the claimed compound and the compound disclosed in the '282 application can be shown in the table below:

Structure of compound in Claim 1	Formula disclosed in '282 Application
	 <p style="text-align: center;">(XI)</p>

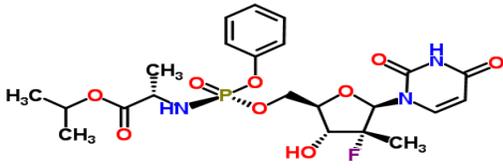
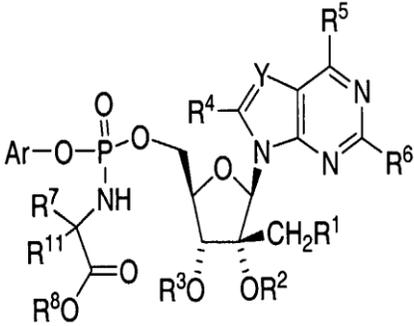
Compound of choice in claim 1- (S)-2-
{[2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-
dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-
hydroxy-4-methyl-tetrahydro-furan-2-
ylmethoxy]-phenoxy-phosphorylam-
ino}-propionic acid isopropyl ester

Base is a purine or **pyrimidine**
base as defined herein;
R₁, R₂ and R₃ are independently H;
phosphate (including
monophosphate, diphosphate,
triphosphate, or a stabilised
phosphate prodrug); acyl
(including lower acyl); alkyl);
alkyl (including lower alkyl);
sulfonate ester including alkyl or
arylalkyl sulfonyl including
methanesulfonyl and benzyl,
wherein the phenyl group is
optionally substituted with one or
more substituents as described in
the definition of aryl given herein;
a lipid, including a phospholipid;
an amino acid; a carbohydrate; a
peptide; a cholesterol; or other
pharmaceutically acceptable
leaving group which when
administered *in vivo* is capable of
providing a compound wherein R₁,
R₂ or R₃ is independently **H** or
phosphate;
R₆ is **hydrogen**, hydroxyl, alkyl
(including lower alky), azido,
cyano, alkenyl, alkynyl, Br-vinyl, -
C(O)O(lower alkyl), -O(acyl),
_O(lower acyl), -O(alkyl), -
O(loweralkyl), -O(alkenyl),
chloro, bromo, **fluoro**, iodo, NO₂,
NH₂, -NH(lower alkyl), -
NH(acyl), -N(lower alkyl)₂, -
N(acyl)₂
R₇ is hydrogen, OR₃, hydroxyl,
alkyl (including lower alkyl),
azido, cyano, alkenyl, alkynyl, Br-
vinyl, -C(O)O(alkyl), -O(acyl),
_O(lower acyl), -O(alkyl), -
O(loweralkyl), -O(alkenyl),
chlorine, bromine, iodine, NO₂,
NH₂, -NH(lower alkyl), -
NH(acyl), -N(lower alkyl)₂, -
N(acyl)₂; and
X is **O**, **S**, **SO₂** or **CH₂**

The '282 Application, therefore teaches 2' substitutions on nucleoside sugars and a delivery mechanism through a stabilised phosphate prodrug.

Nucleoside aryl phosphoramidates as precursors of potent inhibitors known

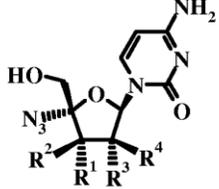
51. WO 2006/012078 titled 'Nucleoside aryl phosphoramidates for the treatment of RNA- Dependent RNA viral infection', hereinafter '078 Application which was published on 02 February 2006 a copy of which is attached and marked herein as "**Exhibit D**" discloses nucleoside aryl phosphoramidates as precursors to potent inhibitors of RNA dependent RNA viral replication. [See internal page 2 of the '078 Application]. The application further discloses that these nucleoside phosphoramidates are useful to treat in particular HCV infection. The structural formula of the nucleoside aryl phosphoramidates is disclosed on internal page 4 of the '078 Application and is reproduced herein below:

Structure of compound in Claim 1 of the present application	Formula disclosed in '078 Application
	 <p style="text-align: center;">(I)</p>

52. These aryl phosphoramidates can act as prodrugs of the corresponding nucleoside 5'- monophosphates. Endogenous kinase enzymes convert the 5'- monophosphates into their 5'- triphosphate derivatives which are the inhibitors of the RNA polymerase. [See internal page 5 of the '078 Application]. The process for preparation of these nucleoside aryl

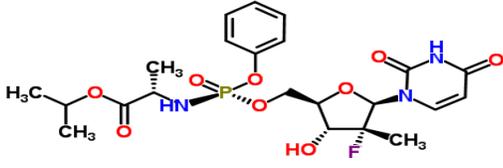
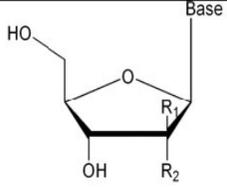
phosphoramidates is disclosed on internal page 22-26 of the '078 Application.

53. The '078 Application therefore teaches the role of nucleoside aryl phosphoramidates as prodrugs of corresponding nucleosides, its method of preparation and its application in the treatment of HCV.
54. WO 2007/020193, titled 'Antiviral Phosphoramidates', hereinafter '193 Application which was published on 22 February, 2007 a copy of which is attached and marked herein as "**Exhibit E**" teaches modification of furanose ring of the nucleosides to have afforded them with antiviral activity and discloses that modification of 2' and the 3'- position has been extensively investigated. [See internal page 3 of the '193 Application]. It is also disclosed that phosphoramidate derivatives of 4'- substituted on nucleoside compounds have improved physicochemical and pharmacokinetic properties. [See internal page 5 of the '193 Application]

Structure of compound in Claim 1 of the present application	Substitution at 2' and 3' disclosed in '193 Application
	 <p>2a: R¹ = OH, R² = R³ = R⁴ = H 2b: R³ = OH, R¹ = R² = R⁴ = H 2c: R³ = OH, R² = F, R¹ = R⁴ = H 2d: R¹ = R² = H, R³ = R⁴ = F 2e: R¹ = OMe, R³ = OH, R² = R⁴ = H</p>

55. The '193 Application therefore teaches that the modification of the furanose ring affords antiviral activity and modifications at 2' and the 3'- position is an area of interest in context of developing nucleoside inhibitors for treatment of HCV.
56. Eisuke Murakami *et al*, 'Mechanism of Activation of β -D-2'- Deoxy-2'- Fluoro-2'-c-Methylcytidine and Inhibition of Hepatitis C virus NS5B RNA

polymerase' Antimicrobial Agents and Chemotherapy, published on 13 November 2006, a copy of which is attached and marked herein as "**Exhibit F**" explores the antiviral activity of β -D-2'- Deoxy-2'- Fluoro-2'- c-Methylcytidine and identifies it as a potent specific inhibitor of HCV RNA replication which also contains 2'- fluoro substitution.

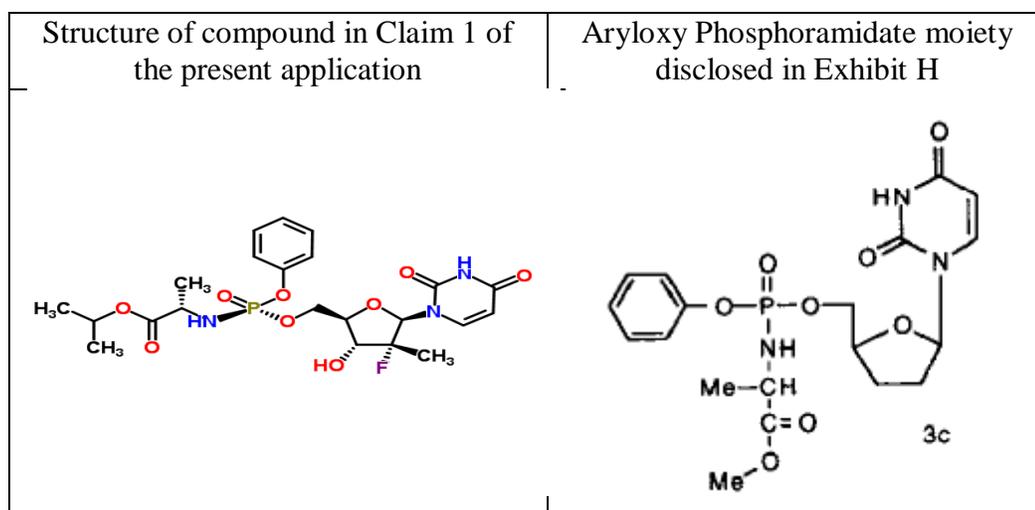
Structure of compound in Claim 1 of the present application	Fluoro substitution at 2' disclosed in Exhibit F																												
	 <table border="1" data-bbox="901 798 1356 987"> <thead> <tr> <th>Compound</th> <th>R₁</th> <th>R₂</th> <th>Base</th> </tr> </thead> <tbody> <tr> <td>PSI-6130</td> <td>CH₃</td> <td>F</td> <td>C</td> </tr> <tr> <td>2'-C-Me-C</td> <td>CH₃</td> <td>OH</td> <td>C</td> </tr> <tr> <td>2'-C-Me-A</td> <td>CH₃</td> <td>OH</td> <td>A</td> </tr> <tr> <td>2'-C-Me-dC</td> <td>CH₃</td> <td>H</td> <td>C</td> </tr> <tr> <td>2'-F-dC</td> <td>H</td> <td>F</td> <td>C</td> </tr> <tr> <td>Gemcitabine</td> <td>F</td> <td>F</td> <td>C</td> </tr> </tbody> </table>	Compound	R ₁	R ₂	Base	PSI-6130	CH ₃	F	C	2'-C-Me-C	CH ₃	OH	C	2'-C-Me-A	CH ₃	OH	A	2'-C-Me-dC	CH ₃	H	C	2'-F-dC	H	F	C	Gemcitabine	F	F	C
Compound	R ₁	R ₂	Base																										
PSI-6130	CH ₃	F	C																										
2'-C-Me-C	CH ₃	OH	C																										
2'-C-Me-A	CH ₃	OH	A																										
2'-C-Me-dC	CH ₃	H	C																										
2'-F-dC	H	F	C																										
Gemcitabine	F	F	C																										

57. Murakami *et al*, therefore expressly teaches fluoro substitution at 2' position on the furanose ring as one of the preferred embodiments.

Effectiveness of masking is known

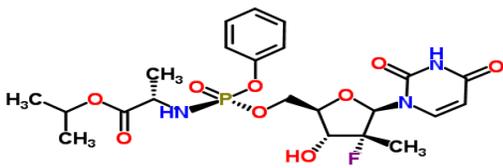
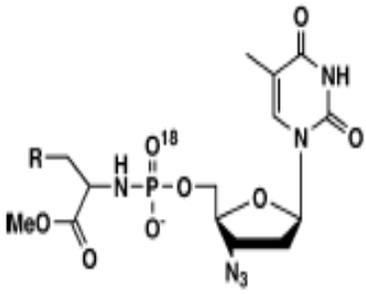
58. Christopher P. Landowski *et al*, 'Targeted delivery to PEPT1-overexpressing cells: Acidic, basic, and secondary floxuridine amino acid ester prodrugs' Molecular Cancer Therapeutics, published in or about April 2005 a copy of which is attached and marked herein as "**Exhibit G**" teaches that prodrug strategies are generally adopted to improve the undesirable properties of therapeutic drugs to overcome barriers, such as poor oral absorption, chemical instability, and toxicity. [See internal page 664]. Landowski *et al*, therefore motivates a person skilled in the art to adopt prodrug strategies to improve disadvantages in undesirable properties of therapeutic drugs.
59. Christopher McGuigan, *et al* in 'Certain phosphoramidate derivatives of dideoxy uridine (ddU) are active against HIV and successfully by-pass

thymidine kinase', FEBS Letter 351, published on 29 August 1994, a copy of which is attached and marked herein as "**Exhibit H**" discloses that masking of the phosphate groups in nucleoside analogues is known to improve their therapeutic potential. Especially in nucleoside analogue dideoxy uridine, judicious phosphorylation in which leads to the introduction of a significant antiviral effect which is retained in thymidine kinase-deficient cells indicating a successful bypass of this enzyme. The success of this strategy is reported with aryloxy phosphoramidates. [See internal page 11, column 1& 2]. It is further reported that the aryloxy phosphoramidate is a potent agent, being approximately 50 – times more active than the parent nucleoside analogue. [See internal page 13, column 2]



60. Christopher McGuigan, *et al*, therefore motivates a person skilled in the art to employ aryloxy phosphoramidate prodrugs to penetrate cell membranes and liberate bio-active nucleosides intracellularly.
61. Jisook Kim *et al*, 'Direct Measurement of Nucleoside Monophosphate Delivery from a Phosphoramidate Pronucleotide by stable isotope labelling and LC-ESI-MS/MS', Molecular Pharmaceutics, published in or about March 2004, a copy of which is attached and marked herein as "**Exhibit I**" teaches that amino acid phosphoramidates of nucleosides

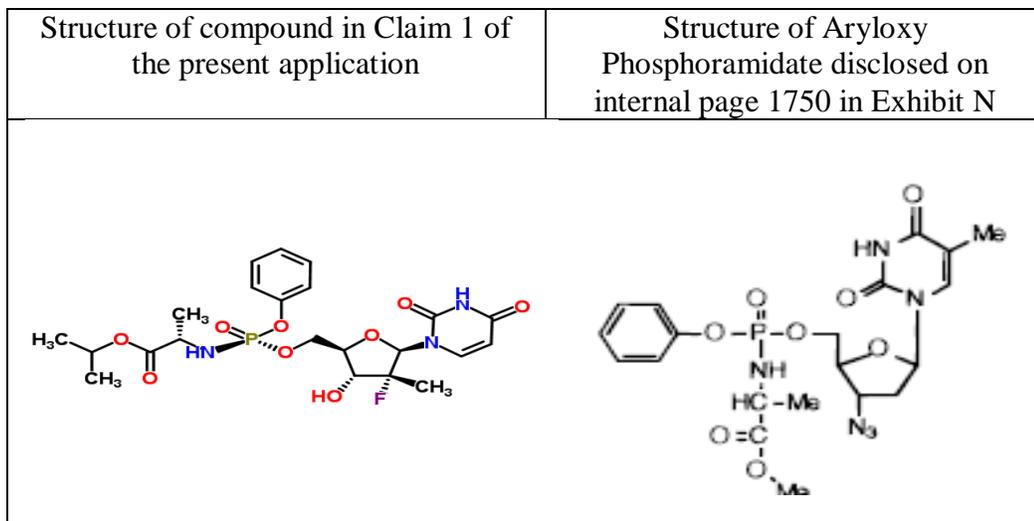
have been shown to be potent antiviral and anticancer agents with the potential to act as nucleoside monophosphate prodrugs. [see Abstract, *ibid*] It further discloses that the pronucleotide approach as a solution to overcome metabolic instability of nucleotide monophosphates and their incapability of crossing cellular membranes. [See internal page B column 1 and 2, internal page C, column 1]

Structure of compound in Claim 1 of the present application	AZT Amino acid phosphoramidate disclosed in Exhibit I
	

Therefore, Jisook Kim *et al*, motivates a person skilled in the art to prefer amino acid phosphoramidate as prodrugs for delivery of nucleoside monophosphates.

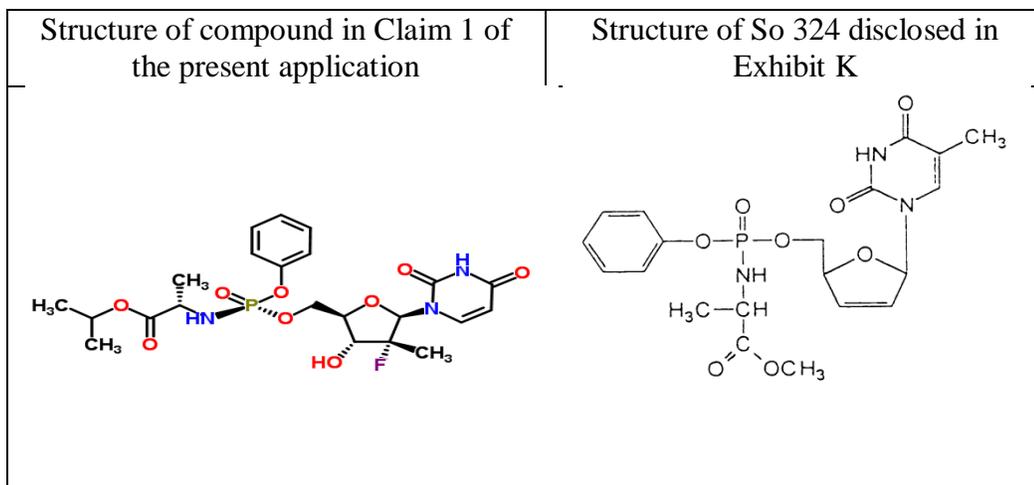
62. Christopher McGuigan *et al*, 'Aryl Phosphoramidates of d4T have improved anti-HIV efficacy in tissue culture and may act by the general of novel intracellular metabolite', Journal of Medicinal Chemistry, published on 12 April 1996, a copy of which is attached and marked herein as "**Exhibit J**" suggests overcoming of dependence on nucleoside kinase activation by the development of a suitable nucleotide development strategy with (aryloxy) phosphoramidates derived from AZT. These phosphoramidates retained good activity in thymidine kinase deficient cells, by comparison to thymidine competent cells. [See internal page 1748]. Christopher McGuigan *et al*, therefore teaches better activity

aryloxy phosphoramidates in thymidine kinase deficient cells in comparison to thymidine dependent cells.



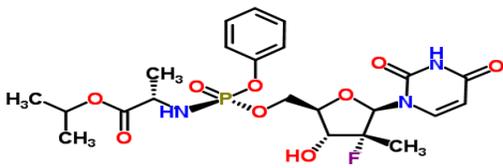
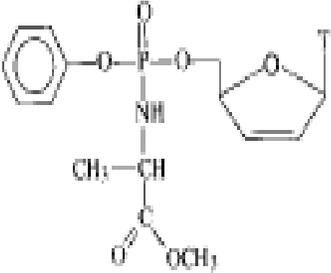
Specific Amino acids involved in the masking were known

63. J. Balzarini *et al*, 'Mechanism of anti-HIV action of masked alaninyl d4T-MP derivatives', Proc Natl Acad Sci U S A. published on in or about July 1996, a copy of which is attached and marked herein as "**Exhibit K**" discloses that alaninyl d4T-MP reached about 13-fold higher levels in So324-exposed cells than d4T-MP which means that the presence of alanine increased the activity of the monophosphate. [See internal page 7928, column 2]



J. Balzarini *et al*, therefore teaches a person skilled in the art to choose alanine over other amino acids while choosing the amino acid moiety.

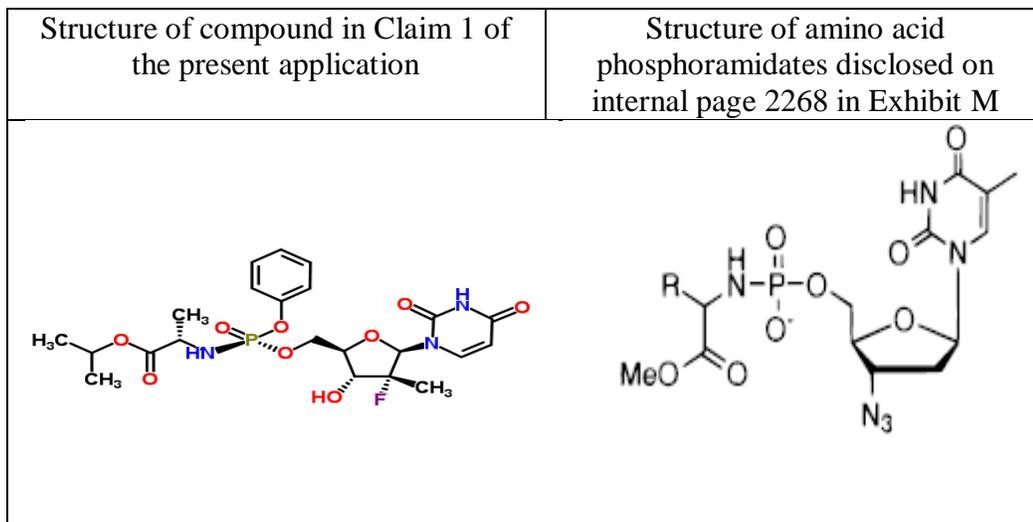
64. Dider Saboulard *et al*, 'Characterization of the activation pathway of phosphoramidate trimer prodrugs of stavudine and zidovudine', *Molecular Pharmacology*, which was published on 1 October 1999, a copy of which is attached and marked herein as "**Exhibit L**" discloses that while selecting of phosphoramidate trimer derivatives of d4TMP and AZTMP, carrying different were evaluated for their antiviral activity and it was found that L- alanine was shown to be the preferred amino acid. The L- alanine compound was found to be 40-, >3000-, and 80 fold more active than the corresponding D- alanine, β - alanine, or glycine prodrugs.[See internal page 696, column 2]

Structure of compound in Claim 1 of the present application	Methyl L- alanine derivative of d4TMonoPhosphate disclosed in Exhibit L
	

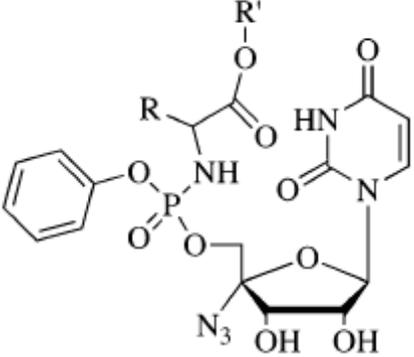
Dider Saboulard *et al*, therefore teaches a person skilled in the art to prefer the L- alanine moiety over other stereoisomeric forms.

65. Vidhya V. Iyer, *et al* 'Synthesis, *in vivo* anti-breast cancer activity, and intracellular decomposition of amino acid methyl ester and alkyl amide phosphoramidate monoesters of 3'-azido-3'-deoxythymidine (AZT)', *Journal of Medicinal Chemistry*, which was published on 21 April 2000, a copy of which is attached and marked herein as "**Exhibit M**" suggests

various phosphoramidate monoesters containing amino acid methyl ester and N-alkyl amide moieties were found to be more cytotoxic. A marked stereochemical preference of L-amino acid was observed. [See internal page 2266]. Vidhya V. Iyer, *et al*, therefore further teaches the person skilled in the art to prefer the L-alanine stereoisomeric form in the phosphoramidate monoesters.



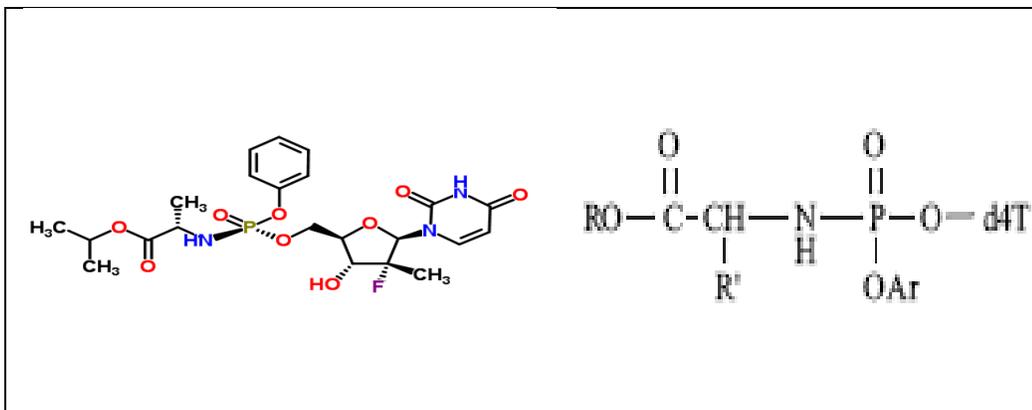
66. Plinio Perrone, 'Application of the phosphoramidate ProTide approach to 4'-Azidouridine confers sub-micromolar potency versus Hepatitis C virus on an inactive nucleoside', *Journal of Medicinal Chemistry*, which was published on 17 March 2007, a copy of which is attached and marked herein as "**Exhibit N**" suggests aryloxy phosphoramidate ProTide approach which allows the bypass of the initial kinase dependence of intracellular delivery of the monophosphorylated nucleoside analogue as a membrane permeable "ProTide" form leads to improved activity over the parent compound. [See internal page 1]. Moreover, the ProTide prodrugs tested by the authors included the alanine isopropyl ester as the phosphoramidate. [See internal page 4, table 1 compound 14]. This document therefore teaches both aryloxy phosphoramidates and the L-alanine moiety under the ProTide approach.

Structure of compound in Claim 1 of the present application	Structure of 4'-Azidouridine phenyl phosphoramidate disclosed on internal page 1841 in Exhibit N
	

This document too, therefore teaches a person skilled in the art to prefer the L-alanine form for masking the monophosphorylated nucleoside analogue.

67. Dominique Cahard *et al*, 'Aryloxy Phosphoramidates Triesters as ProTides, Mini-Reviews in Medicinal Chemistry, published in or about May 2004, a copy of which is attached and marked herein as "**Exhibit O**" discloses that aryloxy phosphoramidates are highly active antivirals. There is a preference for alanine, wherein a preference for L- alanine over D- alanine (5-60), a preference for one phosphonate diastereomer over the other was observed. [See internal page 376-378]. Dominique Cahard *et al*, also, therefore, teaches a preference for L- alanine.

Structure of compound in Claim 1 of the present application	Structure of Aryloxy Phosphoramidate disclosed on internal page 379 in Exhibit O
-------------------------------------------------------------	----------------------------------------------------------------------------------



68. WO 2006/067606 published on 29 June 2006, a copy of which is attached and marked herein as "**Exhibit P**" discloses nucleoside derivatives as antiviral drugs against flaviviridae, especially HCV. [See internal page 5, *placitums*31-37]. The '606 application further discloses alanine esters as potential prodrugs. The '606 application therefore discloses alanine esters as potential prodrugs.
69. WO 2002/08241 published on 31 January 2002 a copy of which is attached and marked herein as "**Exhibit Q**" discloses identical prodrug and diastereomers as claimed in the '3658 application and provides the procedure of the diastereomer separation. [See internal page 30-33].

Summary

70. In light of the above, it becomes clear that 2' substitution at the tetrahydrofuran ring in the nucleoside base was known to increase antiviral activity in a nucleoside analog. For these nucleoside analogs to be delivered *in vivo*, there was sufficient motivation for the person skilled in the art to employ the use of an aryloxy phosphate prodrug including an L-alanine moiety using the Pro-Tide approach. Claims 1 to 14 of the present application are therefore obvious to a person skilled in the art. They do not involve any technical advance over the existing knowledge. They lack inventive step. The mere fact that routine tests and experiments would have to be conducted in order to verify the expected advantages does not confer inventive step to the alleged invention described in the present

application. Therefore, Claims 1 to 14 should be rejected under Section 25 (1)(e) of the Patents Act.

VI.C. Claims 1-3 and 8-10 fail under Section 3(d), are not an invention within the meaning of this Act and should be rejected under Section 25(1)(f) of the Patents Act.

71. Section 25(1)(f) of the Patents Act provides a ground for opposition if the subject matter of any claim of the Complete Specification is not an invention within the meaning of the Act.
72. Under Section 3(d) of the Patents Act, a new form of a known substance is not an invention unless it results in enhancement of efficacy over the known efficacy of the known substance. The explanation to Section 3(d) states that combinations of known substances are to be considered to be the same substance.
73. Section 3(d) of the Patents Act was amended in 2005 to prevent patents on modifications of known substances, such as combinations and salts, esters, ethers and other derivatives of known substances. Under the law, each product claim that relates to a new form of a known substance has to satisfy Section 3(d) of the Patents Act.
74. It is an established position of law that Section 3(d) has to be satisfied independently of Sections 2(1)(j) and 2(1)(ja) [*see Novartis AG v. Union of India and others*, (2013) 6 SCC 1].
75. As held by the Hon'ble Madras High Court, the burden of proof is on the patent applicant to satisfy the requirements of Section 3(d), i.e. that of showing enhanced efficacy [*see Novartis AG and another v. Union of India and others*, (2007) 4 MLJ 1153, para 13]. As held by the Hon'ble Intellectual Property Appellate Board, this data is required to be in the Complete Specification [*Novartis AG v. Union of India and others*, MIPR 2009 (2) 0345, para 9(xvii)].

76. It is also an established position of law that the term “efficacy” in Section 3(d) means therapeutic efficacy for pharmaceutical products [*see Novartis AG v. Union of India and others*, (2013) 6 SCC 1].
77. Christopher Mcguigan *et al*, ‘Phosphoramidate derivatives of stavudine as inhibitors of HIV: unnatural amino acids may substitute for alanine’, published in or about April 2000, a copy of which is attached and marked herein as "**Exhibit R**" discloses that aryl substitution, carboxyl ester variation has little impact on the antiviral activity of aryl phosphoramidates. It therefore emerges that the L-alanine moiety is the key determinant of intracellular phosphate delivery.
78. There are numerous alternative amino acid moieties for a person skilled in the art to investigate. For instance, a variety of alternative unnatural amino acid moieties including α -n-alkylglycine, α -phenylglycine or α,α -sym-n-alkyl-glycine are known [Exhibit R], L- valine, L- leucine, L-tyrosine, L- phenylalanine, L- tryptophan, D-phenylalanine, and D tryptophan [page 2267, column 1, *placitum* 24, Exhibit-M] etc.
79. In order to discharge the burden of Section 3(d), the Applicant ought to have compared therapeutic efficacy of at least one aryl phosphoramidate ester prodrug containing other amino acid moieties which has high efficacy with the present prodrug containing L- alanine amino acid moiety. The Patent Applicant has failed to discharge this burden. The only evidence that has been supplied is the evidence of antiviral effect through an HCV replicon assay. This evidence cannot be considered to be evidence of improvement in therapeutic efficacy over the phosphoramidate esters containing other amino acid moieties.
80. In the alternative, the alleged invention claimed in the present application amounts to a new use of a known substance described in ‘327 Application marked as Exhibit A which discloses the use of various phosphoramidate derivatives of nucleotides for use in the treatment of cancer.

81. In view of the above, the subject matter claimed in the present invention amounts to a new use of a known substance and therefore not an invention in accordance with Section 3(d) of the Patents Act.

VI.D. Claims 4- 5 and 11- 12 fail under Section 3(i) for being method of treatment claims and should be rejected under Section 25(1)(f) of the Patents Act.

82. Without prejudice to other grounds raised herein, the Opponent states that certain claims fail for falling within the proscription of method of treatment claims.

83. Section 3(i) of the Patents Act provides that any process for the medicinal, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment of human beings or any process for similar treatment of animals to render them free of disease or to increase their economic value or that of their products is not an invention within the meaning of the Patents Act. Section 25(1)(f) provides a ground for opposition if the subject of the claim is not an invention within the meaning of the Patents Act.

84. Claims 3 relates to the method of treating a Hepatitis C virus with a composition containing the compound claimed in claim 1. Further claim 4 specifically relates to administering an effective amount of compound claimed in claim 1 for treatment of Hepatitis C virus, West Nile Virus, a yellow fever virus, a dengue virus, a rhinovirus, a poliovirus, a Hepatitis A virus, a bovine viral diarrhoea virus, and a Japanese encephalitis virus. Claim 5 specifically relates to a method of treating Hepatitis C virus with an effective amount of compound or a stereoisomer claimed in claim 1. Similarly claim 10 relates to a diastereomer of the compound claimed in claim 1 and claims 11 and 12 relate to a method of treating a number of viruses including Hepatitis C virus with an effective amount of compound claimed in claim 8.

85. Therefore, Claims 3 to 5 and 10 to 12 fail under Section 3(i) and ought to be rejected under Section 25(1)(f) of the Patents Act.

VI.F. The complete specification does not sufficiently and clearly describe the invention as claimed in Claims 2 & 9 and should be rejected under 25(1)(g) of the Patents Act.

86. Section 25(1)(g) of the Patents Act provides a ground for opposition if the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed.
87. Section 10(4) of the Patents Act requires the complete specification to fully and particularly describe the inventions and its operation or use.
88. Without prejudice to other grounds raised herein, the complete specification does not sufficiently and clearly describe all the claims of the present application.
89. Claim 2 and 9 relate to compositions comprising compounds or stereoisomers thereof and a pharmaceutically acceptable medium claimed in claims 1 and 8 respectively. The specification does not support the claims with adequate description as to how a person skilled in the art can arrive at the composition involving a pharmaceutically acceptable medium. The specification on page 662 broadly defines excipients, carriers and diluents with no specific identification the excipients/ carriers or diluents of the manner in which the compound claimed in claim 1 and 8 can be made into a composition.

VI.G. The Patent Applicant has not complied with the requirements of Section 8. Therefore, the present application should be rejected under Section 25(1)(h) of the Patents Act.

90. Section 25(1)(h) of the Patents Act provides a ground for opposition if the Patent Applicant has not furnished information required under Section 8 of the Patents Act, within the time prescribed by law.
91. Without prejudice to other grounds raised herein, the present application should be rejected because the Patent Applicant has not complied with the mandatory requirements of Section 8 of the Patents Act.

92. Section 8 of the Patents Act read with rule 12(1) of the Patents Rules requires, *inter alia*, a patent applicant, who is prosecuting, either alone or jointly with any other person, an application for a patent in any country outside India in respect of the same or substantially the same invention, to file a statement setting out the particulars of such application (Form 3) within six months of the date of filing of such application in India. Along with such statement, the patent applicant is also required to furnish an undertaking that, up to the grant, it would keep the Controller informed in writing, from time to time, of detailed particulars of applications filed in other jurisdictions after Form 3 was filed in India within six months of the date of such filing in other jurisdictions. This is done by filing Form 3 as prescribed by the Patents Rules. The Patent Applicant is also required to keep the Hon'ble Patent Controller informed of the developments of the corresponding or similar patent applications in other jurisdictions.
93. The prosecution history for the present application, available online on the IPAIRS website, shows that the Patent Applicant had not furnished the information required under Section 8 of the Patents Act, within the time prescribed by law. Thus, *prima facie*, the Patent Applicant has not complied with the requirements of Section 8 of the Patents Act.
94. In the present case, it appears that the latest Form 3 was filed by the Patent Applicant on 18 June 2013 which omits several substantially similar applications filed in 2009- 2013 in other countries/ jurisdictions, the particulars of these applications were not set out in Form 3 that was filed on 18 June 2013. These applications in other jurisdictions include:

Country	Date of filing	Application No.
Taiwan	1 February 2009	TW 200904453A
Argentina	23 September	AR 066898 A1

	2009	
Mexico	10 November 2009	MX200901040 1A
United States	21 January 2010	US2010/001625 1 A1
Republic of Korea	12 February 2010	KR2010001604 1
Israel	31 May 2010	IL201239 D0
Europe	7 July 2010	EP2203462 A2
Japan	14 October 2010	JP2010532747 A
China	15 December 2010	CN 101918425
Colombia	22 March 2011	CO 6260023
Russian Federation	10 May 2011	RU2009139968
United States	20 October 2011	US2011/025712 2A1
Israel	31 January 2012	IL 217228 D0
Taiwan	1 February 2012	TW 1357332 B
Republic of Korea	12 April 2012	KR2012003480 A
China	27 April 2012	SG 179445 A1
New Zealand	25 May 2012	NZ579880 A
Japan	28 June 2012	JP2012121903
Australia	16 August 2012	AU2008/23282 7B2
Malaysia	30 November	MY147409

	2012	
United States	18 December 2012	US8334270B2
Israel	31 December 2012	IL222810D0
United States	31 January 2013	US2013/002992 9A1
Israel	24 March 2013	IL201239

95. Post filing the last form 3, till date there have been more applications filed details of which are as below:

Country	Date of filing	Application No
Israel	29 August 2013	IL217228A
New Zealand	30 August 2013	NZ 599206
Japan	16 October 2013	JP5318085
United States	12 November 2013	US 8580765B2
United States	12 February 2014	US2014/0045783

96. Therefore, the Patent Applicant has failed to comply with the requirements of Section 8 of the Patents Act.
97. The Opponent submits that even if the Patent Applicant were to file any petition to condone the delay or irregularity caused by the delay in filing the information required under Section 8 of the Patents Act, such petition

must be decided in favour of the Patent Applicant only if it provides sufficient and clear and convincing reason for failure to provide the data within the time prescribed by the law. Such delay should not be condoned where the Patent Applicant has failed to exercise due diligence, has been negligent or has delayed the submission of such information in a *mala fide* manner to prevent such information from being available to the Patent Office. Otherwise, the provisions of Section 8 of the Patents Act read with rule 12 of the Patents Rules that mandates timely filing will be rendered otiose. The Patent Applicant should be put to the strict proof of its pleadings in any such application/petition.

98. Therefore, in view of the fact that the Patent Applicant has evidently not complied with the requirements of Section 8 of the Patents Act, the Patent Application should be rejected under Section 25(1)(h) of the Patents Act.

VII. HEARING REQUESTED

99. The Opponents hereby request a hearing under Section 25(1) of the Patents Act and rule 55 of the Patents Rules.

VIII. CONCLUSION

100. Given all of the foregoing, the Opponents humbly pray:
- (i) For an order rejecting patent application 3658/KOLNP/2009 for reasons as stated above:
 - (ii) For such further and other orders as may become necessary in the facts and circumstances of the case or in the interest of justice, equity and good conscience.

Drafted by: Ms. Geetanjali Sharma, Advocate

Settled by: Mr. Anand Grover, Senior Advocate

Place: New Delhi

Date: 25 August, 2014

On Behalf of _____

(Eldred Tellis, Authorised signatory, Sankalp Rehabilitation Trust)

On Behalf of _____

(Ketholelie Angami, Authorised signatory, HepCon)

On Behalf of _____

(Shibananda Sharma Phurailatpam, Authorised signatory, APN+)