

FORM 7A
THE PATENTS Act, 1970 (39 of 1970)
AND
THE PATENTS RULES, 2003
REPRESENTATION FOR OPPOSITION TO GRANT OF PATENT
[Section 25(1) and rule 55]

We, **Sankalp Rehabilitation Trust, Hepatitis Coalition of Nagaland (HepCoN) and Asia Pacific Network of People Living with HIV/AIDS (APN +)** hereby give representation by way of opposition to the grant of patent in respect of application no. **853/DELNP/2009** dated **05th February, 2009** made by Bristol-Myers Squibb Company and published on **12th June, 2009** on the grounds of section **25 (1)(e), 25 (1) (f), 25 (1) (g) and 25 (1)(h).**

Our address for service and correspondence in India in respect of above application is –

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New Delhi -110 014. Phone No. : 011- 4680 5555, Fax No. : 011 – 2437 2236.

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Rameshwari,
Advocate,
Agent for the Opponents.

To,
The Controller of Patents,
The Patent Office,
Intellectual Property Office Building,
Plot No. 32, Sector 14,
Dwarka, New Delhi 110075.

Before the Controller of Patents, New Delhi

**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.
853/DELNP/2009 filed by Bristol-Myers Squibb
Company on 05th February 2009 titled “Hepatitis
C Virus Inhibitors.”**

AND

**In the matter of representation by way of
opposition by Sankalp Rehabilitation Trust,
Hepatitis Coalition of Nagaland (HepCoN) and
Asia Pacific Network of People Living with
HIV/AIDS (APN +).**

STATEMENT OF FACTS AND EVIDENCE

I. INTRODUCTION

1. The Opponents are community based, non-profit organizations representing the needs of people living with Hepatitis-C and HIV/AIDS.
2. 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.

3. 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.
4. 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.
5. 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.

6. 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

7. The present application relates to the inhibitors of the Hepatitis C Virus. Viral Hepatitis is a group of infectious disease, which can be caused by five Hepatitis viruses – Hepatitis A, B, C, D and E. Out of these, Hepatitis –C virus (HCV) is one of the major causes of both acute and chronic hepatitis infection and chronic hepatitis may develop into liver cirrhosis or liver cancer. The HCV is a blood borne virus and is commonly transmitted through blood transfusion, unsafe injection practices, and inadequate sterilization of medical equipment, unscreened blood and blood products.
8. According to the World Health Organization's Report in 2013, almost 170 million people across the globe are HCV infected almost 5 Lakhs deaths are reported per year due to HCV. In India alone, it is estimated that almost 12 million people are infected by the Hepatitis Virus out of which a majority suffers from chronic Hepatitis –C infection.
9. The present patent application pertains to antiviral compounds for the treatment of viral diseases, particularly Hepatitis C. The Hepatitis C Virus (HCV) is cleaved by viral proteases resulting in three structural proteins (core, E1 and E2) and six non-structural proteins (NS2, NS3, NS4A, NS4B, NS5A and NS5B).
10. The compounds disclosed in the present application are generally directed towards anti-viral compounds, and more specifically directed to compounds which can inhibit the function of the NS5A protein encoded by the HCV.
11. NS5A is a large phosphoprotein of unknown function. In the recent past, studies have suggested that the NS5A protein has a direct role in the replication of the HCV because of its great ability of adaptive mutations and stimulating HCV replication. It has been found in numerous studies that the NS5A also serves as a regulator of replication. Studies show that the NS5A interacts with many proteins in mitogenic (cell division) and apoptotic (cell death) signaling,

resulting in the modulation of cellular growth and survival that may be important for the development and maintenance of HCV persistent infection. The alteration of these pathways by NS5A may represent a causative link between HCV infection and hepatocellular carcinoma (HCC).

12. The exact mechanism of antiviral action of NS5A inhibitors is unknown and numerous studies show that they have multiple effects. The present patent application claims allegedly novel compounds which are directly acting antivirals that inhibit non-structural protein, NS5A.
13. Daclatasvir is one such antiviral drug and is an oral, once-daily, NS5A inhibitor with the broad coverage of HCV genotypes and is known to be most effective against genotype 1a and is believed to produce high rates of sustained virological response among patients with HIV and hepatitis C virus infection when taken in combination with other anti viral medicines.
14. While there are many approved medications available in the market, they are not accessible to the patients across the world. Increasingly, in India and throughout the developing world, there is an urgent need to secure an affordable source of Hepatitis –C medicines. At the current prices for many of Hepatitis-C medicines, however, the goal of providing continued lifesaving treatment to millions of those in need, remains far out of reach.
15. 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.
16. 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.

17. 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.
18. 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).
19. 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.
20. The Opponent firmly believes 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 Opponent, therefore, humbly requests 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

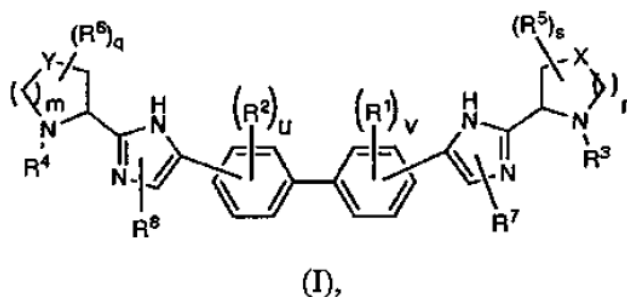
21. On 05th February 2009, the Patent Applicant filed the national phase entry of International Application No. PCT/US2007/075544 (international Publication No. WO/2008/021927) in India, which was subsequently allotted Indian Patent Application No. 853/DELNP/2009, i.e. the present Application. The said international application claims priority from a patent application filed in the United States on 11th August 2006, bearing US Application Serial No. 60/836,996 (hereinafter referred to as the "US '996 Application").
22. The present application relates to compounds useful for treating HCV-infected patients which inhibit HCV viral replication. In particular, the present application relates to direct acting antivirals that inhibit the non-structural protein, NS5A encoded by the Hepatitis-C Virus. The present application relates to a base compound of biphenyl-imidazole through a Markush claim, along with thousands of substituents which inhibit HCV replication by inhibiting NS5A protein.

IV. SUMMARY OF CLAIMS

23. The claims of the present application can be summarised as follows:
 - (i) Claim 1 is an independent claim and relates to a markush structure and claims several possible thousands of compounds.

A compound of formula (I) is reproduced below, from the claims for reference:

A compound of Formula (I)



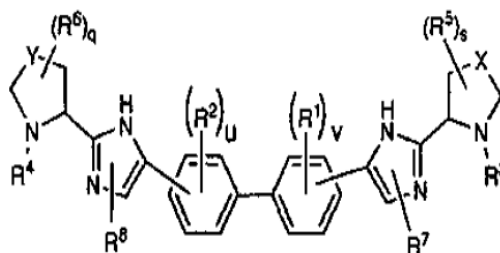
The claim includes biphenyl imidazoles and five membered-nitrogen containing rings with several possible variations through the Markush structure. Claim 1 also claims the pharmaceutically acceptable salts of the claimed compound.

- (ii) Claim 2 is dependent on claim 1 and claims the pharmaceutically acceptable salts of claim 1 wherein, from the variants of formula (I) *m* and *n* are each 1.
- (iii) Claim 3 is dependent on claim 1 and wherein *u* and *v* are independently selected from 0, 1 or 2 and R¹ and R² are selected from numerous substituents.
- (iv) Claim 4 is dependent on claim 1 where in *u* and *v* is selected from 0 or 1 and R¹ and/or R² are selected from halo when present. This claim also claims the pharmaceutically acceptable salt forms.
- (v) Claim 5 is dependent on claim 4 wherein the halo is fluoro.
- (vi) Claim 6 is dependent on claim 1 where in at least one of X and Y is S. This claim also claims the pharmaceutically acceptable salt forms of the disclosed compound.

- (vii) Claim 7 is dependent on claim 6 wherein X and Y are S. This claim also claims the pharmaceutically acceptable salt forms of the disclosed compound.
- (viii) Claim 8 is dependent on claim 1 wherein X is selected from CHR^5 , and $\text{C}(\text{R}^5)_2$, and Y is selected from CH_2 , CHR^6 , and $\text{C}(\text{R}^6)_2$ and also claims the pharmaceutically acceptable salt forms of the disclosed compounds.
- (ix) Claim 9 is dependent on claim 1 wherein R^7 and R^8 are independently selected from hydrogen, alkoxycarbonyl, carboxy, haloalkyl and $(\text{NR}^a\text{R}^b)\text{Carbonyl}$.
- (x) Claim 10 is dependent on claim 9 wherein R^7 and R^8 are hydrogen. This claim also claims the pharmaceutically acceptable salt forms of the claimed compound.
- (xi) Claim 11 is dependent on claim 1 wherein q and s are independently 0, 1 or 2 and R^5 and R^6 are selected from numerous substituents.
- (xii) Claim 12 is dependent on claim 1 wherein q and s are independently 0 or 1 and R^5 and R^6 represents and/or halo.
- (xiii) Claim 13 is dependent on claim 12 wherein, the halo is fluoro. This claim also claims the pharmaceutically acceptable salt forms of the claimed compound.
- (xiv) Claim 14 is dependent on claim 1 wherein at least one of R^3 and R^4 are hydrogen. This claim also claims the pharmaceutically acceptable salt forms of the claimed compounds.
- (xv) Claim 15 is dependent on claim 1, wherein R^3 and R^4 are each $\text{R}^9\text{-C(O)-}$. This claim also claims the pharmaceutically acceptable salt forms of the claimed compounds.
- (xvi) Claim 16 is dependent on claim 15, wherein each R^9 is selected from several substituents mentioned there under. This claim also claims the pharmaceutically acceptable salt forms of the said compound.

- (xvii) Claim 17 is an independent Markush claim called compound of formula II, and is represented below:

A compound of Formula (II)

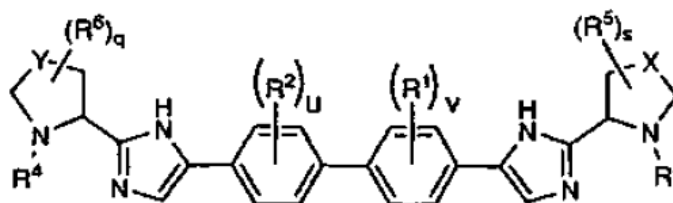


(II),

This claim provides for several possible substitutions through the elaborate Markush formula provided there under. This claim also claims the pharmaceutically acceptable salt forms of the thousands of compounds claimed through the Markush structure.

- (xviii) Claim 18 is another independent Markush claim of compound of formula III, with several possible thousands of compounds. The compound is reproduced below for reference.

A compound of Formula (III)

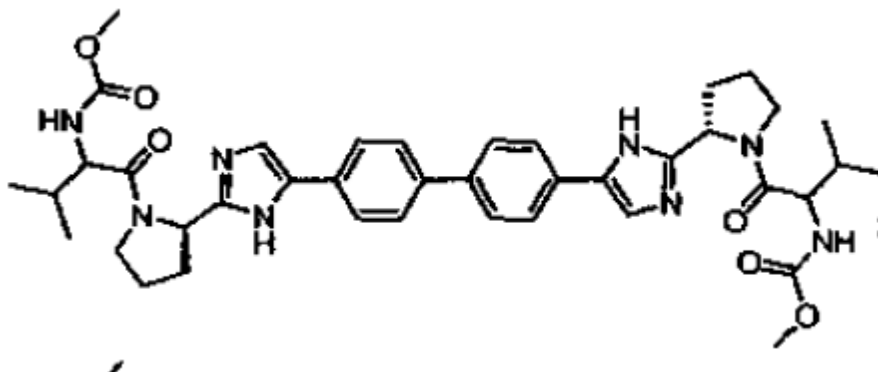


(III),

This claim also claims the pharmaceutically acceptable salt forms of the above disclosed thousands of compounds through the Markush formula.

- (xix) Claim 19 lists almost one thousand compounds by their IUPAC names along with their pharmaceutically acceptable salts.
- (xx) Claim 20 is an independent claim and lists several compounds by their structural representation along with their pharmaceutically acceptable salts.

Claim 20 is also claims a compound whose IUPAC name is - Methyl [(2*S*)-1-{(2*S*)-2-[4-(4'-{2-[(2*S*)-1-{(2*S*)-2-[(methoxycarbonyl)amino]-3-methylbutanoyl]-2-pyrrolidinyl]-1*H*-imidazol-4-yl}-4-biphenyl)-1*H*-imidazol-2-yl]-1-pyrrolidinyl}-3 methyl-1-oxo-2-butan-1-yl] carbamate which is otherwise commonly known as **Daclatasvir** of the following structure:



- (xxi) Claim 21 is an independent claim and lists various compounds by their IUPAC names along with their pharmaceutically acceptable salt forms.
- (xxii) Claim 22 is dependent on claim 21 and claims the pharmaceutically acceptable dihydrochloride salt forms of compounds in claim 21.
- (xxiii) Claims 23-34 are independent claims which claim different compounds and their pharmaceutically acceptable salt forms.
- (xxiv) Claim 35 is dependent on claim 1 and relates to a composition comprising the compound claimed in claim 1 or a pharmaceutically acceptable salt of claim 1 and a pharmaceutically acceptable carrier.
- (xxv) Claim 36 is dependent on claim 35 and comprises of a composition which includes compound claimed in 35 and one or two additional compounds having anti-HCV activity.
- (xxvi) Claim 37 is dependent on claim 36 and is a composition claim wherein the additional compounds having anti-HCV activity is an interferon or a ribavirin.

- (xxvii) Claim 38 is dependent on claim 37 and is a composition claim wherein the interferon is selected from interferon alpha 2 a, pegylated interferon alpha, consensus interferon, interferon alpha 2 a, and lymphoblastoid interferon tau.
- (xxviii) Claim 39 is dependent on claim 36 and is a composition claim where in one of the additional compounds having anti-HCV activity is selected from interleukin 2, interleukin 6, interleukin 12, a compound that enhances the development of a type 1 helper T-cell response, interfering RNA, anti-sense RNA, Imiquimod, ribavirin, an inosine 5- monophosphate dehydrogenase inhibitor and rimantadine.
- (xxix) Claim 40 is again dependent on claim 36 and is a composition claim wherein at least one of the additional compound is effective to inhibit the function of a target selected from HCV metalloprotease, HCV serine protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV NS5A protein, and IMPDH for the treatment of HCV infection.

V. SUMMARY OF GROUNDS OF OPPOSITION

24. The Opponent brings this opposition under the following grounds, amongst others, each of which are without prejudice to one another:
25. Claims 1-34 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;
26. Claims 20 and 22 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 over the efficacy of a known substance. 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.

27. Claims 35 to 40 fail under section 3(e) and are not an invention within the meaning of this Act and should to be rejected under section 25(1)(f) of the Patents Act.
28. Claims 1-34 fail under Section 10(4) (a), (b) and (c) of the Act and should therefore be rejected under section 25(1) (g) of the Patents Act. 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).
29. 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.

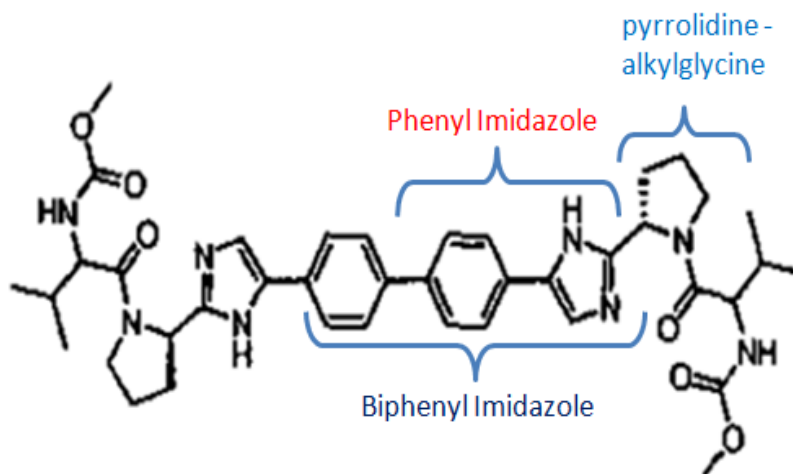
VI. DETAILED GROUNDS:

a. Claims 1 to 34 are obvious, do not involve a technical advance and lack inventive step as defined under Section 2(1)(ja) and should therefore, be rejected under Section 25(1)(e) of the Patents Act.

30. Section 2(1) (j) defines an “invention” as “a new product or process involving an inventive step and capable of industrial application”. 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”.

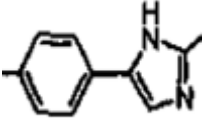
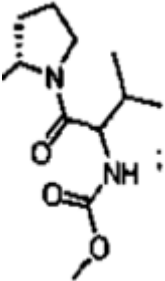
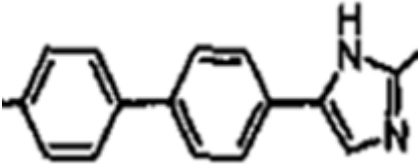
31. Sub-sections (j) and (ja) of Section 2(1) of the Patents Act thus require a Patent Applicant to show that the feature of the alleged invention involves a technical advance and that it is not obvious to a person skilled in the art. These requirements are laid down to ensure that patents, which result in a monopoly, are granted only to genuine inventions.
32. As stated previously, Daclatasvir has been claimed in claim 20 and the present application pertains to other biphenyl imidazole derivative compounds for the treatment of Hepatitis-C infection.
33. Daclatasvir can also be represented by the IUPAC name which is : Methyl[(2S)-1-{(2S)-2-[4-(4'-{2-[(2S)-1-{(2S)-2[(methoxycarbonyl) amino]-3-methylbutanoyl]-2-pyrrolidinyl]-1H-imidazol-4-yl}-4 biphenyl)-1H-imidazol-2-yl]-1-pyrrolidinyl}-3-methyl-1-oxo-2 butanyl] carbamate.
34. The said compound is a symmetrical compound which can be represented by the following structure:



35. The above structure can be divided into four parts but with two moieties as it is a symmetrical compound. The two moieties in the claimed compound are:
- (1) phenyl imidazole moiety

(2) pyrrolidine – alkylglycine moiety.

36. The structural moieties in the above structures are labelled below:

S. No.	Moiety	Structural depiction
1.	Phenyl Imidazole	
2.	Pyrrolidine – alkylglycine moiety	
3.	Biphenyl imidazole	

37. The present patent application relates to the moieties depicted above and notes that the moieties haven't been used before in treatment of Hep – C infection.

38. As stated by the applicants, the critical components of the compound include the following – (a) saturated N-containing rings, (b) addition of the pyrrolidine – alkylglycine components and (c) followed by inversion of configuration.

39. At the time of the alleged invention, as will be explained below, the following were well known to the persons skilled in the art (Supporting exhibits for all the statements are provided along with the explanations below):

A. Phenyl imidazole derivatives which inhibit HCV replication or inhibit the HCV protein were already known.

B. Pyyrolidine-alkylglycine components were already known and used for treatment of HCV.

C. Bis (phenyl –imidazole) derivatives were known for the treatment of Hepatitis-C Virus.

D. Mechanism used by the applicants to combine the symmetrical structure was a standard procedure which was known.

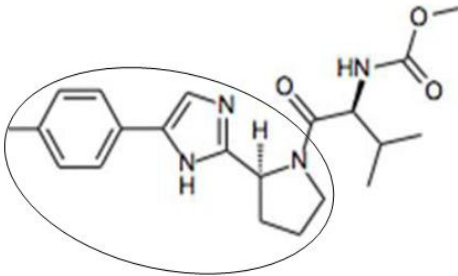
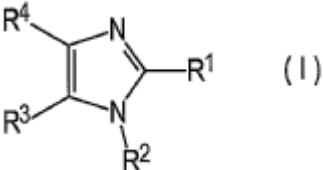
40. Using the above mentioned existing knowledge, the applicants in the present application have claimed alleged inventions. But, it will be shown further that the alleged invention claimed in the present application is obvious to a person skilled in the art and does not involve any technical advancement as compared to existing knowledge.

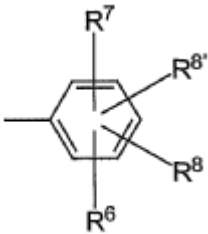
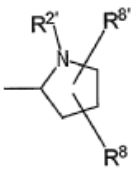
A. Phenyl imidazole derivatives which inhibit HCV replication or inhibit the HCV protein were already known.

41. *Firstly*, WO Patent Application 2004/005264 A2 titled ‘Imidazole compounds and human cellular protein kinases casein kinase I Alpha, Delta and Epsilon as targets for medical Intervention against Hepatitis C infections’ which bears an international publication date of 15th January 2004 (hereinafter referred to as the “WO ‘5264 application”), a copy of which is hereto annexed and marked as **Exhibit – A**, discloses imidazole compounds which are particularly useful against the Hepatitis C Virus infections by inhibiting the NS5A protein and also discloses the use of the compounds in other diseases associated therewith. The application furthermore relates to human cellular protein casein kinase I

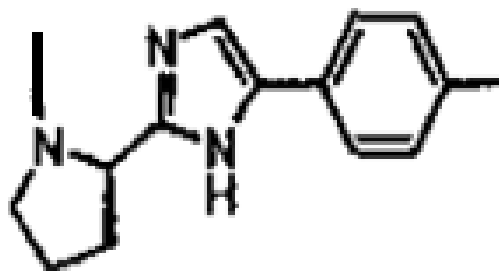
alpha (α), delta (δ) and epsilon (ϵ) as targets for medical intervention against HCV infections and diseases. Furthermore, it discloses methods for the identification of compounds which are useful for the prophylaxis and/or treatment of infections and diseases caused by the HCV, methods for treating HCV infections and diseases, as well as the pharmaceutical compositions useful for the prophylaxis and/or treatment of the HCV infections and diseases. It also discloses solid supports useful for the identification of compounds suitable for preventing and/or treating infections and diseases caused by said HCV. [See internal page 4]

42. The structure mentioned in the application is disclosed below and which is claimed in claim 1 of the present application: [See internal page 48-55]

Claimed Compound	Elements disclosed in '5264 Applicaiton.
	<p>The prior art discloses the claimed compound through the below mentioned Markush (See internal, Page 4, 8 and 9)</p> <div style="text-align: center;">  <p>(I)</p> </div> <p>R³ represents R^{1'}, -R^{1''} [.....]</p> <p>Wherein, R¹, R^{1'}, and R^{1''} represent independently of each other:</p>

	 <p>R¹ also represents the following structure:</p>  <p>R² represents – H.</p>
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43. From the reading of the Markush in the '5264 Application, when R^3 and R^1 are substituted from the Markush provided, the following structure and its derivatives are disclosed:



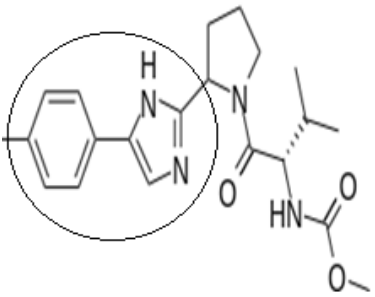
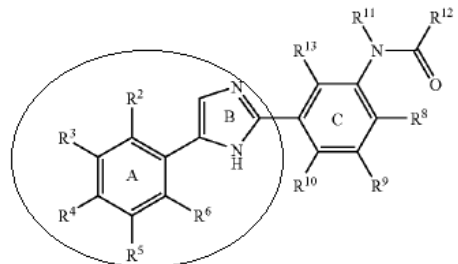
44. As described previously, Daclatasvir It is a dimeric compound with exact structural features on either side of the centre line of symmetry. It has (just looking at one half of the molecule) a phenylimidazole moiety with a pyrrolidine ring attached at 2-position of the imidazole ring. These portions, referred hereafter as phenyl imidazole moiety, has already been disclosed in

Exhibit –A and its potential to show activity against Hepatitis C Virus (HCV) by inhibiting the NS5A has been reported in the Exhibit A.

45. To arrive at the above structure, R⁴ also need to represent Hydrogen atom. The ‘5264 Application discloses that R3 and R4 represent independently of each other –R1’, -R1’’, -R6, -R6’, [...] (See internal, Page 53, and Para 2, *placitum* 1). Further, it discloses that R6 and R6’ represent independently of each other –R2’, -R2’’ [...] (See internal, page 54, *placitum* 2). Further, in the ‘5264 Application, R2, R2’ and R2’’ represent independently of each other –H and several other substituents. (See internal, Page 53, *placitum* 1).
46. It is claimed in the present application that the nitrogen containing heterocyclic rings are crucial for the inhibition of the Hepatitis-C Virus infection. A comparison of the complete specification and the claims of the present application and the ‘5264 Application shows that with the substitutions mentioned in the table above, the structural moiety of **Benzene Imidazole Pyrrolidine** and its substituents were already known for the inhibition of **Hepatitis –C virus replication**. As disclosed above, the structures mentioned in the present application are symmetrical in nature. In the present application, numerous moieties are substituted to the pyrrolidine moieties in different structures. And evidently, the ‘5264 Application discloses one half of the structure as compared to the present application and it is evident from the claims of the present application that the benzene imidazole moieties are the core structures of the claimed compound and are found twice as it is a symmetrical compound. From ‘5264 Application, it is evident that the core moieties have been disclosed earlier for the same function of NS5A inhibition. Therefore, there is no technical advancement as compared to existing knowledge in the present application (*Emphasis added*).
47. The ‘5264 application recognizes that phosphorylation of NS5A and its homologues is a conserved feature among different members of the *Flaviviridae* family and it appears likely that phosphorylation of NS5A plays

an essential role during the HCV replication cycle. It also discloses that cellular protein kinases involved, particularly in cellular kinases responsible for NS5A phosphorylation *in vivo*, could therefore serve as promising targets for antiviral therapeutic intervention. [See internal page 44, *placitum* 7-24]

48. From the disclosures made in the '5264 Application, as of priority date, phenyl imidazole containing compounds had already been identified as NS5A inhibitors. The same has been claimed in the present application by the applicants. (See internal Page 31, Paragraph 2 of the '5264 Application). Therefore, from the above, it can be noted that Exhibit- A shares the same technical utility as claimed in the present application.
49. Secondly, **US patent No. 7,220,745 B2** which also has the international publication number of **WO 2004/103366 A1** (hereinafter referred to as the '366 Application) which was published on December 02nd, 2004 is titled 'Heterocyclic compounds useful to treat HCV' which is hereto annexed and marked as '**Exhibit-B**' relates **to diphenyl heterocycle compounds and pharmaceutical compositions thereof that inhibit replication of the Hepatitis C virus**. This patent also discloses the use of biphenyl heterocyclic compounds and/or compositions to inhibit HCV replication and/or proliferation and to treat or prevent HCV infections. The structure of the compound is disclosed below:

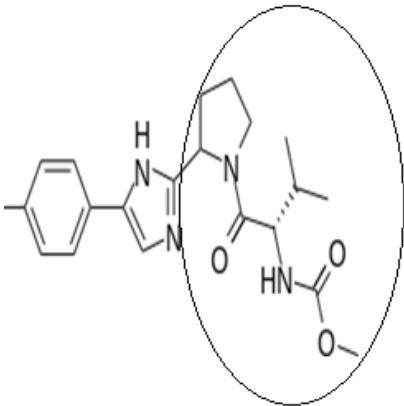
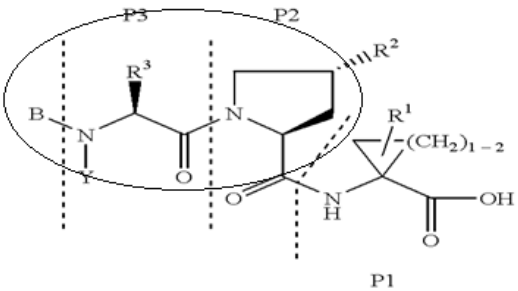
Claimed Compound	Elements disclosed in '366 Application
	

50. A comparison of the complete specification and claims of the present Application and the '366 Application shows that phenyl imidazoles with elaborated chain structures have been used previously for the treatment of HCV infection and for the inhibition of the Hepatitis-C replication. (*See internal page 8*).
51. From the disclosures above, it is evident that the phenyl-imidazoles were used for inhibiting the replication of the Hepatitis-C virus.
52. In the '366 Application, in the structure disclosed above, along with the benzene imidazole, a benzene ring and other moieties are attached to the imidazole ring. It would have been obvious for the applicants to try and replace it with a pyrrolidine alkylglycine due to use of pyrrolidine alkylglycine in Hepatitis-C treatment previously and from the reading of the '5264 Application which also contains a benzene imidazole pyrrolidine moiety.
53. Disclosed further are the documents which pertain to the pyrrolidine-alkylglycine moieties which have been used previously for the treatment of Hepatitis-C virus infection.

B. Pyrrolidine-alkylglycine moieties were already known and used for treatment of HCV.

54. **Thirdly, US Patent No. US 6,323,180 B1** (hereinafter known as the '180 patent), titled 'Hepatitis C Inhibitor Tri-peptide' published on 27th November 2001, which is hereto annexed and marked as "**Exhibit- C**" discloses Hepatitis C Virus Inhibitors which inhibit the replication of the HCV.
55. The '180 patent relates to the compounds for the treatment of the HCV. It discloses peptide analogs and methods for using the analogs in the treatment of the HCV infection. The '180 patent discloses inhibitors of the NS3 proteases and is advantageous because it does not inhibit other serine proteases in the human body. (*See internal Page 4, column 3, para 2*).

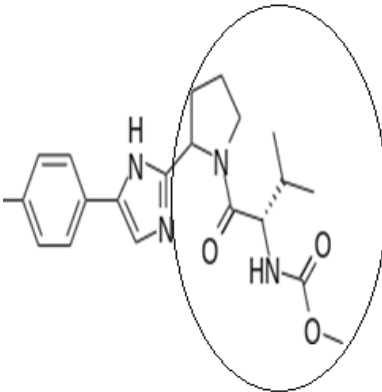
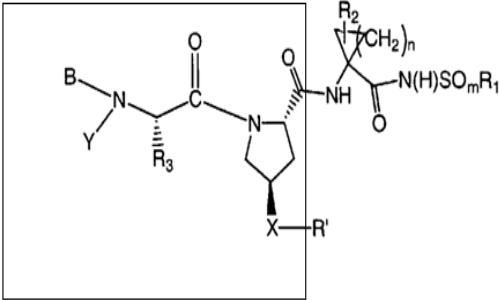
56. The Pyrrolidine-alkylglycine components in the present application can also be found in the claim 1 of the '180 patent and the structure of which is represented below. (See internal page 73, Column 142, figure – I).

Claimed Compound	Elements disclosed in the '180 Patent
	 <p>Wherein;</p> <p>B is H, [.....]; or</p> <p>B is an acyl derivative of formula $R_4-C(O)-$; a carboxyl derivative of formula $R_4-O-C(O)-$;[.....]</p> <p>Y is H or C_{1-6} alkyl;</p> <p>R³ is C_{1-8} alkyl,[....]</p>

57. *Fourthly*, It is also important to note that a WO Patent Application **WO03/099274 A1** titled 'Hepatitis C Virus inhibitors' (hereinafter referred to as the '274 Application) published on 04th December 2003 also filed by the

current applicant, i.e Bristol-Myers Squibb Company, which is hereto annexed and marked as **“Exhibit-D”** discloses antiviral compounds which inhibit the functioning of the NS3 protease encoded by the Hepatitis C Virus.

58. In the present Application, the alkylglycine moieties are attached to the pyrrolidine rings. From the ‘274 Application, it is evident that the alkylglycine components have already been used in the treatment of Hepatitis-C. Therefore, when the applicants are producing new compounds for the treatment of Hepatitis-C, it was obvious for them to combine the same with the moieties disclosed in the present application.
59. The application discloses and claims a pyrrolidine-alkylglycine cap and the elaboration thereof. (See internal page 665, Claim 1). The structure from the ‘274 Application is depicted below:

Claimed compound	Elements disclosed in the ‘274 Application
	<div style="text-align: center;">  <p>(I)</p> </div> <p>Wherein:</p> <p>(a) R₃ is C₁₋₈ alkyl [.....]</p>

	<p>(b) Y is H,[.....]</p> <p>(g) B is H, C,-6 alkyl, R₄-(C=O)-, R₄O(C=O)-, R₄-N(R₅)-C(=O)-, R₄-N(R₅)-C(=S)-, R₄SO₂-, or R₄-N(R₅)-SO₂-;</p> <p>(h) R₄ is (i) Ci-io alkyl optionally substituted with phenyl, carboxyl, C₁₋₆ alkanoyl, 1-3 halogen, 25hydroxyl, [.....]</p>
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60. From the tables set out above and the reading of the '5264 Patent together, it is clear that the compounds disclosed in the present application have been previously used for the treatment of Hepatitis-C Virus infection. Also it is pertinent to note that the combination of the Benzene-Imidazole- Pyrrolidine moieties have already been disclosed for the NS5A inhibition.

C. Bis (phenyl –imidazole) derivatives were known for the treatment of Hepatitis-C Virus.

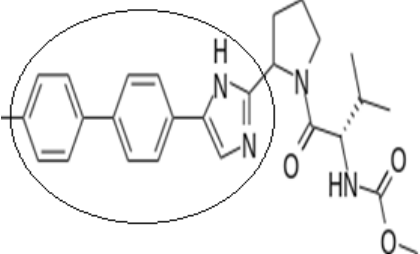
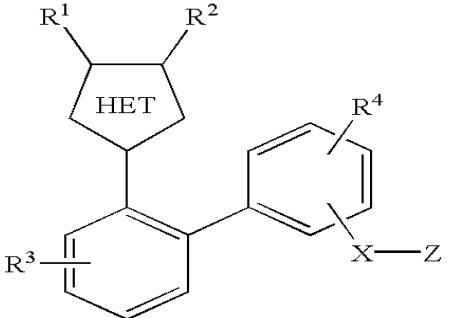

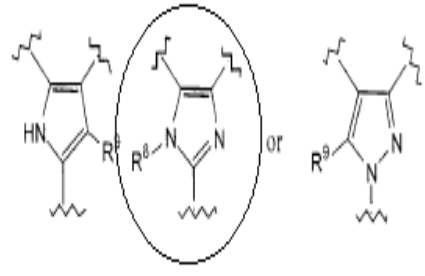
61. From the reading of the complete specification and the claims, it is clear that the alleged invention pertains to bis (phenyl – imidazole) moieties. The documents mentioned below provide that di-phenyl imidazole containing compounds have been known to be used for hepatitis-C Virus infection.

62. Bis – phenyl imidazole chain structures have been known as early as 1963. Schubert Herman *et al* in “Diimidazole. III. Synthese von aromatischüberbrückten 4(5),4'(5')-Diimidazolen” *Journal Fuer praktische Chemie, Leipzig*, DE, vol. 22, no. ¾, 1 January 1963 (1963-01-01), pages 140-152, XP002473762 ISSN: 0021-8383], a copy of which is hereto annexed and marked as “**Exhibit – E**” discloses the below mentioned : [See internal Page 151, para 4]. A translated copy of the same has been attested and annexed and marked as “**Exhibit-E (translation)**”.

Claimed Compound	Methyl[(2S)-1-{(2S)-2-[4-(4'-{2-[(2S)-1-{(2S)-2[(methoxycarbonyl) amino]-3-methylbutanoyl}-2-pyrrolidinyl]-1H-imidazol-4-yl}-4 <u>biphenyl</u>)-1H-imidazol-2-yl]-1-pyrrolidinyl}-3-methyl-1-oxo-2 butanyl] carbamate.
Features disclosed in Schubert Herman <i>et al</i>	<p>1,4-Bis-[4(5)-phenylimidazolyl-5(4)]-benzol: a) 1 g vorst. Bromketon wird in 80 ml Formamid unter Erwärmen gelöst, dann wird am Steigrohr 2 Stunden im schwachen Rückfluß erhitzt. Die gelborange Lösung wird wie oben beschrieben mit verd. HCl aufgearbeitet. Aus verd. Alkohol erhält man feine Nadeln vom Schmp. 319–320°, die sich an der Luft sehr schnell rosa färben. Ausbeute: 25–30% d. Th.</p> <p>b) 1 g vorst. Acyloin wird mit 20 ml Formamid umgesetzt. Nach beendeter Reaktionszeit wird in verd. NH₃ eingerührt und der Niederschlag aus verd. Alkohol umkristallisiert. Nadeln vom Schmp. 319–320°. Ausbeute: 35% d. Th.</p> <p>C₂₄H₁₈N₄ (362,41) gef.: C 78,1; H 5,2; N 15,1; ber.: C 79,6; H 5,0; N 15,4.</p>

63. From the above disclosure, it is evident that there is no inventive step in producing bis (phenyl imidazoles) as they have been produced as early as 1963. From the combined reading of the prior arts disclosed above, it is clear that the same compounds have been used for the treatment of Hepatitis-C. Therefore, it is said that there is no technical advancement in the present application as compared to the prior arts disclosed above.
64. **US patent** with international publication number **WO 0059506 A1** (hereinafter referred to as the '506 Patent) titled 'Heterocyclic containing biphenyl AP2 inhibitors and method', published internationally on 12th October 2000 **is assigned to the present applicant – Bristol-Myers Squibb Company**, a copy of which is hereto annexed and marked as "**Exhibit-F**". The '506 patent relates to heterocyclic containing biphenyls which are inhibitors of aP2 and to the method for treating diabetes, as well as hyperglycemia and other chronic inflammatory and autoimmune/inflammatory diseases. [See internal Page 1 and 2]

65. The '506 patent discloses biphenyl compounds containing imidazole (See internal Page 189) which were used for chronic inflammatory and autoimmune/inflammatory diseases. The structural comparison of the elements of the claimed inventions in the present applicant and the elements disclosed in the prior art are reproduced below for reference:

Claimed Compound	Elements disclosed in the '506 Patent
	<div data-bbox="889 766 1339 1081">  </div> <p data-bbox="889 1087 1421 1176">Wherein, (the structure of imidazole is disclosed below)</p> <div data-bbox="901 1260 1096 1438">  <p data-bbox="901 1407 1096 1438">15 is</p> </div> <div data-bbox="950 1480 1372 1753">  </div>

66. From the comparison of the compound disclosed in the present application and the structures disclosed above in the prior documents, it is obvious for a person skilled in the art to arrive at the structures claimed compounds using the existing knowledge.
67. It would therefore, suffice to say that the applicants have previously produced compounds having similar structure as disclosed in the present application. Therefore, there is no technical advancement even in the production of the moieties disclosed in the present application.
68. Therefore, from the above disclosures, it is clear that all the components of claim 20 has been previously described in the prior arts mentioned above and all that was needed was to combine the compounds.

Motivation to combine the compounds to be used for Hepatitis-C treatment is obvious:

69. Shintaro Hirashima *et al* in their article titled ‘Benzimidazole derivatives bearing substituted Biphenyls as Hepatitis C Virus NS5B RNA-Dependent RNA polymerase inhibitors: Structure – Activity Relationship Studies and identification of a potent and highly selective inhibitor JTK-109 published in June 2006 in the Journal of Medicinal Chemistry 2006, 49: 4721-4736, a copy of which is hereto annexed and marked as “**Exhibit-G**” discloses that following the discovery of a new series of benzimidazole derivatives bearing diarylmethyl group as inhibitors of HCV NS5B RNA-dependent RNA polymerase, study was extended to the structure-activity relationship (SAR) to analogues bearing substituted biphenyl groups and it showed a significant advancement of activity in inhibiting the HCV non-structural proteins.
70. It also recognizes that compared to a previous study, improvement of activity was a major challenge in the anti-HCV drugs. Therefore, when phenyl rings were substituted, it showed more distinct SARs and **generated significant**

improvement in potency with favourable pharmacokinetic and safety profiles.

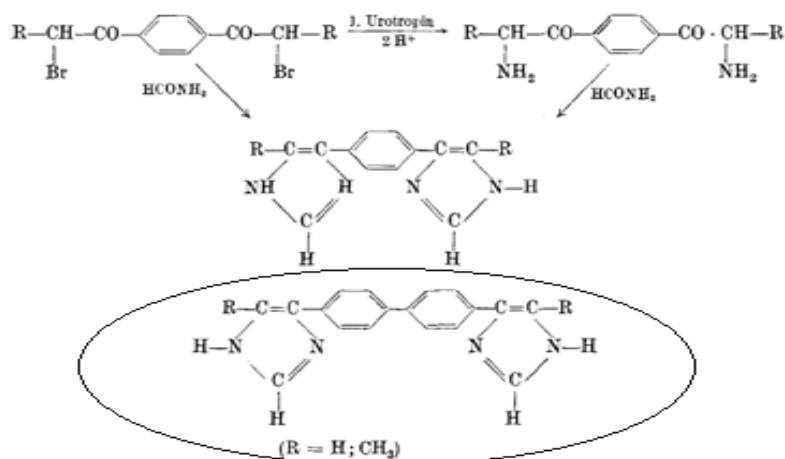
[See internal – page 4721, RHS, para 2, *placitum* 10-16]

71. Further, it was obvious to combine both the compounds because, it is clear from the **US Patent 4,868,207** (hereinafter referred to as the US ‘207 patent) which was published on 19th September 1989, a copy of which is hereto annexed and marked as “**Exhibit-H**”, discloses biphenyl containing compounds having desirable effects without side effects as the therapeutic agents for chronic hepatitis (See internal Page 2, column 1, para 2)
72. **US Patent 7, 091, 247 B2** (hereinafter referred to as the ‘247 patent) which was published on January 03rd, 2002, a copy of which is hereto annexed and marked as “**Exhibit-I**” titled ‘Biphenyl Compound’ discloses biphenyl compounds which are responsible for the regulation of somatostatin (a regulator hormone which regulates several other hormones in the body and also the growth hormone) (See internal Page 2 column 2, para 2) and also discloses the uses of biphenyl compounds and its derivatives for treating numerous diseases. ‘247 Patent also discloses that the biphenyl containing compounds are useful as a preventive or therapeutic drug for alcoholic hepatitis, hepatitis A, hepatitis B and Hepatitis C. (See internal Page 27, Column 52 *placitum* 53-58).

Symmetrical bis (phenyl imidazoles) were known:

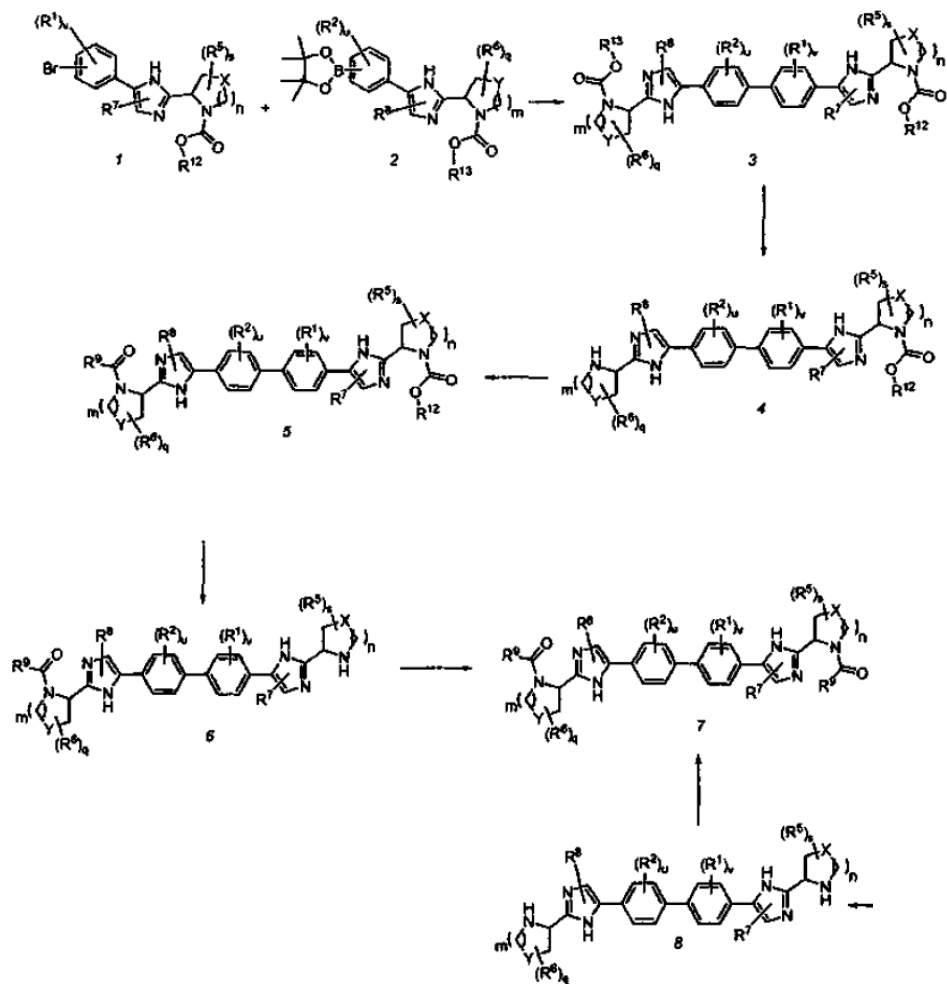
73. The complete specification of the present application pertains to elaborated chain structure containing diphenyl imidazoles and the same has already been disclosed in **Exhibit –E** which also discloses the procedure for synthesis of the compound (See internal Page 141). Therefore, it can be seen from the above disclosed prior art that biphenyl imidazole containing structures were known, barring the substitutions bonded to the imidazole ring in the present application.

74. In the complete specification of the present application, symmetrical biphenyl imidazoles are disclosed and allegedly termed as non-obvious according to the applicants. But from the above disclosures and the structure depicted below, it is clear that there is no technical advancement over the existing knowledge and in the presence of findings regarding the significant improvement of potency in presence of biphenyl moieties, it is obvious for a person skilled in the art to produce biphenyl imidazole containing moieties.



D. Mechanism used by the applicants to combine the elements to create the symmetrical structure was a standard procedure which was known.

75. The applicants, in the complete specification, refer to schemes for the synthesis of the compound disclosed in the application. The complete specification refers to the synthesis of symmetric or asymmetric biphenyls based on a reaction called the Suzuki-Miyaura reaction (See - specification, Page 31). The scheme is reproduced below for the sake convenience:



76. From the disclosures made previously and from the reading of the complete specification of the present application, it is clear that compound 1 and 2 as mentioned in this scheme were previously known compounds, as also admitted by the applicants. It is also evident from the disclosures made above that procedure of synthesizing biphenyl imidazole moieties has been performed previously. Therefore from the reading of the complete specification of the present application and scheme of the synthesis, it is obvious for the person skilled in the art to arrive at the compound 3 (bi-phenyl imidazole) moieties which is disclosed in scheme depicted above. It would also suffice to say that

the synthesis of biphenyl imidazole moieties in addition to being obvious, does not lead to any technical advancement as compared to existing knowledge.

77. Further, the mechanism used to react phenyl imidazoles was a commonly used reaction called the Suzuki-Miyaura coupling reaction which also involves inversion of configuration of the compound. The Suzuki-Miyaura coupling condition has been extensively used for the synthesis of biologically active natural and non-natural product and this common mechanism was used in the present application to create the claimed compounds.
78. Timothy E. Barder *et al* in their article titled “Catalysts for Suzuki-Miyaura Coupling Processes: Scope and Studies of the effect of the ligand Structure” in the *Journal of the American Chemical Society* 2005, 127 (4685-4696), published in 2005, a copy of which is hereto annexed and marked as “**Exhibit-J**” note aryl and heteroaryl halides with aryl-, heteroaryl- and vinyl boronic acids proceed in very good to excellent yields. [See internal page 4688, RHS *placitum* – 14-17] The article also discloses that originally, the Suzuki-Miyaura creported coupling reactions of alkenyl boronates with alkenyl bromides. But recently, the Suzuki-Miyaura reaction has been improved upon to prepare extremely hindered biaryls and proceeds in excellent yields with the help of specific catalysts.
79. Admittedly, as of the priority date, Sherry R. Chemler *et al* in their article titled – *The B-Alkyl Suzuki-Miyaura Cross-Coupling Reaction: A versatile C-C bond-forming tool* published in the *Angewandte Chemie International Edition* 2001, 40, 4544-4568 in 2001, a copy of which is hereto annexed and marked as “**Exhibit-K**” notes that the Suzuki-Miyaura cross coupling reaction is a valuable resource for the coupling of complex molecular fragments. The article also discloses that the reaction has proved to be an extraordinarily useful tool for construction of carbon frameworks and the products created may ultimately be converted into useful compounds. (See internal Page 4546, Para 2, *Placitum* 5-6).

80. The Suzuki-Miyaura coupling reaction is a standard method to produce coupled reactants. Norio Miyaura and Akira Suzuki, in their article titled 'Palladium Catalyzed Cross-Coupling Reaction of Organoboron Compounds' in Chemical Reviews, 1995, 95, 2457-2483 published in 1995 which is hereto annexed and marked as "**Exhibit-L**" notes that coupling reaction with benzylic halides proceeds with a **complete inversion**(See internal Page 2460, RHS, para 2, placitum 1-6).
81. Therefore, from the disclosures made in Exhibit-K and Exhibit-L, it is clear that the inversion of the configuration was a result of the use of the Suzuki-Miyaura reaction which has been observed in numerous reactions previously in the Suzuki-Miyaura coupling conditions.
82. In the light of the above disclosures, it is stated that the disclosures made in the complete specification are obvious and do not lead to technical advancement as compared to existing knowledge, therefore the alleged invention in the present application lacks inventive step.

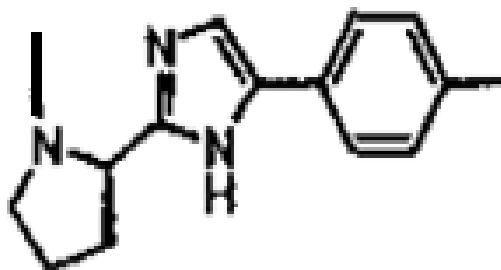
Summary

83. Therefore, in the light of the above, it is respectfully submitted that NS5A has been identified as a target for inhibiting the replication of HCV and anti-HCV therapies pertaining to the moieties disclosed in the present application were already known. Also, the mechanism employed by the applicants was standard procedures used to produce elaborated symmetric and asymmetrical compounds. The production of the moieties consisting of bi-phenyl imidazoles is also obvious because bi-phenyl imidazoles were known and used as anti-HCV treatment. Therefore, in the light of the above, claims 1-34 are obvious for a person skilled in the art and do not involve technical advance over the existing knowledge. Claims 1-34 lack inventive step and should therefore be rejected under section 25 (1) (e) of the Patents Act.

b. Claims 20 and 22 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.

84. 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.
85. 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.
86. 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.
87. 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].
88. 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)].
89. 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].

90. Without prejudice to other grounds raised herein, Claims 20 and 22 fail under section 3(d) of the Patents Act.
91. Claims 20 and 22 essentially covers the derivatives of phenyl imidazole compounds which are useful in the inhibition of the HCV replication.
92. Without prejudice to the contention that the claims in the present application do not involve an inventive step and other grounds raised therein, the Opponent states that the claims of the present application do not satisfy the test of section 3(d) of the Patent Act. The Patent Application has not provided data to demonstrate enhanced therapeutic efficacy of the claimed compounds over the known efficacy of the compounds disclosed in the '5264 Patent (Exhibit –A). The applicants have thus, failed to discharge their burden. The applicants, in the present application, have not provided any data to demonstrate the efficacy of the claimed compounds as compared to the compounds disclosed previously.
93. In the present application, it is disclosed that the, compounds useful for treating HCV infected patients are desired which selectively inhibit HCV viral replication and in particular, compounds which are effective to inhibit the function of the NS5A proteins are desired.
94. It cannot be disputed that the Exhibit – A also discloses derivatives of phenyl imidazoles which are basically useful for the inhibition of the HCV replication. Exhibit-A discloses phenyl imidazole containing compounds and its derivatives which are also useful in the treatment of the HCV infected patients through inhibition of the NS5A protein. As disclosed previously, the following compound can be derived from Exhibit –A:



95. From the comparison the Exhibit-A along with the present application, it is therefore, submitted that the compounds disclosed in the present application are therefore ‘same substances’ as disclosed in Exhibit-A and the numerous compounds claimed in the present application are the derivatives of phenyl imidazoles as disclosed in Exhibit-A.
96. Further, from the reading of Exhibit E and F, which discloses the phenyl imidazole containing compounds, it can be stated that the present application discloses the derivatives of biphenyl imidazoles which were previously known substances.
97. Therefore, in the light of the above, it is respectfully submitted that the present application claims derivatives of known substances and therefore, the Applicant has therefore failed to discharge the onus of fulfilling the requirement under section 3(d) of the Act.
98. In view of the above, the compounds claimed in the present application are derivatives of previously known substances and therefore not an invention in accordance with section 3(d) of the Patents Act.
- c. Claims 35 to 40 fail under section 3(e), are not an invention within the meaning of this Act and should be rejected under section 25(1)(f) of the Patents Act.

99. Under section 3(e) of the Patents Act, claims relating to “a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof” are not eligible for a patent.
100. Without prejudice to other grounds raised herein, the pharmaceutical composition claimed by the Patent Applicant in Claims 35 to 40 are substances obtained by a mere admixture. The Patent Applicant has not shown that the compounds claimed exhibit any synergistic effect, whether improved and unexpected or otherwise, over and above the aggregation of the properties of the components thereof.
101. Claims 35 to 40, in as much as they describe the various compositions to be used for the treatment of Hepatitis-C treatment, from Exhibit-A it is evident that the same compositions have been used previously for the treatment of Hepatitis-C.
102. Therefore, Claims 35 to 40 fail under section 3(e) and should be rejected under section 25(1) (f) of the Patents.

d. The complete specification does not sufficiently and clearly describe the invention as claimed in Claims 1-34 and should be rejected under section 25(1)(g) of the Patents Act.

103. Section 25(1)(g) of the Patents Act provides a ground for opposition of patent application if the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed.
104. In the present application, the claim covers thousands of compounds. The detailed synthesis of and characterization of each of the compounds claimed should be provided. The present application is too wide and fails to narrow down the scope of the invention.
105. Section 10 (4)(a) of the patents act provides that every complete specification shall fully and particularly describe the inventions and its operation or use

and method by which it is to be performed and Section 10 (4) (b) provides that every complete specification shall disclose the best method of performing the invention which is known to the applicant and for which he is entitled to claim protection; and section 10 (4) (c) provides that that even a complete specification shall end with claim or claims defining the scope of the invention for which protection is claimed.

106. The applicants have claimed over a thousand compounds for which a detailed synthesis and characterization of each of the compound has not been provided. The applicants have taken the opportunity to widen the scope of the invention to the maximum and therefore the thousands of compounds cannot be regarded as a solution to the problem of treating Hepatitis-C.
107. Without prejudice to the other grounds raised herein, the present application claims thousands of compounds in the markush claims which are defined only by reference to a desired functional activity. The present application does not give a specific technical guidance to arrive at thousands of compounds which have been claimed in the claims and this could be seen as a mere invitation to the skilled person to perform a research program in order to find the suitable variants to arrive at the thousands of compounds which have been claimed in the present application.
108. Without prejudice to the other grounds raised herein, it is also submitted that the present application claims so many variations that it is difficult to ascertain the actual scope of the invention. In the present application there are thousands of combinations and variations and do not even fall within a single inventive concept while section 10 (5) of the Patents Act mandates that the claim or claims in the complete specification shall relate to a single invention, or to a group of inventions linked so as to form a single inventive concept, shall be clear and succinct and shall be fairly based on the matter disclosed in the specification. It is pertinent to note that in the present application, with the vast number of independent claims, it is difficult to ascertain whether all the

claims relate to a single inventive concept. The Markush claims impose an arduous task in examining different categories of claims which then effectively conceals the boundary of the invention.

109. Time and again it has been emphasized that the patent applicant must therefore provide necessary information in order to identify the claimed subject matter of the application in order to not make it unduly burdensome. However, the Markush group in the present application is so vastly populated that a person skilled in the art cannot accurately measure the boundaries of the claimed invention. Therefore, the present application should be rejected for indefiniteness.

110. From the present application, it appears from the mere size of the claims that the scope of claims has been enlarged with the intent to confuse the patent office. Therefore, as stated above, the present application should be rejected for the lack of clarity and indefiniteness.

e. The patent applicant has not complied with requirements of section 8. The present application, should thus be rejected under section 25(1)(h) of the Patents Act.

111. 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.

112. 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.

113. 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.

114. The prosecution history for the present Application, available online on the IPAIRS website, shows that the Patent Applicant had not furnished any 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.
115. In the present case, it appears that the Patent Applicant first filed Form 3 on 05th February, 2009 and listed only the applications filed in the United States, from which priority is claimed, and the PCT Application.
116. The applications filed by the applicant in numerous other jurisdictions include the following:

Country	Date of filing	Application No.
Argentina	11 th February, 2009	AR063684
Australia	21 st February, 2008	AU2007286222 (A1)
Australia	28 th June, 2008	AU2007286222 (B2)
Canada	21 st February 2008	CA2660520
Chile	16 th May, 2008	CL2007002327

China	14 th October, 2009	CN101558059 (A)
China	03 rd December, 2014	CN101558059 (B)
Columbia	20 th April, 2010	CO6150171 (A2)
Denmark	07 th July, 2014	DK2049522 (T3)
Eurasian Patent Organization (EAPO)	30 th October, 2009	EA200900298 (A1)
European Patent Organization (EPO)	22 nd April, 2009	EP2049522 (A2)
Spain	15 th July, 2014	ES2476592 (T3)
Hong Kong, (SAR)	15 th August, 2014	HK1126486 (A1)
Israel	30 th April, 2014	IL 196813 (A)
Japan	07 th January, 2010	JP2010500413
Republic of Korea	27 th April, 2009	KR20090040909 (A)
Mexico	17 th February, 2009	MX2009001426 (A)
Norway	02 nd March, 2009	NO20090447 (A)
New Zealand	30 th September, 2011	NZ574805 (A)
Peru	16 th May, 2008	PE05422008 (A1)
Portugal	20 th August, 2014	PT2049522 (E)

Slovenia	31 st December, 2014	SI2049522 (T1)
Taiwan	16 th August, 2009	TW200934486 (A)

117. The applicants have made no further efforts to keep the Controller informed in writing regarding the applications relating to the same or substantially same invention as the present application filed in any country outside India subsequent to the filing of the application in the Indian jurisdiction.
118. Further, it appears from the prosecution history available online that, following the filing of the present Application in 2009, the Patent Applicant did not even attempt subsequently to comply with the requirements of section 8 of the Patents Act once the corresponding international application entered national phase in other jurisdictions.
119. Even though it filed the request for examination on 09th August, 2010, the patent applicant took no step even at or around that time to comply with the requirements of section 8 of the Patents Act.
120. Subsequently, via examination report dated 26th June, 2014, the Examiner ordered that regarding the search and/or examination report including claims of the application allowed, as referred to in Rule 12(3) of the Patent Rule, 2003, in respect of same or substantially the same invention filed in all the major patent offices along with appropriate translation where applicable, should be submitted within a period of Six months from the date of receipt of this communication as provided under section 8(2) of the Indian Patents Act. The applicants haven't furnished any information in this regard.
121. Therefore, the Patent Applicant has failed to comply with the requirements of section 8 of the Patents Act.
122. 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.

123. In the first examination report dated 26th June, 2014, the Hon'ble Patent Controller has also sought information from the Patent Applicant under section 8(2) of the Patents Act read with rule 12(3) of the Patents Rules regarding search and / or examination report, including claims of application allowed, in respect of the same or substantially the same invention filed in all the major patent offices within a period of six months from the date of receipt of communication of the first examination report. The applicants, to this date, haven't furnished any information in this regard even after the examination report was circulated.

124. 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

125. The Opponent hereby requests a hearing under section 25(1) of the Patents Act and rule 55 of the Patents Rules.

VIII. PRAYER:

126. Given all the foregoing, the Opponent humbly prays:

- (i) For an order rejecting patent application 853/DELNP/2009 for the reasons stated above;
- (ii) For a copy of any reply statement and evidence and/or amended specifications and/or claims that may be filed by the Patent Applicant and a further opportunity to file a rejoinder and rebut the same;
- (iii) For leave to amend the opposition and/or raise further grounds and file further documents or evidence, as and when required;
- (iv) For a hearing under section 25(1) of the Patents Act read with rule 55 (1) of the Patent rules;
- (v) 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. Rameshwari, Advocate

Settled by: Mr. Anand Grover, Senior Advocate

Place: New Delhi

Date: 18th April, 2015

On Behalf of _____

(Eldred Tellis, Authorised signatory, Sankalp Rehabilitation Trust)

(Contd.)

(Contd. from the previous page)

On Behalf of _____

(Ketholelie Angami, Authorised signatory, HepCoN)

On Behalf of _____

(Shibananda Sharma Phurailatpam, Authorised signatory, APN+)