THE PATENTS ACT, 1970 (AS AMENDED)

&

THE PATENTS RULES, 2003 (AS AMENDED)

SECTION 25(1)

In The Matter of

An Application for Patent No. 202017034452

AND

In The Matter of

A Pre-grant opposition to the grant of a patent thereon under section 25(1)

And

Hearing u/s 14

FMC corporation.....The Applicant

Haryana Pesticides Manufactures'Association… ..... The Opponent

Appeared in the hearing held on January 23, 2025 under section 25(1)

Ms.Archana Shanker, Sh.Devinder Singh Rawat, Ms.Vashima Miglani..... **For the Applicant**

Dr. Pinki Chakraborty and Ms.Haneet Papreja..... **For the opponent**

- **Grounds of opposition for a patent.**

1) Lack of Novelty (u/s 25(1)(b)): The Opponent argued that the subject matter of the patent

application is not novel and is anticipated by prior art.

2) Lack of Inventive Step (u/s 25(1)(e)): It was contended that the application lacks an inventive step, as the claimed invention would be obvious to a person skilled in the art in light of the prior art.
3) Non-patentability and Not an Invention (u/s 25(1)(f)): The Opponent submitted that the invention does not meet the criteria of patentable subject matter under the applicable patent
laws and regulations.
4) Insufficiency of Disclosure (u/s 25(1)(g)): The Opponent argued that the patent application
fails to provide sufficient disclosure to enable a person skilled in the art to practice the invention.

- **Timelines:**

Applicant Name Priority No.	FMC Corporation
Priority No. & Date US	US 62/629,154 dated February 12, 2018 US 62/631,665 dated February 17, 2018 US 62/657,647 dated April 13, 2018
PCT Application No. & Date	PCT/US2019/016260 dated February 01, 2019
PCT Publication No. & Date	WO2019/156903 dated August 15, 2019
Indian Application Filing Dated	August 11, 2020
Request for Examination	February 10, 2022
Publication Date u/S 11A	September 25, 2020
FER date	February 17, 2022
FER reply	November 16, 2022
Pre-grant Opposition filed on	August 03, 2021, by Haryana Pesticides Manufactures' Associatio
Date of Notification of Opposition	February 28, 2023
Reply statement filed on	May 15, 2023
Reply statement filed on	04th November, 2024
Adjournment request filed by the Applicant	January 31st , 2025
Hearing Notice issued appointing hearing u/s 25(1) on 10-Mar-2025	February 03, 2024

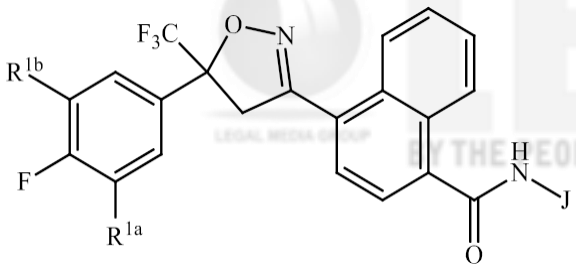
- The Opponent has relied on the following documents in the Opposition Statement and filed on 03rd August 2021.

Sr. No	Documents	Publication Date
D1	WO2009002809 A2	2008

D2	US2012077765 ≈ WO2012038851	2012
D3	WO2008154528 A2	2008
D4	US2017020848 ≈ WO2016164487	2017
D5	WO2009/045999 A1	2009
D6	DK2576523T3 = WO2011149749	2016
D7	Shoop et al., Discovery and mode of Action of Afoxolaner, a new isooxazoline Parasiticide for dogs, 2014	2014

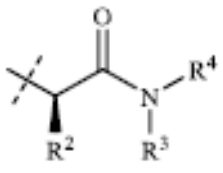
- Claims as amended by the applicant and presented during the hearing :

1. A compound selected from Formula **1**,



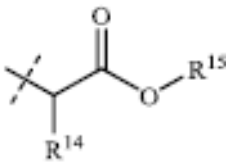
wherein

J is



J-1

or

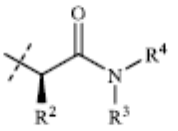


J-5

-

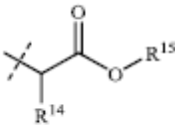
wherein

J is



J-1

or



J-5

R^{1a} is Cl or CF_3; R^{1b} is H or Cl;

R^2 is methyl, ethyl, iso-propyl, tert-butyl; R^3 is H; or methyl;

R^4 is H, methyl, ethyl, iso-propyl, CH2CF3

R^{14} is H or methyl;

R^{15} is H, methyl, ethyl, iso-propyl, CH2CF3.

2. The compound as claimed in claim 1 wherein

R^{1a} is Cl and R^{1b} is Cl; or

R^{1a} is CF_3 and R^{1b} is H.

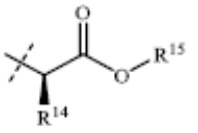
3. The compound as claimed in claim 1 wherein

R^2 is methyl;

R^3 is H or methyl; and

R^4 is H or methyl.

4. The compound as claimed in claim 1 wherein J-5 is



J-5a

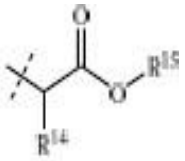
5. The compound as claimed in claim 4 wherein
R^{14} is H or methyl; and
R^{15} is methyl, ethyl, iso-propyl,

6.. A composition comprising a compound as claimed in Claim 1 and at least one additional component selected from the group consisting of surfactants, solid diluents and liquid diluents, said composition optionally further comprising at least one additional biologically active compound or agent preferably wherein the at least one additional biologically active compound or agent is selected from the group consisting of abamectin, acephate, acequinocyl, acetamiprid, acrinathrin, afidopyropen, amidoflumet, amitraz, avermectin, azadirachtin, azinphos-methyl, benfuracarb, bensultap, bifenthrin, bifenazate, bistrifluron, borate, , buprofezin, carbaryl, carbofuran, cartap, carzol, chlorantraniliprole, chlorfenapyr, chlorfluazuron, chlorpyrifos, chlorpyrifos-methyl, chromafenozide, clofentezin, clothianidin, cyantraniliprole, cyclaniliprole, cycloprothrin, cycloxaprid, cyflumetofen, cyfluthrin, beta-cyfluthrin, cyhalothrin, gamma-cyhalothrin, lambda-cyhalothrin, cypermethrin, alpha-cypermethrin, zeta-cypermethrin, cyromazine, deltamethrin, diafenthiuron, diazinon, dieldrin, diflubenzuron, dimefluthrin, dimehypo, dimethoate, dinotefuran, diofenolan, emamectin, endosulfan, esfenvalerate, ethiprole, etofenprox, etoxazole, fenbutatin oxide, fenitrothion, fenothiocarb, fenoxycarb, fenpropathrin, fenvalerate, fipronil, flometoquin, flonicamid, flubendiamide, flucythrinate, flufenerim, flufenoxuron, flufenoxystrobin, flufensulfone, fluorpyram, flupiprole, flupyradifurone, fluvalinate, tau-fluvalinate, fonophos, formetanate, fosthiazate, halofenozide, heptafluthrin, hexaflumuron, hexythiazox, hydramethylnon, imidacloprid, indoxacarb, insecticidal soaps, isofenphos, lufenuron, malathion, meperfluthrin, metaflumizone, metaldehyde, methamidophos, methidathion, methiodicarb, methomyl, methoprene, methoxychlor, metofluthrin, monocrotophos, monofluthrin, methoxyfenozide, nitenpyram, nithiazine, novaluron, noviflumuron, oxamyl, parathion, parathion-methyl, permethrin, phorate, phosalone, phosmet, phosphamidon, pirimicarb, profenofos, profluthrin, propargite, protrifenbute, pyflubumide,

pymetrozine, pyrafluprole, pyrethrin, pyridaben, pyridalyl, pyrifluquinazon, pyriminostrobin, pyriprole, pyriproxyfen, rotenone, ryanodine, silafluofen, spinetoram, spinosad, spirodiclofen, spiromesifen, spirotetramat, sulprofos, sulfoxaflor, tebufenozide, tebufenpyrad, teflubenzuron, tefluthrin, terbufos, tetrachlorvinphos, tetramethrin, tetramethylfluthrin, thiacloprid, thiamethoxam, thiodicarb, thiosultap-sodium, tolfenpyrad, tralomethrin, triazamate, trichlorfon, triflumuron, all strains of *Bacillus thuringiensis*, entomopathogenic bacteria, all strains of *Nucleo polyhedrosis* viruses, entomopathogenic viruses and entomopathogenic fungi more preferably wherein the at least one additional biologically active compound or agent is selected from the group consisting of abamectin, acetamiprid, acrinathrin, afidopyropen, amitraz, avermectin, azadirachtin, benfuracarb, bensultap, bifenthrin, 3-bromo-1-(3-chloro-2-pyridinyl)-*N*-[4-cyano-2-methyl-6-[(methylamino)carbonyl]phenyl]-1*H*-pyrazole-5-carboxamide, buprofezin, carbaryl, cartap, chlorantraniliprole, chlorfenapyr, chlorpyrifos, clothianidin, cyantraniliprole, cyclaniliprole, cycloprothrin, cyfluthrin, beta-cyfluthrin, cyhalothrin, lambda-cyhalothrin, gamma-cyhalothrin, cypermethrin, alpha-cypermethrin, zeta-cypermethrin, cyromazine, deltamethrin, dieldrin, dinotefuran, diofenolan, emamectin, endosulfan, esfenvalerate, ethiprole, etofenprox, etoxazole, fenitrothion, fenothiocarb, fenoxycarb, fenvalerate, fipronil, flometoquin, flonicamid, flubendiamide, flufenoxuron, flufenoxystrobin, flufensulfone, flupiprole, flupyradifurone, fluvalinate, formetanate, fosthiazate, heptafluthrin, hexaflumuron, hydramethylnon, imidacloprid, indoxacarb, lufenuron, meperfluthrin, metaflumizone, methiocarb, methomyl, methoprene, methoxyfenozide, metofluthrin, monofluthrin, nitenpyram, nithiazine, novaluron, oxamyl, pyflubumide, pymetrozine, pyrethrin, pyridaben, pyridalyl, pyriminostrobin, pyriproxyfen, ryanodine, spinetoram, spinosad, spirodiclofen, spiromesifen, spirotetramat, sulfoxaflor, tebufenozide, tetramethrin, thiacloprid, thiamethoxam, thiodicarb, thiosultap-sodium, tralomethrin, tetramethylfluthrin, triazamate, triflumuron, all strains of *Bacillus thuringiensis* and all strains of *Nucleo polyhedrosis* viruses.

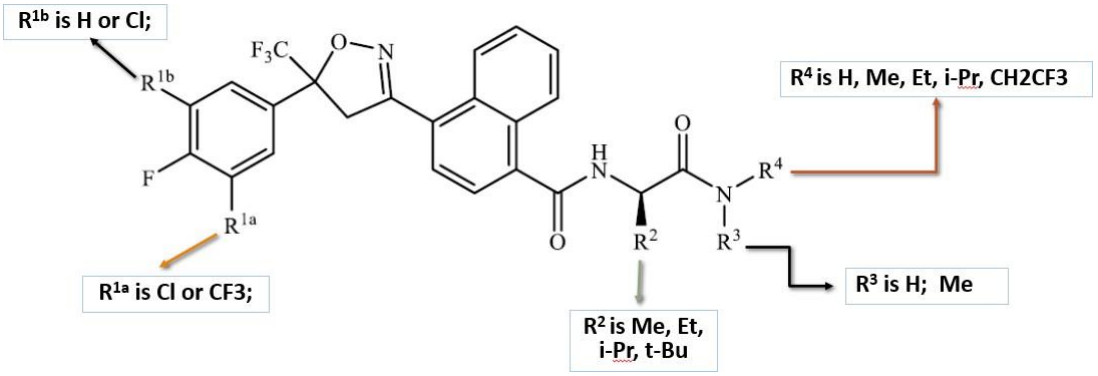
In summarized form the specific substituents for J in the impugned invention are narrowed to:

J-1

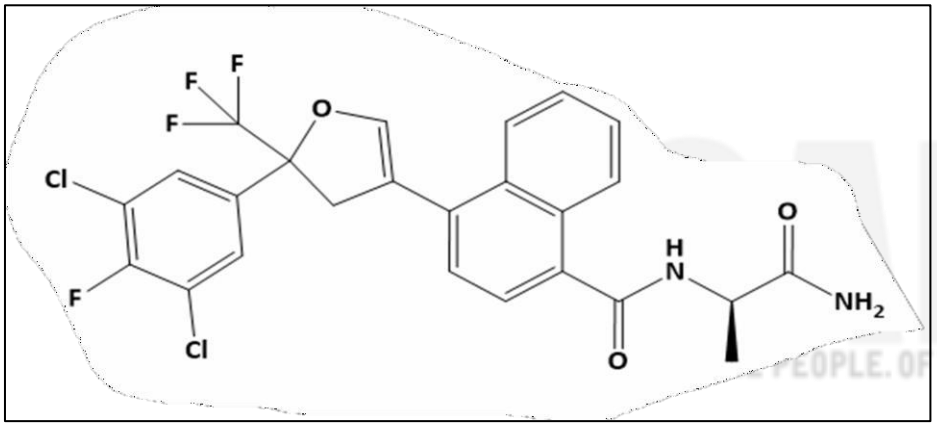


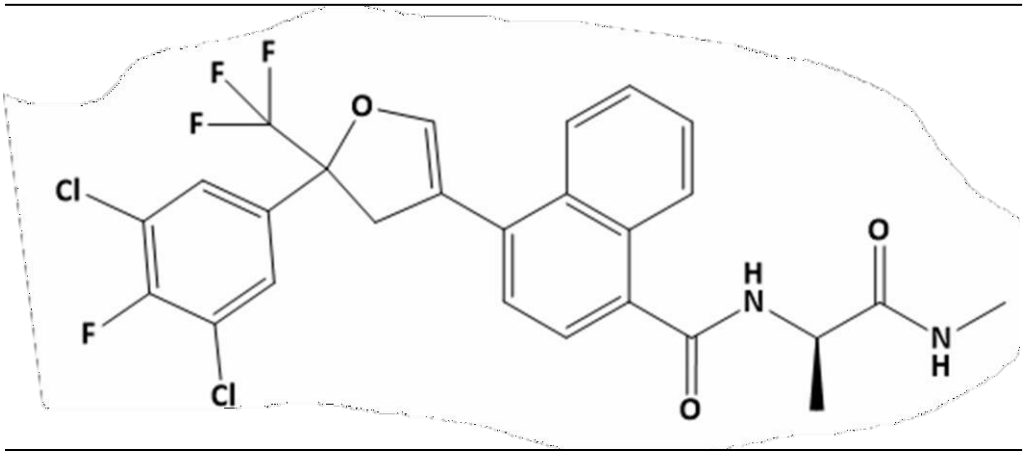
J-5

The compounds of the revised claims are listed in Table 1-1 of the complete specification (Page 34) of IN'452, as depicted below: .



. Compounds that fall within the limited revised scope of Formula I have been specifically provided in amended claim 3 that have the following chemical structure: and,





- Specifically, the application highlights two significant inventive selections that distinguish the claimed compounds of the present invention from the prior art.

a) The chiral center on J = J1 or J5 is specified to be the (R)-stereochemistry

b) Narrow choice of substituents on the aryl ring appended to the 5-position of the isooxazoline, where a 4-F is required with a narrow group of substituents, where Rla is CI or CF3 and Rl b is H or Cl.

(a) Fluorine atom at the 4-position of the phenyl ring attached to the 5-position of the isoxazoline ring a. This selection is crucial, as outlined on page 20 of the complete specification, where it is explained that bioaccumulation of pesticides in nontarget organisms is an important safety consideration. It is often desirable to limit the systemic exposure and/or accumulation of pesticides and their metabolites in non-target organisms.

For example, if a compound is to be applied as an insecticide to a crop plant, it is essential that the compound does not accumulate in the plasma or fat of a vertebrate animal. Compounds of Formula 1, as selected, are believed to exhibit favorable pharmacokinetic properties in vertebrate animals. Specifically, these compounds have been found to have rapid clearance from vertebrate animal plasma/blood and low distribution into vertebrate animal fat, thereby reducing the potential for unwanted bioaccumulation. This inventive selection of the fluorine atom at the specified position plays a key role in achieving these desired pharmacokinetic properties.

Test	Pest	Conc. (ppm)	Efficacy (%)	Plant Damage (%)	Mortality (%)
Test A	**Diamondback Moth *(Plutella xylostella)***	250 ppm	Very Good to Excellent	≤40%	100%
		50 ppm	Very Good to Excellent	≤40%	100%
		10 ppm	Very Good to Excellent	≤40%	100%
Test B	**Fall Armyworm (*Spodoptera frugiperda*)**	250 ppm	Very Good to Excellent	≤40%	100%
		50 ppm	Very Good to Excellent	≤40%	100%
		10 ppm	Very Good to Excellent	≤40%	100%
		2 ppm	Very Good to Excellent	≤40%	100%
Test C	**Corn Planthopper (*Peregrinus maidis*)**	50 ppm	NA	NA	80%

Test D	**Potato Leafhopper (*Empoasca fabae*)**	250 ppm	NA	NA	80%
		50 ppm	NA	NA	80%
		10 ppm	NA	NA	80%
		2 ppm	NA	NA	80%

Test E	**Green Peach Aphid (Myzus persicae)**	250 ppm	Very Good to Excellent	NA	80%
		50 ppm	Very Good to Excellent	NA	80%
		10 ppm	Very Good to Excellent	NA	80%
Test F	**Cotton Melon Aphid (*Aphis Gossypii)***	250 ppm	Very Good to Excellent	NA	80%
		50 ppm	Very Good to Excellent	NA	80%
		10 ppm	Very Good to Excellent	NA	80%
Test G	**Sweetpotato Whitefly (Bemisia tabaci)**	250 ppm	NA	NA	70%
		50 ppm	NA	NA	70%
		10 ppm	NA	NA	70%
		2 ppm	NA	NA	70%
Test H	**Western Flower Thrips (*Frankliniella occidentalis)***	250 ppm	Very Good to Excellent	≤30%	80%
		50 ppm	Very Good to Excellent	≤30%	80%
		10 ppm	Very Good to Excellent	≤30%	80%
		2 ppm	Very Good to Excellent	≤30%	80%

Expert Affidavit: The Applicant has filed and relied on the evidence affidavit of Dr. Ming Xu, enclosed as Annexure A2.

The said evidence demonstrates that the selection of the (R)-stereochemistry is critical for achieving the desired biological activity, and it significantly impacts the compound's interaction with its target, distinguishing it from the compounds disclosed in D6. Further, as demonstrated by the effect of structural changes on activity, bioefficacy tests were conducted on Western Flower Thrips (*Frankliniella accidentalis*) to compare the control efficacy of the compound with those disclosed in D6 and D7.

The selection of compounds in our invention is based on two important factors, which are further supported and backed by the following case laws:

- **Novartis AG vs UOI, IPAB, 100/20091**
- **Apotex Inc. v. Sanofi Synthelabo Canada Inc. et al. (2008)2**
- **E.I. Du Pont De Nemours & Co. (Witsiepe's) Application (1982)3**

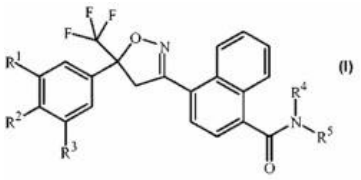
The prior art are not discussed separately as they have been discussed during the discussion in this document extensively under the grounds of Novelty and inventive step.

❖ GROUND I: LACK OF NOVELTY U/S 25(1)(b)

OPPONENT'S SUBMISSION:

D1 WO2009002809 [herein after referred as D1 **[**Abstract, Claim 1] discloses

compounds of Formula (I),



Wherein,

Rl is halogen, C1-C2 haloalkyl or C1-C2 haloalkoxy;

R2 is H, halogen or cyano;

R3 is H, halogen or CF3;

R4 is H, C2-C7 alkylcarbonyl or C2-C7 alkoxycarbonyl; and

R5 is C1-C6 alkyl or C1-C6 haloalkyl, each substituted with one substituent independently selected from hydroxy, C1-C6 alkoxy, C1-C6 alkylthio, C1-C6 alkylsulfonyl, C1-C6 alkylsulfonyl, C2-C7 alkylaminocarbonyl, C3-C9 dialkylaminocarbonyl, C2-C7 haloalkylaminocarbonyl and C3-C9 halodialkylaminocarbonyl.

Herein, the Opponent argues that when the above highlighted substituents are considered in the context of D1's Formula (I), they clearly resemble the structure of compound Formula 1 in the present impugned application, under two scenarios:

A. Earlier Claim 1: If R1 is halogen or C1-C2 haloalkyl, R2 is halogen, R3 is halogen or CF3, and R4 is hydrogen, the possible R5 substituents (like C1-C6 alkylsulfonyl, C2-C7 alkylaminocarbonyl, C3-C9 dialkylaminocarbonyl, C2-C7 haloalkylaminocarbonyl andC3-C9 alodialkylaminocarbonyl.) resemble the structure of compound of Formula 1 in the present application's compound, pecifically for all claimed subtituents of J.

B. Amended Claim 1: If R1 is halogen or C1-C2 haloalkyl, R2 is halogen, R3 is halogen or CF3, and R4 is hydrogen, the possible R5 substituents (like C2-C7 alkylaminocarbonyl, C3-C9

dialkylaminocarbonyl, C2-C7 haloalkylaminocarbonyl and C3-C9 halodialkylaminocarbonyl) also resemble the structure of compound of Formula 1 in the present impugned application, particularly J-1.

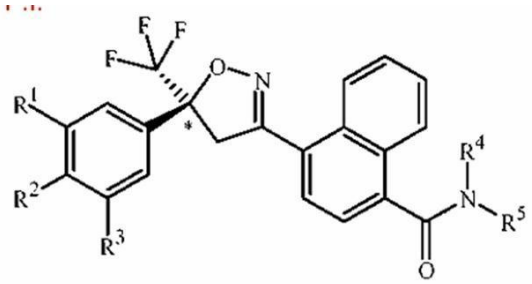
Summary: Thus, the opponent asserts that the prior art D1 discloses the possibility of the same compound of Formula 1 of the present impugned application that are structurally same suggesting that the present invention to be already in public domain before the filing of the said application and thereby critically challenging the novelty of the invention.

POINT-2:

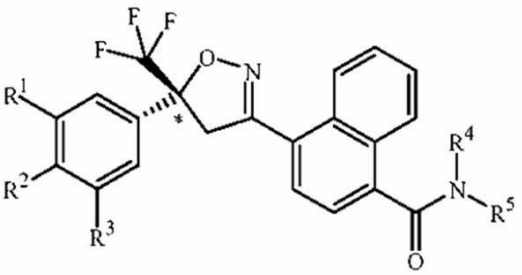
'D1 discloses the use of the composition made of the D1's Formula (I) can be used for invertebrate pest control in both agronomic and nonagronomic applications wherein the list of crops, animals and other products mentioned exactly resembles with the disclosure of the specification of the present application [Annexure -1: On Page 5, 6 and 81-88 of the Annexure].

POINT-3:

D1 discloses the existence of D1's Formula (I) as one or more stereoisomers which include enantiomers, diastereomers and atropisomers The compounds of the invention may be present as a mixture of stereoisomers, individual stereoisomers or as an optically active form.Further, 'D1 (Annexure 2)' [Page 120 of Annexures] presents following two structures supporting the afore-mentioned disclosure of 'D1' as:



1a



1b

Wherein, it is also mentioned that two possible enantiomers of Formula I are depicted as Formula la and Formula lb involving the Isoxazoline chiral center identified with an asterisk (*) with further mention that analogously, other chiral centers are possible at, for example, R5.

The Opponent submits that the potential existence of stereoisomeric forms of the compounds, particularly with the presence of an Isoxazoline chiral center and additional stereoisomeric possibilities related to the chiral centers of substituent "R5" in the prior art reference (D1) is explicitly disclosed in the specification of the present impugned patent application. The relevant sections of the application, namely [Annexure 1-Pages 8, 9, 13,14, and 19 of Annexures, outline that the compound of Formula 1 exists in stereoisomeric forms. These forms involve the Isoxazoline chiral center, as well as other potential stereoisomeric configurations of the substituent "J," which closely resembles the substituent "R5" as described in D1.

Therefore, it is clear from the application's specification that the existence of these stereoisomeric forms is contemplated and aligning with prior art disclosure and raising question regarding the novelty of the present impugned application.

POINT-4:
Further, the embodiment on D1 also showing resemblances in substituents wherein 'R2' in D1 is defined as 'Fluorine' and 'R1' and 'R3' analogous to substituents 'R^{1a}' and 'R^{1b}, of the present invention are exactly matching with the disclosure of 'Present Claim 3' of the impugned patent application.

POINT-5:
D1 discloses the 'scheme' of formation of such Naphthalene isoxazoline' compounds wherein, the 'Scheme 1' matches with 'Scheme 2' of the present impugned invention on [Page 23 of Annexures] and 'Scheme 2' matches with 'Scheme 1' of the present impugned invention on [Page 22 of Annexures] and 'Scheme 3' matches with 'Scheme 5' of the present impugned invention on [Page 25 of Annexures].

POINT-6:
'D1 discloses the invertebrate compositions made of such 'Naphthalene isoxazoline' compounds of Formula I can be made to useful formulations include both liquid and solid compositions wherein the list of names disclosed for liquid formulations, solid formulations, sprayable formulations along with the weight percentage table of the compositions and the names of diluents, surfactants are exactly resembling the broad disclosure for the same mentioned in the present impugned application specification [[Annexure 1-Page 73-76, 97, 99-100 of Annexures].

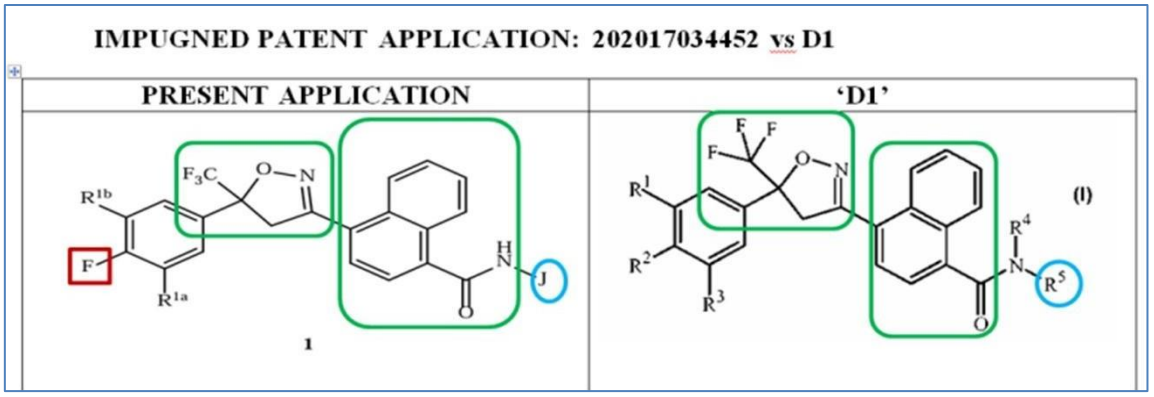
POINT-7:
Further,'D1 discloses the exact same formulations with same weight percentages of active and inactive components as disclosed in the present impugned application specification [Annexure 1-Page 78-80 of Annexures].

POINT-8:
Also, 'D1 [Claim 8, 9 and 10 of 'D1'] discloses a laundrylistofoneormoreotherbiologically active compounds or agents which are capable of forming suitable formulation with such 'Naphthalene isoxazoline' compounds of 'Formula I' which exactly matches with the large laundry list of compounds disclosed in the present application [Annexure 1-Page 73 and 90 of Annexures] and on 'Present amended claim 6'.

POINT-9:
D1[Claim 8, 9 and 10 of 'D1']discloses the 'Biological efficacy' of the composition wherein control efficacy (20% or less feeding damage or 80% or more mortality) is already mentioned and if any skilled artisan review the disclosures of the present impugned application [Annexure 1- From Page 102 onwards of Annexures] can understand that the present application also disclosing the similar control efficacy for the biological efficacy tests which

evidently proves that the disclosure of prior art 'D1' are enough anticipating for the present application.

COMPARISON OF PARENTAL STRUCTURES OF COMPOUNDS OF THE PRESENT APPLICATION AND PRIOR ART 'D1'



OVERALL OBSERVATION:

Based on the disclosures in D1 (Annexure 2), the Opponent asserts that the present impugned patent application lacks novelty. The substantial overlap in the chemical structures, formulations, methods, uses, and biological efficacy between the disclosures in D1 and the present application demonstrates that the invention claimed in the present patent is already in the public domain. The Opponent contends that the claimed invention is anticipated by prior art D1 and therefore does not meet the requirements of novelty, raising significant concerns about the patentability of the present application.

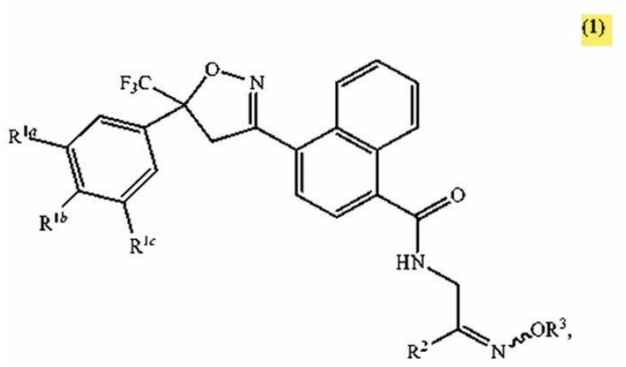
Herein, the Opponent highlights the 'The Patent manual which mentions that: "A specific disclosure in the prior art takes away the novelty of a generic disclosure" Clearly, the disclosures and present claim 1 of 'D1' exactly resembles certain specific prototypes of broad Compound 1 of the P.I. with highlighted substituents matching with certain 'J' substituents.

Therefore, the present claims of the impugned invention lacks novelty in view of the cited prior arts D1 following the provisions of 'Section 25(1)(b)' with the 'Section 2(1)(j)' and '2(1)(l)', therefore the patent application shall not be granted and is liable to be rightly rejected on this ground on the grounds of 'Section 25(1)(b)-Lack of Novelty'.

2. **D2: US2012077765A1** [published on 29/03/2012] Title:
"ISOXAZOLINE OXIMES AS ANTIPARASITIC AGENTS"
Field of Invention: This invention relates to isoxazoline oxime derivatives having parasiticidal activity. The compounds of interest are substituted naphthyl isoxazoline oxime derivatives. The invention also relates to compositions and methods of use thereof.

POINT-1:

D2 US2012077765 hereinafter referred as D2 – [CLAIM 1] and [Abstract, Summary] discloses:
Isoxazoline oxime derivatives of Formula (1):



wherein

(1) R1a,R1b,and1careeachindependentlyselectedfromhydrogen,halo, cyano, C1-C6 alkyl, C1-C6haloalkyl, C1-C6 alkoxy,
R2isH,C1-C6alkyl, C1-C6 alkyl phenyl,…….
R3 is H, C1-C6 alkyl, C0-C6 alkyl, C3-C6 cycloalkyl, C0-C6 alkenyl, C0- C6 alkyl phenyl, C1-C4 alkyl-O-phenyl, C0-C6 alkyl heterocycle, or C0-C6 alkyl heteroaryl; each of R2 and R3 C1-C6 alkyl or C0-C6 alkyl, C3- C6 cycloalkyl can be optionallyand independently substituted by at least one substituent selected from cyano, halo,……
Herein, the Opponent argues that when the above highlighted substituents are considered in the context of D2's Formula (1) clearly resemble the structure of compound Formula 1 in the present impugned application Under both the scenarios:
A. Earlier Claim 1: If R1a,R1b,and1careeachindependentlyselectedfromhydrogen, halo, C1-C6haloalkyl, and R2isH,C1-C6alkyl, R2isH,C1-C6alkyl, then the structure of compound in prior D2 is found to resemble with the structure of compound of Formula 1 in the present application, with J-3.
B. Amended Claim 1: In amended claim 1, as J-3 substituent have been deleted.
Herein, the Opponent asserts that the structure of the compound in prior art D2, after the deletion of J-3 from the original list of compounds the earlier is now not in the scope of the current set of claims but still the other similarity of disclosures as detailed below shows the represent invention to be anticipating in comparison to the disclosures of 'D2'.

POINT-2:
Further, Claim 4 and 5 of prior art 'D2 (Annexure 3)' [Page 306 of Annexures] mentions that if selectively the substituents, R^{1a}, R^{1b} and R^{1c} are each independently selected from hydrogen, chloro, fluoro, and C1- C6 haloalkyl, and R3 is H, C1-C6 alkyl, Co-C6 alkyl, C3- C6 cycloalkyl, or C1-C6 alkyl substituted with halo then exactly the same compound of Formula 1 of the present impugned patent application would get deduced as claimed in present amended claim 1-5.

POINT-3:
Further, 'D2 (Annexure 3)' ['Summary-Para 0008] discloses: The present invention provides Formula (1) compounds, geometric isomers, stereoisomers thereof, which act as parasiticides, in particular, ectoparasiticides; therefore may be used to prevent, treat, repel, and control acarids and insect infection and infestation in animals.

Herein, the Opponent would like to stress on the fact that the compound of Formula (1) in D2 is also used with the objective of prevent and inhibiting invertebrates pest/insects on animals as parasites. Hence, it is to be noted that the nature of the Naphtahlene Isoxazoline compounds to show the invertebrate pesticidal control would remain and shown equally whether applied on crops or on animals, the purpose of such compounds to be used for their invertebrate pescital effect is already known as per disclosure of 'D2' prior art. So, point of whether it is applied on crops or on animals cannot be the point to male the present invention 'novel' wherein evidently the compound is found to be existing in public domain.
Moreover, the present invention disclosure [Annexure 1- Page 20 of Annexures] itself also discloses the use of such compounds show favorable pharmacokinetic properties in vertebrate animals.

POINT-4: D2 discloses the existence of D2's Formula (1) as one or more stereoisomers which include enantiomers, diastereomers and atropisomers The compounds of the invention may be present as a mixture of stereoisomers, individual stereoisomers or as an optically active form. The Opponent submits that the potential existence of stereoisomeric forms of the compounds, particularly with the presence of an Isoxazoline chiral center and additional stereoisomeric possibilities the prior art reference (D12 is explicitly disclosed in the specification of the present impugned patent application. The relevant sections of the application, namely Pages 8, 9, 13, 14, and 19, outline that the compound of Formula 1, as disclosed in the present invention, exists in stereoisomeric forms. These forms involve the Isoxazoline chiral center, as well as other potential stereoisomeric configurations of the substituent "J," which closely resembles the substituent comprising 'R2' and 'R3' as described in D2.

POINT-5:

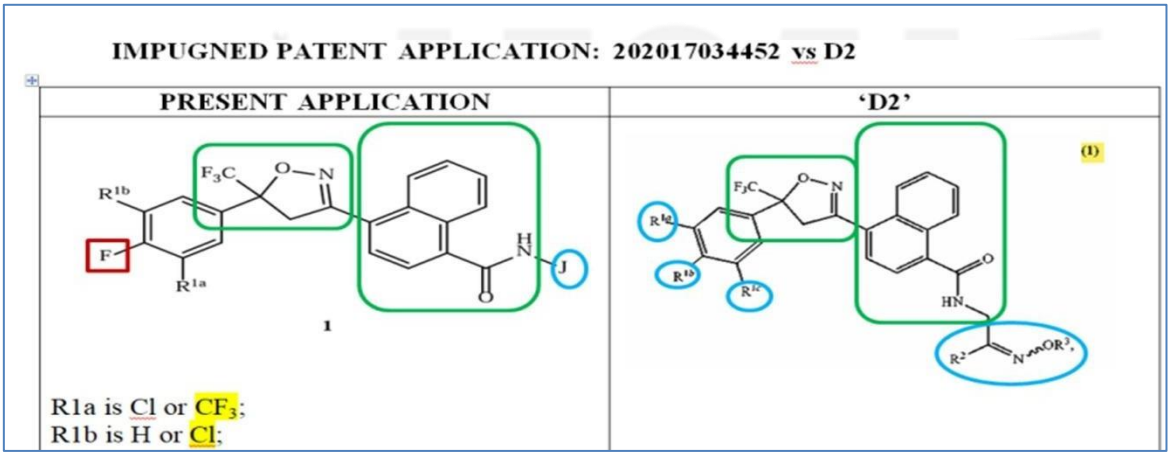
D2 discloses that the said isoxaline compound of Formula (1) in 'D2' is used for typical formulation is prepared by mixing a Formula (1) compound with a pharmaceutically or veterinarily acceptable carrier, diluent or excipient. Suitable carriers, diluents and excipients are well known to those skilled in the art which exactly coincides with the disclosures of present impugned application [on Annexure 1- Page 73 of Annexures].

POINT-6:
'D2 discloses compounds may be administered alone or in combination with at least one additional veterinary agent including laundry list of other biologically active compounds or agents which are capable of forming suitable formulation with such 'Isoxazoline' compounds

of 'Formula 1' which exactly matches with the large laundry list of compounds disclosed in the present application [Annexure 1- Page 73 and 90 of Annexures] and on 'Present amended claim 6'.

The Opponent asserts that as per present claim 1 filed by the Applicant after the Opponent deliberations were completed in the pre-grant opposition deliberations and as that now though exact structural similarities between the compounds of Formula (1) in D2 and the present application is not shown but just mere change of one substituent does not change the surprising resemblances of the parental structures in both the documents. Moreover, the present impugned application lacks novelty due to its substantial similarity to the prior art disclosed in D2 considering the functional use of these compounds as parasiticides for invertebrate pest control, suggest that the present invention is anticipated by prior art. Additionally, the formulation techniques, stereoisomeric forms, and administration with other veterinary agents are all disclosed in D2, further supporting the claim that the present application does not meet the requirements for patentability.

COMPARISON OF PARENTAL STRUCTURES OF COMPOUNDS OF THE PRESENT APPLICATION AND PRIOR ART 'D2'

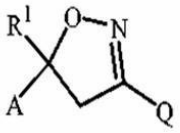


3. **D3: WO2008154528A2** Title: "Isoxazoline insecticides"

Field of Invention: This invention relates to certain isoxazolines, their //-oxides, salts and compositions suitable for agronomic, nonagronomic and animal health uses, methods of their use for controlling invertebrate pests such as arthropods in both agronomic and nonagronomic environments, and for treatment of parasite infections in animals or infestations in the general environment.

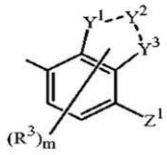
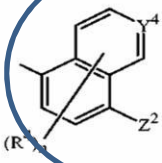
POINT-1:D3 [CLAIM 1] and [Abstract] discloses:Isoxazoline insecticides of Formula (I):

A compound selected from Formula 1, JV-oxides and salts thereof,



1

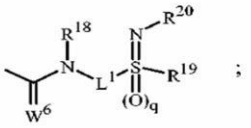
Wherein, Aisa6-memberedaromaticringcontainingwherein, carbonatoms and 0-3 nitrogen atoms as ring members, saidringoptionallysubstituted with1-5substituentsindependently selectedfromR2;

Q is  or  ;

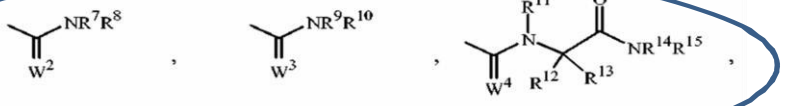
Q-A Q-B

$\gamma^1..\gamma^2..\gamma^3$ is -CH=CH-S-, -CH=CH-O-, -CH=CH-NH-, -CH=N-NH-, -S-CH=CH-, -0-CH=CH-, -NH-CH=CH- or -NH-N=CH-;

Y^4 is CR^4 or N;

Z^1 is  or  ;

Z^1-I Z^1-2 Z^1-3

Z^2 is 

Z2-1 Z2-2 Z2-3

each W1,W2,W3,W4,W5andW6isindependentlyO or S;

with the sub-substituents of R7, R8, R9, R10 , R11, R12, R13, R14 and R15 are suitably disclosed in the prior art 'D3' which clearly matches with the structure of compound of Formula I of the present patent application with J suitable being J-1.

The Opponent asserts that D3 (Annexure 4) discloses Isoxazoline insecticides of Formula (I), which includes a 6-membered aromatic ring with carbon and nitrogen atoms. The substituents, including R2 and the sub-substituents (R7, R8, R9, R10, R11, R12, R13, R14, and R15), are disclosed in D3 and show a close structural match to the compound of Formula I in the present patent application. The Opponent argues that the structure of the compound disclosed in D3 is highly resembling to the compound in the present patent, particularly with the J-1 substituent.

POINT-2:
D3 [Claim 5-7] discloses a laundrylistof one or more other biologically active compounds or agents which are capable of forming suitable formulation with such 'Isoxazoline insecticides' compounds of 'Formula I' which exactly matches with the large laundry list of compounds disclosed in the present application [Annexure 1-Page 73 and 90 of Annexures] and on 'Present amended claim 6'.

POINT-3:
D3 discloses the invertebrate compositions made of such 'Isoxazoline insecticide' compounds of Formula I can be made to useful formulations include both liquid and solid compositions wherein the list of names disclosed for liquid formulations, solid formulations, sprayable formulations along with the weight percentage table of the compositions and the names of diluents, surfactants are exactly resembling the broad disclosure for the same mentioned in the present impugned application specification [Annexure 1-Page 73-77 of Annexures].

POINT-4:
'D3 discloses the exact same formulations with same weight percentages of active and inactive components as disclosed in the present impugned application specification [Annexure 1-Page 78-80 of Annexures].

POINT-5:'D3 discloses a laundry list of one or more other biologically active compounds or agents which are capable of forming suitable formulation with such 'isoxazoline insecticide' compounds of 'Formula 1' which exactly matches with the large laundry list of compounds disclosed in the present application [Annexure 1-Page 73 and 90 of Annexures] and on 'Present amended claim 6'.

POINT-6 D3 (Annexure 4)' [Page 441-445 of Annexures] discloses the 'Biological efficacy' of the composition wherein control efficacy (20% or less feeding damage or 80% or more mortality) is already mentioned and if any skilled artisan review the disclosures of the present impugned application [Annexure 1- From Page 102 onwards of Annexures] can understand that the present application also disclosing the similar control efficacy for the biological efficacy tests which evidently proves that the disclosure of prior art 'D3' are enough anticipating for the present application.

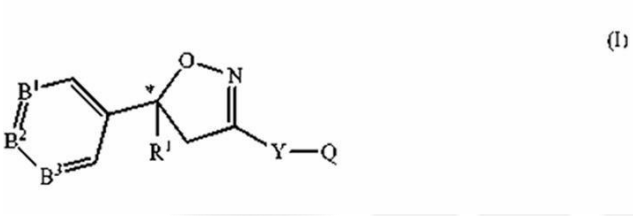
The Opponent submits that D3 (Annexure 4) provides prior art that fully anticipates the claims of the present application. The disclosures in D3, particularly with regard to the structure, formulations, and biological efficacy of Isoxazoline insecticides, directly overlap with the claims in the present application, both before and after amendments. Therefore, the Opponent asserts that the present claims are not novel and are fully anticipated by the prior art in D3.

4. **D4: US2017020848A1** [Annexure 5, published on 26/01/2017]

Title: “Extended release injectable formulations comprising an isoxazoline active agent, methods and uses thereof”Field of Invention: This invention relates to certain isoxazolines, their -oxides, salts and compositions suitable for agronomic, nonagronomic and animal health uses, methods of their use for controlling invertebrate pests such as arthropods in both agronomic and nonagronomic environments, and for treatment of parasite infections in animals or infestations in the general environment.

POINT-1:
‘D4 (CLAIM 2 of D4 discloses): This invention relates to extended release injectable formu lations for combating parasites in animals, comprising at least one isoxazoline active agent, a pharmaceutically acceptable polymer, and a solvent. This invention also provides for improved methods for eradicating, controlling, and preventing parasite infections”

POINT-2:
‘D4 [CLAIM 3] discloses:The extended release injectable composition according to claim 2 comprising:
a) an antiparasitic effective amount of at least one isoxazoline active agent, which is:
i) an isoxazoline compound of formula (I):



wherein:

B1, B2 and B3 areeachindependentlyC-R or N;
each RisindependentlyH,halogen, cyano, —NO2,……
R1 is C1-C3 alkyl or C1-C3haloalkyl;
Y is an optionally Substituted phenylene, naphthalene, indanylene, a 5- or 6-membered heteroarylene or an 8-10-membered fused heterobicyclylene, wherein the optional Substituentsareselectedfromthegroup……
QisX-NR2R3, the group… ..... ;
X is (CH), CH(CH), CH(CN), C(=O) or C(—S);

R2isH, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, cycloalkylalkyl,…….
R3 is H, OR7, NR8R9orQ'; or alkyl, haloalkyl, alkenyl, haloalkenyl, alkynyl, haloalkynyl, cycloalkyl, alkylcy cloalkyl, cycloalkylalkyl, alkylcarbonyl, alkoxycarbo nyl, aminocarbonyl, alkylaminocarbonylordialkylaminocarbonyl,eachoptionallysubstitutedwithoneormore substituentsindependentlyselectedfromR4;
each R4 is independently halogen; alkyl, cycloalkyl, alkoxy, alkylthio,…….. cycloalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylaminocarbonyl, dialkylamin

ocarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, haloalkylaminocarbonyl, dihaloalkylaminocarbonyl,

Q1isaphenylring,a5-or6-memberedheterocyclicring, or an 8-, 9- or 10-membered fused bicyclic ring toms selected from up to 1O. up to 1S and up to 3N, each ring or ring system optionally Substituted with one or more substituents independently selected from R:

Q2 is independently a phenyl ring or a 5- or 6-membered heterocyclic ring, each ring optionally substitutedwithoneormoresubstituentsindependentlyselectedfromR:

Q3isaphenylringora5-or6-memberedheterocyclicring,eachringoptionallySubstituted withoneor moresubstituentsindependentlyselectedfromR:and n is 0,1or2;and/or

Herein, the Opponent argues that when the above highlighted selective substituents when considered in the context of D4's isoxazoline compound of formula (I), exactly matches with the structures of compound Formula 1 in the present impugned application for both earlier 'Claims on record' as well as 'Present Amended Claims'

A. Earlier Claim 1: If the substituents as highlighted above are selected suitable for the isoxazoline compound of formula (I) of D4, then structure of the compound exactly resemble the structure of compound of Formula 1 in the present application's compound, resemble the structure of compound of Formula 1 in the present application's compound, specifically for all claimed subtituents of J.

B. Amended Claim 1: If the substituents as highlighted above are selected suitable for the isoxazoline compound of formula (I) of D4, then structure of the compound exactly resemble the structure of compound of Formula 1 in the present application's compound, specifically for J-1 and J-5As structure with J-1 can be envisage by considering the substituents as 'aminocarbonyl, alkylaminocarbonyl or dialkylaminocarbonyl' and 'alkylaminocarbonyl, dialkylaminocarbonyl'

AND The structure with J-5 can be envisage by considering the substituents as'alkoxycarbonyl' and 'haloalkoxycarbonyl'which is the present amended claim 1 filed by the Applicant which makes the invention completely anticipating and Not acceptable based on the grounds of 'NOVELTY'.

Summary: Thus, the opponent asserts that the prior art D4 discloses the possibility of the same compound of Formula 1 of the present impugned application that are structurally same suggesting that the present invention to be already in public domain before the filing of the said application and thereby critically challenging the novelty of the invention.

POINT-3:Further, Claim 5 along with Claim 18 and 19 also discloses 'isoxazoline compounds' Formula (IIa) and Formula (IIc), wherein on suitable selection of substituents would lead to the same 'Naphthaline Isoxaline' compound of the present impugned patent application.Support of the above-stated submissions can also be found in the embodiments of the prior art 'D4' [on Pages 465-466 of Annexures] which clearly establishes the exact

resemblance in the structures of the compound in question disclosed and claimed in the present impugned application.

POINT-4:'D4 [CLAIM 38] discloses: The use of an isoxazoline in the preparation of an extended release injectable formulation for the treatment or prevention of a parasite infestation or infection on or in an animals.

- APPLICANT'S SUBMISSION ON GROUNDS OF LACK OF NOVELTY U/S 25(1)(b):

CITED PRIOR ARTS CONSIDERED DURING THE PRE-GRANT OPPOSITION

HEARING DELIBERATIONS UNDER SECTION 25(1)(b):

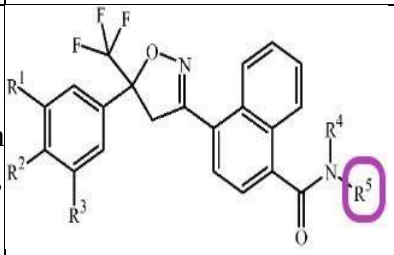
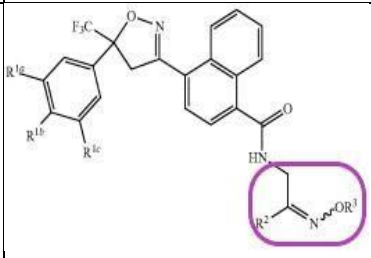
D1: WO2009002809A1 [Annexure 2, published on 31/12/2008]

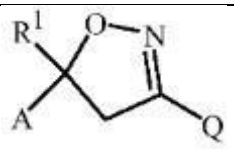
D2: US2012077765A1 [Annexure 3, published on 29/03/2012]

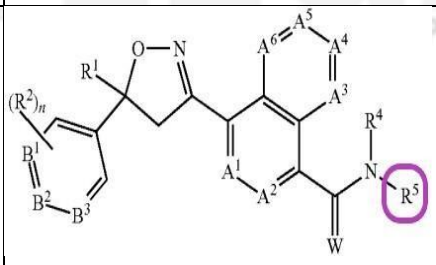
D3: WO2008154528A2 [Annexure 4, published on 18/12/2008]

D4: US2017020848A1 [Annexure 5, published on 26/01/2017]

The Applicant has applied the above legal principle of novelty and has demonstrated that the claimed compounds are novel in view of the documents D1 to D4.

Document / Publication Date	**Teaching of the Document**	**Applicant Submission / Comment / Remark**
D1:WO2009002809; Published on December 31, 2008		**In D1, no exemplifications** were made for compounds bearing the 4-fluorophenyl at C5 of the isoxazoline in combination with the (R)- stereochemistry on the alanine side chain
D2: **US2012077765 ≈ WO2012038851** published on March 29,2012		The marked substitution is totally different w.r.t **J-1 and J-5, the carbonyl group absent.**

D3: WO2008154528, published on December 18, 2008		• Most of the compounds in D3 do not contain a naphthyl ring as in our invention. Only the compounds in Table 25-32 (page 65), 33-40, and page 67 feature the naphthyl ring. However, even in these compounds, the combination of a 4- fluoro substitution with R-stereochemistry, which coincides with the substitutions of J1 or J5, is absent. • Table A in D3 (page 32) defines 30 specific exemplified embodiments, where the 4-fluoro substitution is absent,

Document / Publication Date	**Teaching of the Document**	**Applicant Submission / Comment / Remark**
D4: US2017020848 ≈ WO2016164487 published on January 26, 2017		**D4, non-analogous art** i.e., used in the treatment of parasitic infections.

- DISCUSSION AND CONCLUSION LACK OF NOVELTY U/S 25(1)(b): : On reading through the submission ,it is clearly demonstrated in above table, there is no enabling disclosure or direction of teaching in the cited prior art documents D1 to D4, to arrive at the claimed invention. The broad generic disclosure of the cited prior art, D1 to D4, does not envisage the specific claimed compound of the instant application, IN' 452. Further, the exemplified compounds of D1 to D4 would draw a person skilled in the art to a different direction.The amended claims are not suggested in the cited prior art. Thus, the

Opponent has failed to provide any reasoning why a person skilled in the art would have "envisaged at once" the necessary selections without any teaching to arrive at any particular compound over many other selections that were equally plausible.The ground of opposition for lack of novelty is therefore rejected .

- **GROUND II: LACK OF INVENTIVE STEP U/S 25(1)(e)**
- OPPONENT'S SUBMISSION **:**

OPPOSITION HEARING DELIBERATIONS UNDER SECTION 25(1)(e):

D1- Patent Application No: WO200900280A2

D2- Patent Application No: US2012077765A1

D3- Patent Application No: WO2008154528A2

D4- Patent Application No: US2017020848A1

D6- Patent Application No: DK2576523T3

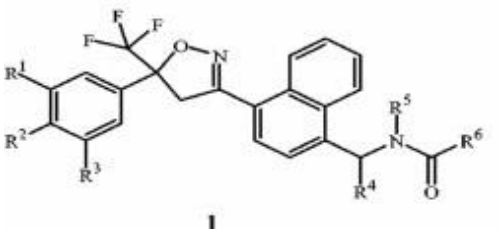
D7 – NPL – "Discovery and mode of action of afoxolaner, a new isoxazoline parasiticide for dogs"

The opponent submits that , based on the arguments presented in the previous sections regarding the prior arts D1-D4 under 'Novelty (u/s 25(1)(b))', the Opponent further contests the present impugned patent application on the grounds of lack of inventiveness (Section 25(1)(e))considering these two prior arts as well. The Opponent asserts that the subject matter of the invention fails to overcome the hurdle of Lack of Inventiveness/Obviousness as after the detailed review of the prior arts D1 to D4, it is amply clear for any person skilled in the art that the subject matter of the present patent application is merely a result of routine workshop improvement and does not reflect any inventive step. Therefore, the application should be rejected for not meeting the inventiveness requirement and being obvious under the applicable grounds of 'Section 25(1)(e)' of 'The Patent Act'.

Other cited prior arts:
D6: DK2576523T3 [Annexure 7, published on 10/04/2013]
D7: Discovery and mode of action of afoxolaner a new isoxazoline parasiticide for dogs published on 02/04/2014, by Wesley L Shoop et al.

D6: DK2576523T3 [Annexure 7, published on 10/04/2013]
Opponent submits
Title: A crystalline form of 4- [5- [3-chloro-5- (trifluoromethyl) phenyl] -4,5-dihydro-5- (trifluoromethyl) -3-isoxazolyl] -N- [2-oxo-2 - [(2,2,2-trifluoroethyl) amino] ethyl] - 1-naphthalenecarboxamide.'D6 discloses a to a solid form of 4- [5- [3-chloro-5- (trifluoromethyl)phenyl] -4,5-dihydro-5- (trifluoromethyl) -3-isoxazolyl] -N- [2-oxo-2 - [(2,2,2-trifluoroethyl)amino] ethyl] - 1-naphthalenecarboxamide
POINT 1:

D6 discloses the structure of the compound as:



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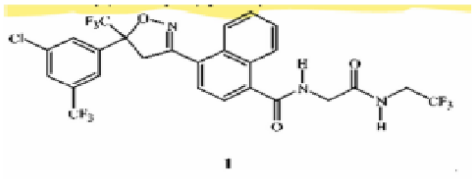
D6 discloses the compound with exact same structure with the 'Naphthaine isoxaline' compound of the present patent application wherein, the parental structure is the same .Moreover, 'D6 further discloses the specific compound with structure:



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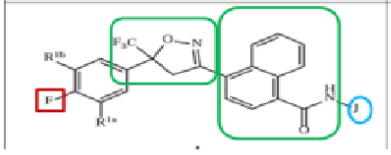
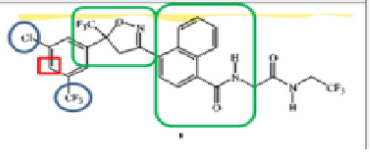
Herein, the Opponent would like to present the following comparison of the structure which shall clearly provide the evidence that both present application **and the prior art 'D6' are centric on the same compound.**

IMPUGNED PATENT APPLICATION: 202017034452 vs D6

PRESENT APPLICATION	'D6'
	

The structural similarity of the compound disclosed in **'D6'** and the **compound Formula 1** in the present impugned application in respect to both earlier **'Claims on record'** as well as **'Present Amended Claims'** are presented herein:

A. **Earlier Claim 1:** The compound of **D6** exactly resemble the structure of **compound of Formula 1** in the present application's compound, wherein the resemblance of the structure of **compound of Formula 1** in the present application's compound, specifically for all claimed subtituent of **J as C(O)NHR17** and **J-1.**

B. Amended Claim 1: The compound of **D6** exactly resemble the structure of **compound of Formula 1** in the present application's compound, wherein the resemblance of the structure of **compound of Formula 1** in the present application's compound, specifically for all claimed substituent of **J-1.**

POINT 2:

D6 (Annexure 7)' [Page 609-Para 0019 of Annexures] further discloses that the molecular structure of the compound of **'D6'** can exist as distinct stereoisomers, moreover such structure are known to be existing as racemic mixtures in form of compositions which resembles with the disclosure of the present impugned patent application [Annexure 1-**Pages 8, 9, 13, 14, and 19 of Annexures]**.

Therefore, it is clear from the application's specification that the existence of these stereoisomeric forms is contemplated and aligning with prior art disclosure of D6.

POINT 3:

D6 (Annexure 7)' [Page 616 and 617-Para 0058-0068 of Annexures] further discloses detailed description regarding the compound can be can be made to useful formulations include both liquid and solid compositions wherein the list of names disclosed for liquid formulations, solid formulations, sprayable formulations along with the weight percentage table of the compositions and the names of diluents, surfactants are exactly resembling the broad disclosure for the same mentioned in the present impugned application specification **[Annexure 1-Page 73-76, 97, 99-100 of Annexures].**

POINT 4:

D6 (Annexure 7)' [Page 618 and 622 of Annexures] discloses the exact same formulations with same weight percentages of active and inactive components as disclosed in the present impugned application specification **[Annexure 1-Page 78-80 of Annexures].**

POINT 5:

D6 (Annexure 7)' [Page 622 of Annexures] discloses use of the compound for pest control in both agronomic and nonagronomic applications wherein the list of crops, animals and other products mentioned exactly resembles with the disclosure of the specification of the present application **[Annexure -1: On Page 81-88 of the Annexure].**

POINT 6:

D6 (Annexure 7)' [Page 626-627, Para 0096 and 0097 of Annexures] discloses a laundry list of one or more other biologically active compounds or agents which are capable of forming suitable formulation with the compound of 'D6' which exactly matches with the large laundry list of compounds disclosed in the present application **[Annexure 1-Page 73 and 90 of Annexures]** and on **'Present amended claim 6'.**

Overall Conclusion

Therefore, the Opponent comprehends that the disclosure in **'D6'** is in alignment with the invention's objectives of the impugned application and hence the Opponent submits that the present invention claimed in the present application is not inventive as it clearly lacks inventive step and is evidently obvious for any person skilled in the art and skilled person in the art can easily arrive at the present invention from the **teachings of the prior art 'D6' combination with the learnings of the prior arts (D1-D4)** and should hence be rejected based on obviousness *and is liable to be out rightly rejected on this ground on the grounds of* ***'Section 25(1)(e)-Lack of Inventive Step'*** *the presently amended claims 1-6 of said impugned patent application must be dismissed.*

4. D7: Discovery and mode of action of afoxolaner a new isoxazoline parasiticide for dogs published on 02/04/2014, by Wesley L Shoop et al.

Our Submissions:

Title: Discovery and mode of action of afoxolaner, a new isoxazoline parasiticide for dogs

'D7 (Annexure 8)' discloses a "compound named as **afoxolaner** as a new isoxazaline parasiticide" **[Abstract, PAGE 646 of Annexures].**

POINT 1:

'D7 (Annexure 8)' [Page 647 of Annexures] discloses the structure of the compound as:

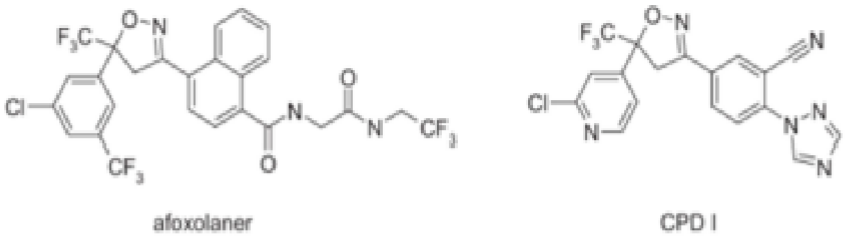
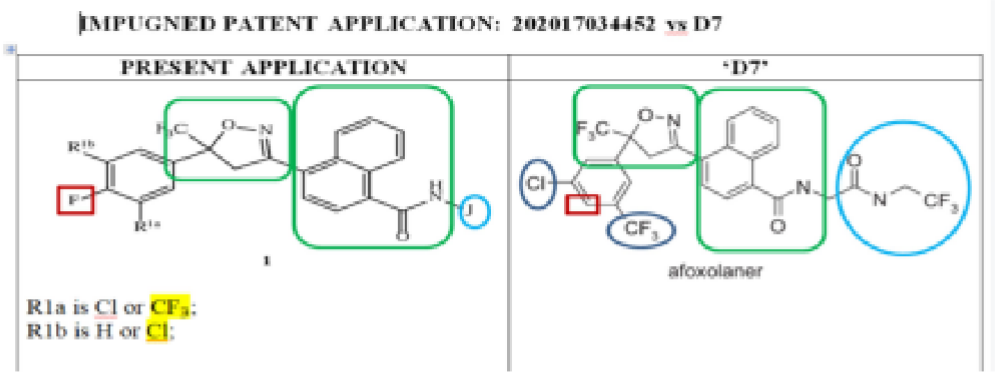


Fig. 1. Molecular structure of afoxolaner and the isoxazoline, CPD I.

Wherein, on the same context the prior art on the same page discloses that the said compound of **'Afoxolaner'** ***which is shows similarity with the structure of the compound Formula I of the present impugned application is known to show remarkable activity of afoxolaner against fleas, and sub sequent in vivo testing in dogs demonstrated outstanding effectiveness against fleas and ticks.***

Herein, the Opponent would like to present the structural similarity between both the compounds of present invention and the prior art **D7** as:



The structural similarity of the compound disclosed in **'D7'** and the **compound Formula 1** in the present impugned application in respect to both earlier **'Claims on record'** as well as **'Present Amended Claims'** are presented herein:

A. **Earlier Claim 1:** The compound of **D7** exactly resemble the structure of **compound of Formula 1** in the present application's compound, wherein the resemblance of the structure of **compound of Formula 1** in the present application's compound, specifically for all claimed subtituent of **J as C(O)NHR17** and **J-1.**

B. Amended Claim 1: The compound of **D7** exactly resemble the structure of **compound of Formula 1** in the present application's compound, wherein the resemblance of the structure of **compound of Formula 1** in the present application's compound, specifically for all claimed substituent of **J-1.**

Therefore, the Opponent would like to stress on the fact that as since the compound is structurally identical in both documents and is used in formulations for pest control, it is irrelevant whether the compound is applied to crops or animals, what matters is that the same compound, in the same formulations, exhibiting the same activity, has already been disclosed in the prior art **'D7'** This prior disclosure is sufficient to negate the novelty of the present impugned application

Overall Conclusion:

Therefore, the Opponent comprehends that the disclosure in **'D7'** is in alignment with the invention's objectives of the impugned application and hence the Opponent submits that the present invention claimed in the present application is not inventive as it clearly lacks inventive step and is evidently obvious for any person skilled in the art and skilled person in the art can easily arrive at the present invention from the **teachings of the prior art 'D7' combination with the learnings of the prior arts (D1-D4 and D6)** and should hence be rejected based on obviousness *and is liable to be out rightly rejected on this ground on the grounds of* ***'Section 25(1)(e)-Lack of Inventive Step'*** *the presently amended claims 1-6 of said impugned patent application must be dismissed*

APPLICANT SUBMISSION ON GROUND II LACKOF INVENTIVENESS :

The applicant submits (1) Legal Principles of Obviousness with the definition of 'inventive step' in The Patents (Amendment) Act reads as under: - Section 2(1) (ja) "inventive step" means a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art.

Non-obviousness is a mixed question of law and fact and, therefore, must be adjudicated by way of legal principles and material facts. (Guidelines for Examination of Patent Applications in the Field of Pharmaceuticals, October 2014, paragraph 8.4) 31. The following principles have been established for a non-obviousness enquiry. The legal test of non-obviousness has been extensively dealt with by the IPAB and Courts in India. The applicant submits that the Opponent failed to apply the inventive step test as laid down in para. 118 of the order of the Division bench of the Delhi High Court in Roche vs CIPLA (enclosed), RFA 92/20128.

The applicant states that

1) **Gilead Pharmasset, LLC vs Sankalp Rehabilitation Trust11, para 22, IPO,** *The opponents have failed to provide anydocument which suggests such general teaching which states that selected specific substituents on phosphoramidate will show same activity for every nucleoside moiety irrespective of its structure. The selection of specific nucleoside moiety having* Structural similarity cannot form basis of selection of lead compound for obviousness: and refers to Hon'ble Justice Mukta Gupta of the Delhi High Court in BMS vs. BDR9 s and Gilead Pharmasset, LLC vs Sankalp Rehabilitation Trust11, para 22, IPO,

2) Biological activity of a molecule has to be seen as a whole

In this regard, reference has been made to the case law Merck vs Glenmark that held that the biological activity of a molecule must **be seen as a whole**.

specific substituents thereon and selection of specific substituents in phosphoarmidate moiety of present invention is considered as non-obvious.

Claimed invention is not obvious in view of cited prior art documents: The Applicant at the hearing submits that:

a) The Opponent in the hindsight manner has identified the prior art and thereafter particularly select a portion of the compound. In that process, the Opponent has ignored the other part of the molecule.

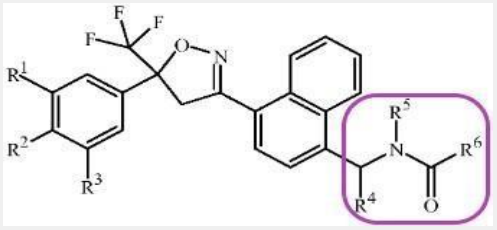
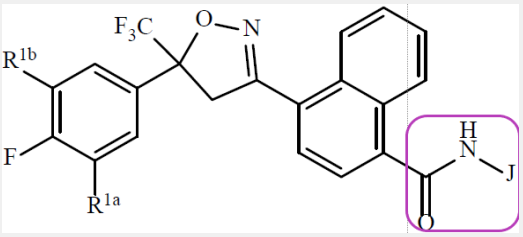
b) There is no indication in D1-D4 that would motivate a person skilled in the art to consider compounds with a 4-fluorophenyl group at C5 of the isoxazoline, combined with the (R)-stereochemistry on the alanine side chain, as no exemplifications of such compounds are provided.

c) The Opponent has, with the benefit of hindsight, identified prior art D6 and D7 solely because the AFOXOLANER moiety is commercially available. However, D6 (DK'253) and D7 teach away from compounds wherein X = F and (R)-configuration on the alanine side chain.

d) There is no coherent thread that combine the alleged prior art, i.e., teaching of one lead to second and so on. On the contrary, the Opponent, having knowledge of the claimed compound, thereafter in the hindsight manner has combine the prior art documents.

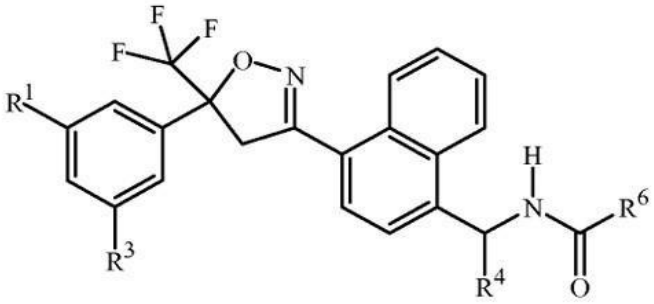
D5 (WO' 999) teaches away structurally different compounds: 37. The Applicant submits that compounds of WO '999 are structurally different having an additional R4 substituent (wherein R4 is H, halogen, cyano, C1-C3 alkyl or C1-C3 haloalkyl; R5 is H, CH3, C2-C7 alkylcarbonyl, C2-C4 haloalkylcarbonyl, C2-C7 alkoxycarbonyl or CH2O(C1-C3 alkyl) and also R6 substituent (wherein R6 is C1-C6 alkyl group optionally substituted with halogen, OR11, S(O)nR12 or NR13C(O)R14; or R6 is C3-C6 cycloalkyl or C4-C7 cycloalkylalkyl, each optionally substituted with 1 to 4 substituents selected from the group consisting of halogen, C1- C2 alkyl, C1-C2 haloalkyl and up to 1 cyclopropyl; or R6 is (CH2)mQ; or R6 is OR8 or NR9aR9b). These differences distinguish the compounds envisaged from D5 than those present in the instant application, IN' 452.

Moreover, the carbonyl part of the amide is directly attached to the napthyl ring in the compounds of the present application in contrast to the compounds of WO '999, wherein the nitrogen of amide is attached to the napthyl ring through an alkyl chain

WO'999	IN'452
	

While the generic disclosure mentions halogen substitutions at 4'-position of the phenyl ring in D5. However, there is no direction of teaching towards halogen substitution at 4'-position. In fact, the exemplified compounds do not even contain a substitution at 4'-position of phenyl ring The 9 exemplified compounds listed in Index Table A (Page 57) of D5 are shown below:

INDEX TABLE A



Cmpd. No.	R^1	R^3	R^4	R^6	m.p. (°C)
1 (Ex. 1)	Cl	Cl	H	cyclopropyl	**
2	Cl	Cl	H	isopropyl	*
3	Cl	Cl	cyano	cyclopropyl	*
4	CF_3	CF_3	CH_3	isopropyl	*
5	Cl	CF_3	H	isopropyl	*
6	Cl	CF_3	H	cyclopropyl	*
7	CF_3	CF_3	CH_3	CH_2CF_3	*
8	CF_3	CF_3	CH_3	$CH(CF_3)_2$	*
9	CF_3	CF_3	CH_3	CF_2CF_3	*

The generic broad structure and the specific compounds of D5, Index Table 5, would not lead a person skilled in the art to arrive at the compounds of instant application, IN' 452. In D5, unlike instant application, the 4'-position of phenyl is unsubstituted.Additionally, the stereochemical configuration at R4 position in D5 is not in Rconfiguration, which further diverges from the compounds in claimed invention.

Therefore, D5 does not provide any motivation for a person skilled in the art to arrive at the compounds of our invention. Thus, the direction of teaching in D5 points towards no substitution at 4-position of the phenyl group attached to the isooxazoline ring, rather than the novel substitution present in instant application, IN' 452.

(b) POSA would not select AFOXOLANER from D6 (DK'253) and D7 as lead compound:

The Applicant submits that the compounds of the present invention are inventive inview of Document D6. While **D6 discloses a subset of naphthyl carboxamides, including afoxolaner for crop protection, the compounds disclosed in D6 aredistinguishable from those of the present invention based on two key structural features:**

a) **Chiral Center and (R)-Stereochemistry:**

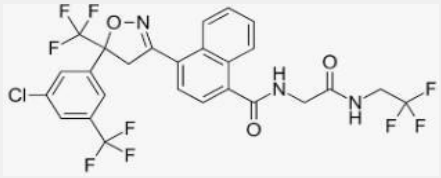
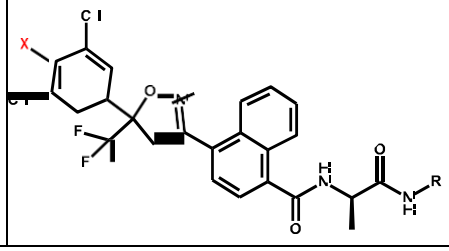
In D6, the chiral centre at J = J1 or J5 is not specified with any stereochemistry, whereas in the present invention, it is explicitly specified that the chiral centre has the (R)-configuration at the R2 and R14 position specifically for J-1 and J-5 substituent respectively.

b) **Substitution at the 5-Position of the Isoxazoline Ring:**

The compounds of the present invention also differ from those disclosed in D6 based on the substitution pattern at the 5-position of the isoxazoline ring. In particular, the present invention requires the substitution of a 4- fluorophenyl group (4-F) at this position, with very specific substituents on the aryl ring. D6 does not disclose any compounds where the 5-position of the isoxazoline ring is substituted with a 4-fluorophenyl group, nor does it provide a motivation to arrive at this specific combination of substituents.

In this regard, the Applicant relied on the evidence affidavit of Dr. Ming Xu, demonstrated that selection of the (R)-stereochemistry is critical for achieving the desired biological activity, and it significantly impacts the compound's interaction with its target, distinguishing it from the compounds disclosed in D6. Further, as demonstrated by the effect of structural changes on activity, bioefficacy tests were conducted on Western Flower Thrips (*Frankliniella accidentalis*) to compare the control efficacy of the compound with those disclosed in D6 and D7.

F

Compound (2ppM)	Structure	X	R	Control on Thrips
1 (D6)		H	H	10%
2 (corresponds to Cmp 3 of current disclosure)		F	Me	90%

D6 focuses on the use of afoxolaner and other amide derivatives as crop protection agents, but it does not provide motivation for a person skilled in the art to **combine the (R)-stereochemistry with the specific 4-fluorophenyl substitution at the 5- position of the isoxazoline ring, as described in the present invention**. The combination of these features results in a compound with enhanced properties that are not disclosed or suggested by D6. Therefore, a skilled person would not have been motivated to arrive at the compounds of the present invention based on the teachings of D6.

D7, **represents a non-analogous art**, as the authors of D7 discovered a group of naphthalene isoxazoline compounds with remarkable activity against the cat flea (Ctenocephalides felis) and dog ticks (Dermacentor variabilis). **First and foremost, compounds used for animal pests cannot be directly compared to those intended for plant pests**. **A skilled person in the art would not consider developing an animal-targeted compound to be a lead for plant protection, as the biological mechanisms and requirements for efficacy are quite different**.

Furthermore, in **Afoxolaner, the R2 substituent is hydrogen, whereas in the compound IN'452, it is an alkyl substituent in R-configuration**. Additionally, Afoxolaner does not have the possibility of forming an ester, unlike what is indicated for J-5 in D7, which presents a different chemical reactivity and structural behaviour.

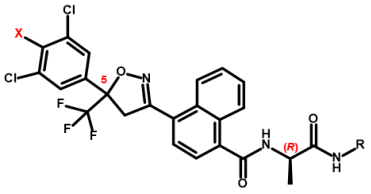
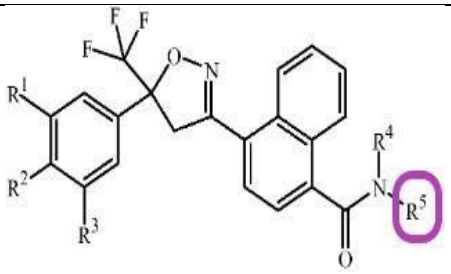
When considering both D6 and D7, neither document provides any motivation to arrive at the compounds of the present invention. D6 and D7 both fail to suggest the specific structural changes that would lead to the novel compounds of our invention. **Furthermore, the bioactivity data disclosed in our application shows significantly better results, highlighting the advantages of the structural modifications we have introduced**. Thus, both D6 and D7 fail to provide any viable pathway for achieving the compounds claimed in our invention, and the activity data strongly supports the inventive step of our compounds.

Further, the Opponent argued that D6 and D7 compound i.e., AFOXOLANER contains the most relevant structure, which allegedly provided the applicant with the motivation to derive the compounds of the present invention by combining the depicted structural changes.

The Applicant humbly submits that the Opponent in the hindsight manner has identified portions of the prior art and focused on specific structural elements. In doing so, the Opponent has overlooked other crucial aspects of the molecule. There is no motivation in Afoxolaner for a person skilled in art to combine the structural changes of the present invention with Afoxolaner, as the structural features that are central to the present invention are not suggested by the prior art.

(c) D1: WO'809 teaches away no 4-fluorophenyl substitution

D1 constitutes a selection invention directed to a subset isooxazoline naphthyl carboxamides **which are structurally distinct** from the compounds of IN '452.

IN'452	**WO'809**
Table 1 	

The structural differences between the compounds are significant. The compound of IN'452 application, the chiral center at J = J1 is specifically defined as having the (R)-stereochemistry, which is absent in the compounds of D1. Furthermore, IN'452 features a narrow selection of substituents on the aryl ring attached to the 5-position of the isoxazoline, where a 4-fluorophenyl group is required, combined with a limited set of substituents—R1a

being Cl or CF3, and R1b being H or Cl. In contrast, D1 does not disclose such a combination of structural features in its exemplified compounds, which sets IN'452 apart from D1.

Taking together, these structural changes provided unexpected improvements in the biological activity of Formula I compounds of the current invention. In this regard, the Applicant refers to evidence of Dr Ming Xu. The compounds of Table 1 below consist of a pair of 4-F/desfluoro compounds, all bearing the (*R*)-Me side chain. **Table 1 describes the efficacy on lepidopteran pests (*Spodoptera exigua, Helicoverpa zea*, and *Spodoptera frugiperda*) of a set of X = F/desfluoro compounds, where R = H or Me.** Compounds **1** and **2** are a pair of F/desfluouro compounds where R = Me and compounds **3** and **4** are a pair of F/desflouro compounds where R = H. Compounds bearing X = F show consistently stronger activity on all three lepidopteran species than their X = H counterparts:

Table 1

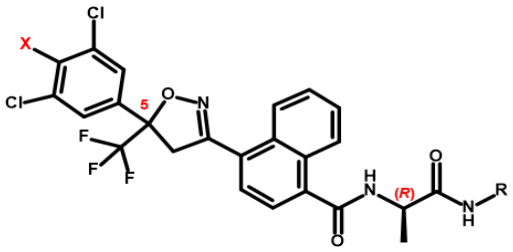
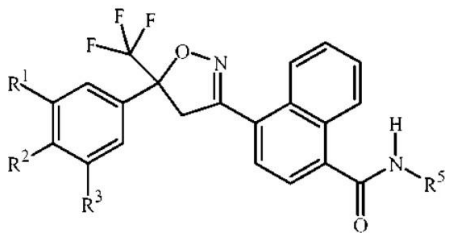


Table 1. Efficacy of Compounds 1-4 on Lepidopteran Species (EC50, ppm)					
Compound			***Spodoptera***	***Helicoverpa***	***Spodoptera***
1. (corresponds to Cmp 1			1.48	1.19	1.73
2. D1			>10	2.14	2.85

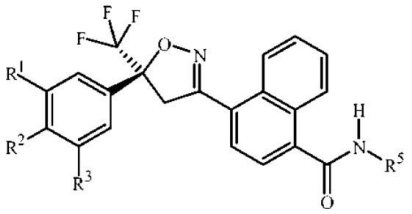
Table 1. Efficacy of Compounds 1-4 on Lepidopteran Species (EC50, ppm)					
Compound	**X**	**R**	***Spodoptera exigua***	***Helicoverpa zea***	***Spodoptera frugiperda***
3. (corresponds to Cmp 3	F	Me	1.1	0.44	0.69
4. D1	H	Me	2.03	0.76	1.04

Apart from this, **three index tables (A-C; Page 136-141)** combine **149 exemplified compounds** with core shown below.

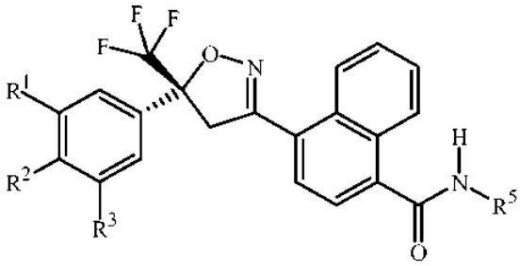
INDEX TABLE A



INDEX TABLE B



INDEX TABLE C



The Applicant submits that the compounds disclosed in D1 do not provide any motivation for a person skilled in the art (POSA) to arrive at the compounds of the present invention, and therefore, the subject matter of the present application involves an inventive step.

In D1, the three index tables (A-C) do not contain **a single compound where R2 is substituted with a fluorine atom**. **The only halogen substitution at R2 is present in Compound 15 (Page 136) and Compound 19 (Page 137), where R2 is substituted with chlorine, not fluorine**. This clearly demonstrates that D1 does not suggest the possibility of **substituting R2 with a fluorine atom**. Therefore, a POSA, based on the teachings of D1, would not be motivated to make the substitution of R2 with a fluorine atom, which is a key feature of the present invention.

Additionally, while several compounds in D1, such as **compounds 16, 29, 33, 60, 83,84, 93, 94, 95, 96, 97, 106, 107, 108, 109, 110, 111, 112, 137, 138, 139, 140, 141, 142,173, and 176, do exhibit the (R)-configuration at the chiral center. However, none of these compounds feature the specific combination of structural changes present in the present invention, particularly the 4-fluorophenyl substitution at the 5-position of the isoxazoline ring. Therefore, even though D1 discloses compounds with the (R)-stereochemistry, it does not suggest the inventive combination that is central to the compounds of IN'452 application**. In conclusion, D1 fails to provide motivation for a POSA to combine the specific structural features, such as the fluorine substitution at R2 and the

combination of the (R)-configuration with the 4-fluorophenyl substitution, as disclosed in IN'452.

The Opponent in the hindsight manner has identified the prior art D1 Annexure A merely because the resemblance with the core moiety i.e., isooxazoline combined with naphthalene ring but the opponent has ignored the fact that the asserted prior art compound must be analysed in terms of its chemical structure as a whole. In this regard, reference has been made to the case law that held that the biological activity of a molecule is dependent on its structure as a whole:

a) **Merck vs Glenmark (enclosed), order of Delhi High Court**, para 105 and para 85.

Para 105

It is readily evident that the two molecules have very little in common when complete structures are compared. It is worth pointing out here that the biological activity of a molecule and its utility as a medicine is completely dependent on the structure as a whole. That is, each part of the molecule makes some contribution to the overall biological effect.

Para 85

Further, having realized the missing parts in the hypothetical patch compound, the Defendant went hop-scotch searching.

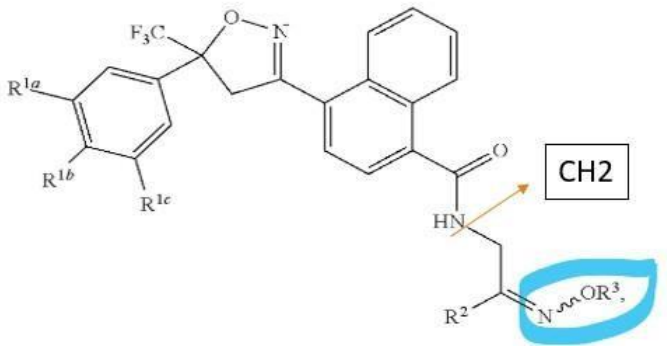
b) Gilead Pharmasset, LLC vs Sankalp Rehabilitation Trust, para 22, IPO,

22. *It may be noted that none of the documents cited by O1, independently or in combination with each other, either discloses the claimed nucleoside moiety or claimed phosphoramidate moiety. Though D1 generically discloses a nucleoside unit in claim-6 which having pyrimidine base may include uracil (but no specific example with uracil as base is provided in the description) but it lacks phenyl phosphoramidate moiety. D8, D10, D14, D15, D16 & D17 generally suggests use of the phosphoramidate ProTide technology to various nucleosides analogues like 4' azidouridine (D14), ddU (D8), d4T (D10) but there is neither any disclosure of specific phosphoramidate moiety claimed in present invention nor any suggestion to modify the known phosphoramidate moieties by having specific substituents therein. On the basis of mere disclosure of phospharamidate moieties attached to structurally different nucleoside moiety it is not reasonable to consider that such teachings can be extended to nucleoside moieties having different sugar molecule with different substituents pattern. Even selection of substituents of phosphoramidate moiety disclosed in cited prior art documents and activity shown thereof is in relation with nucleoside to which it is attached. The opponents have failed to provide any document which suggests such general teaching which states that selected specific substituents on phosphoramidate will show same activity for every nucleoside moiety irrespective of its structure. The selection of specific nucleoside moiety having specific substituents thereon and selection of specific substituents in phosphoarmidate moiety of present invention is considered as non-obvious.*

(d) D2 (US'765) teaches extra methylene group

59. D2 **discloses naphthyl isoxazoline oxime derivatives of Formula (1),**

(1)

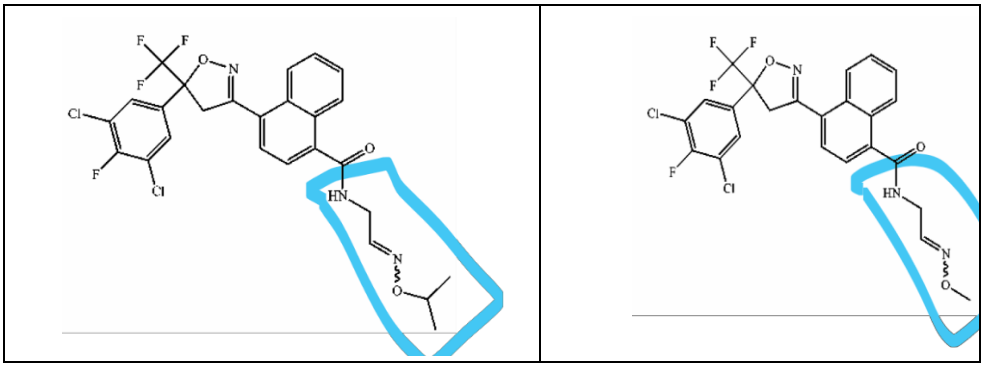


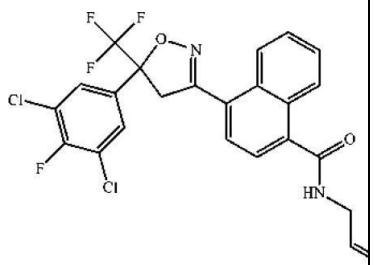
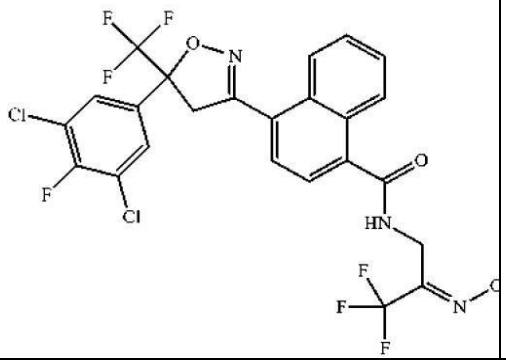
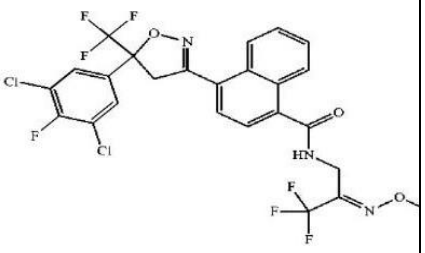
R^3 is H, C_1-C_6alkyl, C_0-C_6alkyl C_3-C_6cycloalkyl, C_2-C_6alkenyl, C_0-C_6alkyl phenyl, C_1-C_4alkyl-O-phenyl, C_0-C_6alkyl heterocycle, or C_0-C_6alkyl heteroaryl;

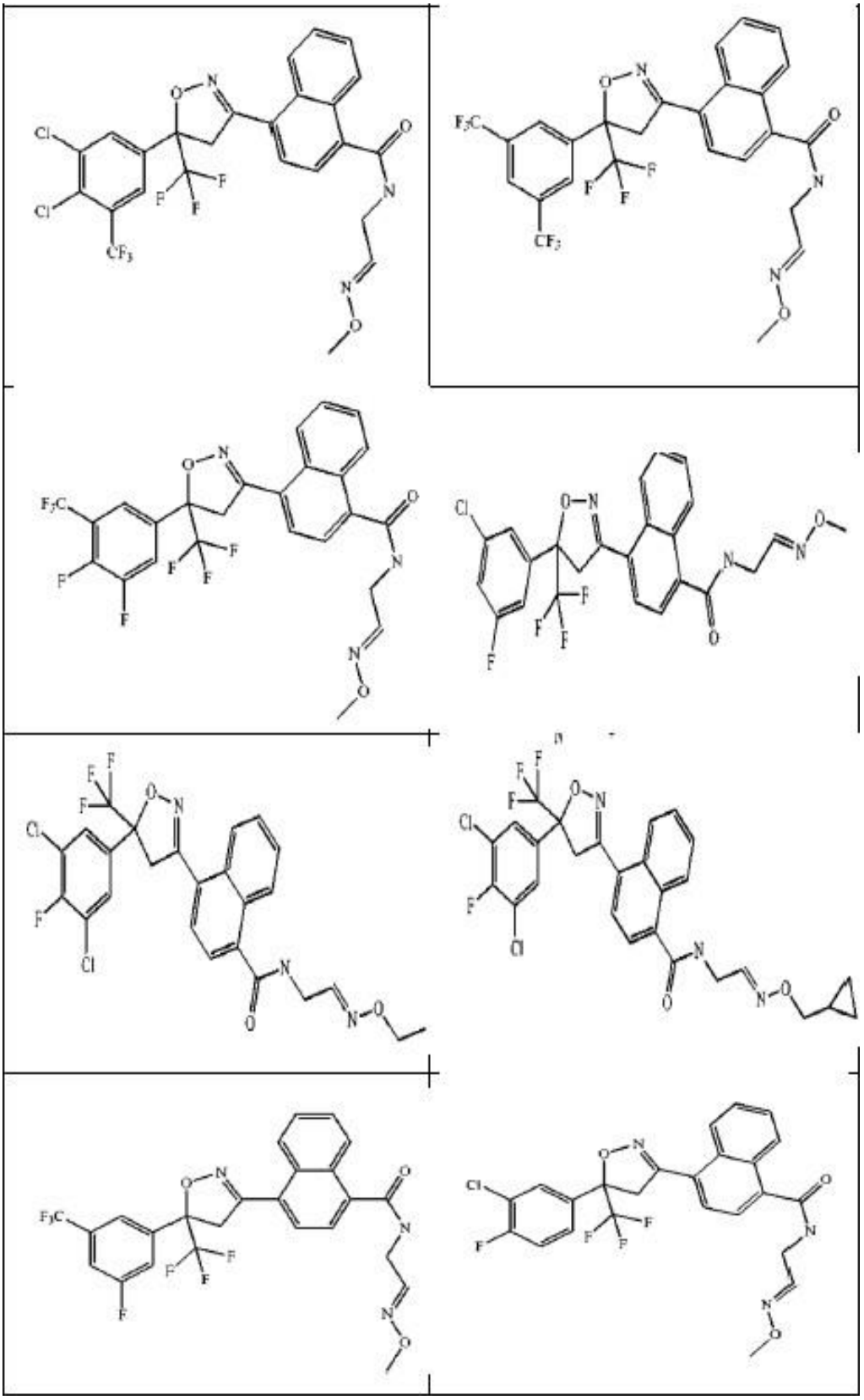
where the substitutions for R3 are specifically limited., i.e.:

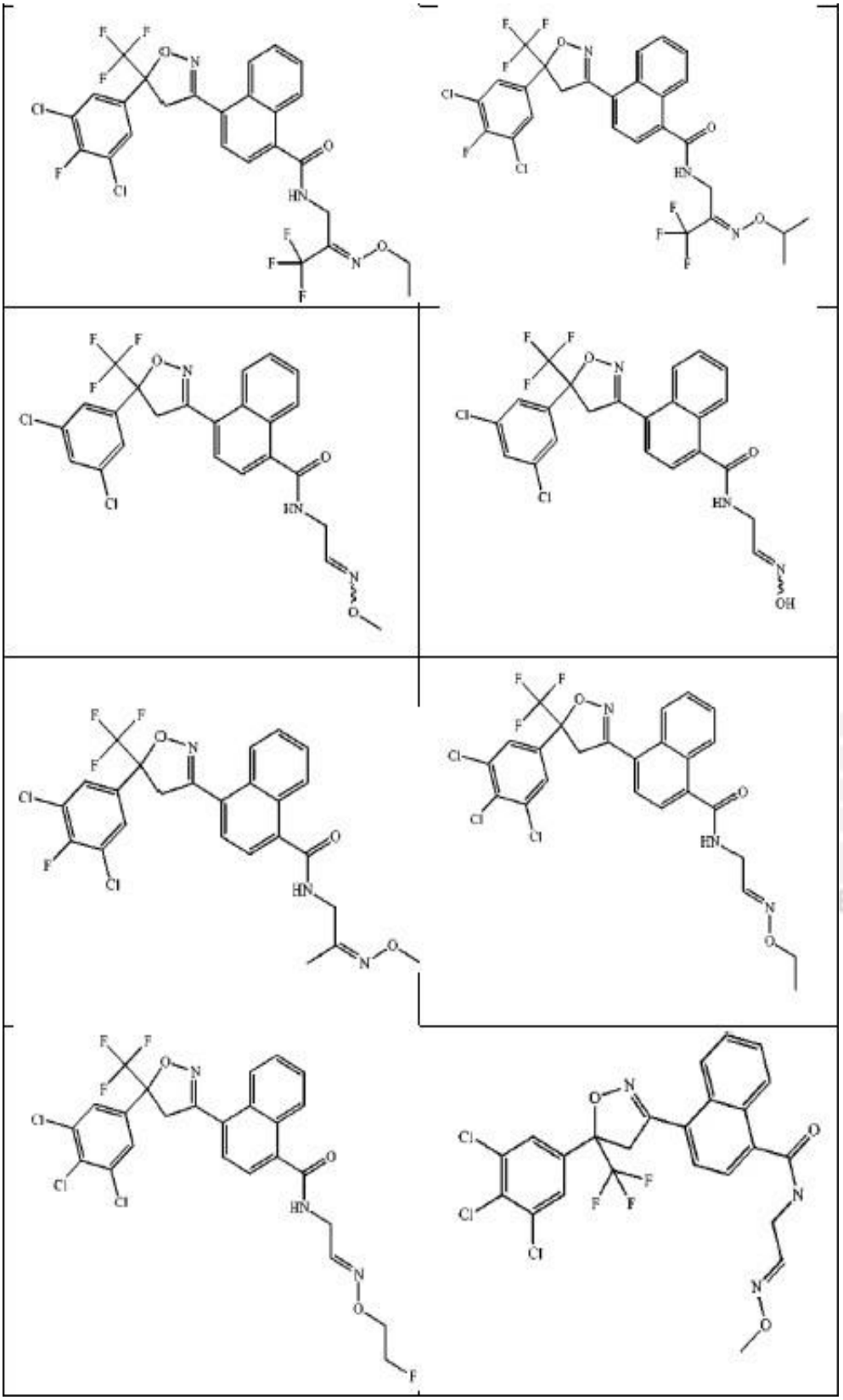
None of the substitutions listed for R3 align with the substitutions of "J" as described in IN'452 **for J1 or J5**. Additionally, **the compounds in D2 feature a "methylene" group (-CH2) adjacent to the amide group**.

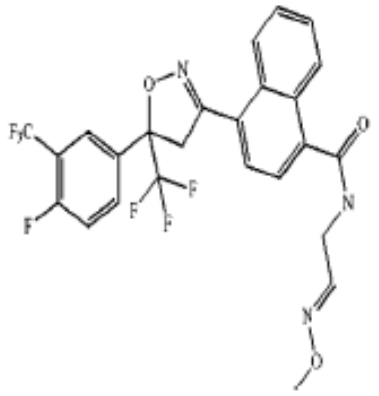
A person of ordinary skill in the art (POSA) would not be motivated to modify the Markush structure by removing the extra methylene group to match the compounds in IN'452. **D2 provides 25 exemplified examples (Pages 16-31), where each differs in the positions of J-1 and J-5, with most having F at the R2 position and notably, none of these examples show the exemplified R stereochemistry as depicted below**:







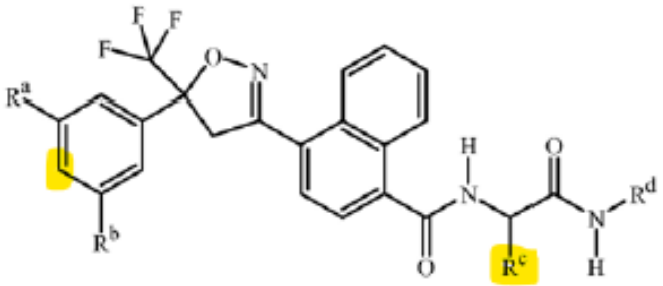
	

47. D2 was selected by the Opponent in hindsight only after having knowledge of the present invention of the Applicant.

(e) D3 (WO'528) teaches no substitution at 4th position

48. D3 relates to certain isoxazolines, their N-oxides, salts, and compositions suitable for agronomic, non-agronomic, and animal health uses. **Table A in D3 (page 32) defines 30 specific exemplified embodiments**. In these embodiments, the concerned substitution is absent, **as the 4-fluoro group is not present**. None of the exemplified compounds teach the presence of this substitution, **nor do any show the presence of R-stereochemistry at the Rc position** as depicted below:

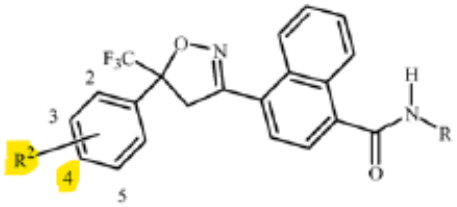
TABLE A



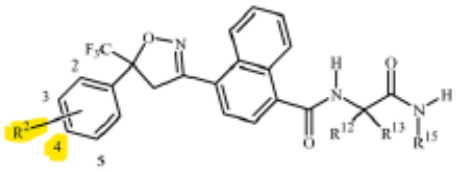
R^a	R^b	R^c	R^d
Cl	Cl	H	*c*-Pr
Cl	Cl	H	CH_2-*c*-Pr
Cl	Cl	H	a)
Cl	Cl	CH_3	*c*-Pr
Cl	Cl	CH_3	CH_2-*c*-Pr
Cl	Cl	CH_3	a)
Cl	CF_3	H	*c*-Pr
Cl	CF_3	H	CH_2-*c*-Pr
Cl	CF_3	H	a)
Cl	CF_3	CH_3	*c*-Pr
Cl	CF_3	CH_3	CH_2-*c*-Pr
Cl	CF_3	CH_3	a)
Cl	OCH_2CF_3	H	*c*-Pr
Cl	OCH_2CF_3	H	CH_2-*c*-Pr
Cl	OCH_2CF_3	H	a)
Cl	OCH_2CF_3	CH_3	*c*-Pr
Cl	OCH_2CF_3	CH_3	CH_2-*c*-Pr
Cl	OCH_2CF_3	CH_3	a)
Br	CF_3	H	*c*-Pr
Br	CF_3	H	CH_2-*c*-Pr
Br	CF_3	H	a)
Br	CF_3	CH_3	*c*-Pr
Br	CF_3	CH_3	CH_2-*c*-Pr
Br	CF_3	CH_3	a)
CF_3	CF_3	H	*c*-Pr
CF_3	CF_3	H	CH_2-*c*-Pr
CF_3	CF_3	H	a)
CF_3	CF_3	CH_3	*c*-Pr
CF_3	CF_3	CH_3	CH_2-*c*-Pr
CF_3	CF_3	CH_3	a)

19. Further, **Index Tables A-G collectively show 111 exemplified compounds** (Page 119-125), where the R2 group can be substituted at the 2nd, 3rd, 4th, and 5th positions on the phenyl ring. **The only substitution of R2 in these embodiments that aligns with our invention is at the 4th position**. However, **it is crucial to emphasize that not a single compound out of the 111 bears a fluoro substitution at this position**. **Only compounds 8, 49, and 95 out of the 111 have a substitution at the 4th position for R2, and in each case, the substitution is chloro**.

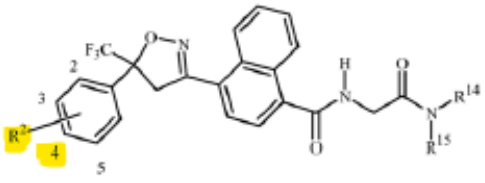
INDEX TABLE A



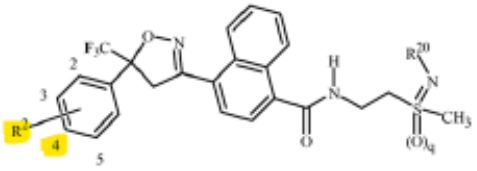
INDEX TABLE B



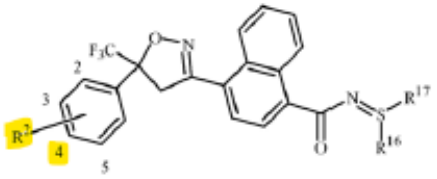
INDEX TABLE C



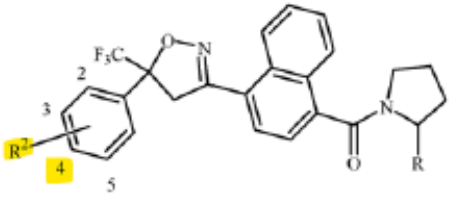
INDEX TABLE D



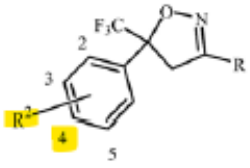
INDEX TABLE E



INDEX TABLE F



INDEX TABLE G



50. The teaching of the document is clear: with so many compounds exemplified and none of them showing a fluoro substitution at the 4th position, there is no motivation for a skilled person to make such a substitution, other than through hindsight. Therefore, there would be no logical or technical reason for the inventor to be motivated to introduce a fluoro substitution to arrive at the compounds of our invention.

51. There is no possibility, other than through hindsight, for a person of ordinary skill in the art to get motivated from the teachings of D3, particularly in relation to 4-fluoro. The distinct nature of each compound, along with their structural and functional differences, makes any such teaching highly unlikely without the benefit of knowing the outcome in advance.

(f) D4: US'848- A non-analogous prior art

52. Referring to D4, **which is a non-analogous art**, he Applicant humbly submits that it relates to extended-release injectable formulations comprising an isooxazoline active agent, methods and uses as antiparasitic agent, and if the art is non-analogous in nature, it cannot be considered valid for our purposes, as its teachings are fundamentally different and not relevant to our invention.

53. The Applicant submits that a person skilled in the art would not consider the prior art document that addresses a different technical solution. In this regard a reference has been made to the following case law.

a) Kuraray Co. Ltd. vs Asst. Controller of Patents (2023 MHC 5222)[12]

54. The Hon'ble Madras High Court in Kuraray vs Controller of patents held in para 16 held as follows

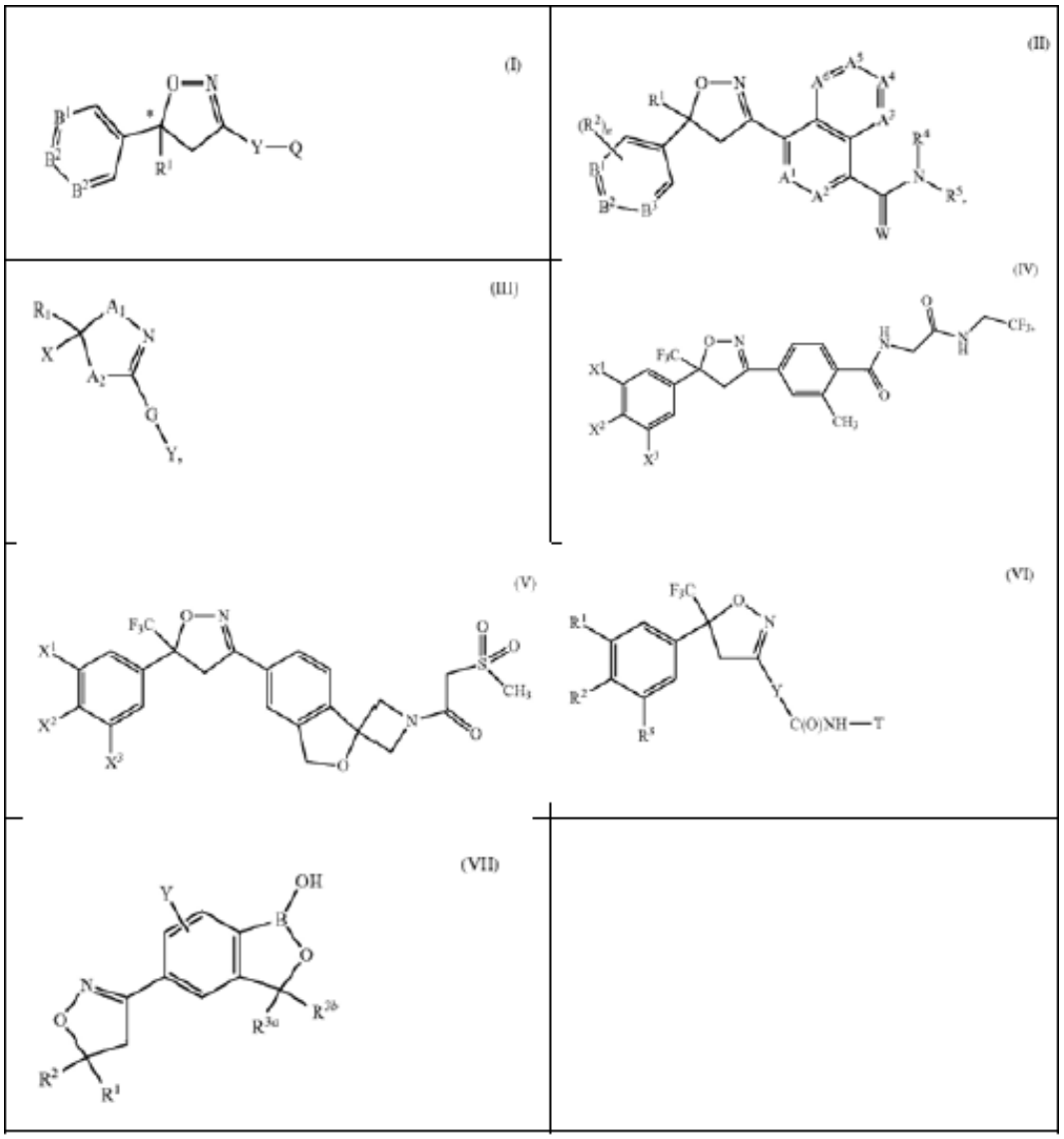
> *Para 16: As discussed above, the invention disclosed in prior art document D1 is intended to resolve a different problem and the said prior art teaches the use of a laminate for such purpose. Consequently, a person skilled in such prior art would not be motivated to consider the use of a PVA film on a standalone basis for resolving the problem that the claimed invention is targeted to resolve.*

b) Titan Umreifungstechnik Vs. Asst. Controller of Patents, (C.A.(COMM.IPD-PAT) 114/2022: 2023 DHC 3832)[13]

> *Hon'ble Justice Sanjiv Narula) came to a similar finding and held that identification of relevant prior art has while assessing lack of inventive step has to be from the same technical field and addressing the same problem. The Court held that if two prior art documents address different problems, it would not be plausible for a person skilled in the art to realistically combine the teachings of the referenced prior art. The Court further held that combining/mosaicking two substantial unrelated prior art in order to invalidate a claim is inappropriate.*

55. Furthermore, the Opponent has failed to provide any reasoning or explanation as to how a person skilled in the art would select specific compounds from this extensive list and arrive at the compounds of the present application without undue experimentation.

56. **The prior art discloses compounds of formulas I-VII, with multiple exemplified compounds for each formula**, providing a large laundry list of options.



57. **Additionally, it is important to highlight that none of the compounds in D4 exhibit a combination of substitutions resembling the 4-fluoro group or the R-stereochemistry of the structures corresponding to J1 or J5, which are key features of our invention**.

58. The Applicant submits that the cited prior art documents, D1-D7, does not teaches in the direction of the modification as alleged by the Opponent. In this regard, the Applicant has relied on the case law.

a) ***Roche v/s Cipla, RFA (OS) 92/2012 from Para 111, 106 and 118***

Obviousness – Mixed question of law and fact and must be strictly and objectively judged.

Para 111*: Obviousness must be strictly and objectively judged. In the decision reported as (1979) 2 SCC 511Bishwanath Prasad Vs. Hindustan Metal Industries (para 25) the Supreme Court laid down the principles to test inventive step 'as under :-*

Teaching of the document as a whole

Para 106: "Teachings in prior art document have to be considered as a whole.

Obviousness test

118*. From the decisions noted above to determine obviousness/lack of inventive steps the following inquires are required to be conducted:*
Step No. 1 To identify an ordinary person skilled in the art,
Step No. 2 To identify the inventive concept embodied in the patent,
Step No.3 To impute to a normal skilled but unimaginative ordinary person skilled in the art what was common general knowledge in the art at the priority date.
Step No.4 To identify the differences, if any, between the matter cited and the alleged invention and ascertain whether the differences are ordinary application of law or involve various different steps requiring multiple, theoretical and practical applications,
Step No.5 To decide whether those differences, viewed in the knowledge of alleged invention, constituted steps which would have been obvious to the ordinary person skilled in the art and rule out a hideside approach

b) ***Enercon vs Aloys Wobben, IPAB, 123/2013[14] from para 43 & 44***

Para 43 "The mere existence in the prior arts, of each of the elements in the invention, will not ipso facto mean obviousness. For after all most inventions are built with prior known puzzle-pieces. There must be a coherent thread leading from the prior arts to the invention, the tracing of the thread must be an act which follows obviously. We must apply this reasoning to test if indeed it is obvious, or if it seems to us to be obvious to the person skilled in the art because of what we know now. If it is the latter, it is hindsight deduction and is not acceptable, but if it is the former, then the patent must go.

Para 44. "We will examine if the person with skill and knowledge, as per our own law, would have arrived at the invention with the benefit of the prior arts. While we look at prior arts and the decisions on how prior arts must be applied, we must never lose sight of the invention in question..... ....."

- DISCUSSION AND CONCLUSION LACK OF INVENTIVE STEP U/S 25(1)(e) : The compounds claimed are small molecule of naphthalene isooxazolines compounds for controlling invertebrate pests. The application highlights two significant inventive selections that distinguish the claimed compounds of the present invention from the prior art:

a) Fluorine atom at the 4-position of the phenyl ring attached to the 5-position of the isoxazoline ring

b) The chiral center on J = J1 and J5 is specified to be in the (R)-stereochemistry .

D1 (WO'809) teaches away from the 4-fluorophenyl substitution at R2, as none of its exemplified compounds feature this substitution. Therefore, a person skilled in the art would not be motivated to make this substitution based on D1.

D2 (US'765) discloses compounds with an additional methylene group adjacent to the amide, and none of the exemplified compounds feature the specific R-stereochemistry or the desired substitution at the R2 position.

D3 (WO'528) teaches towards no substitution at the 4th position of the isoxazoline ring and does not disclose the required R-stereochemistry.

D4 (US'848) is a non-analogous prior art and does not disclose compounds with a combination of key substitutions, such as the 4-fluoro group or R-stereochemistry, critical to the present invention.

None of the cited documents, D1-D7 discloses the claimed compound. None of the exemplified compound discloses the claimed compound. Further, the generic disclosure does not anticipate the specific disclosure. Moreover, none of the cited document teaches towards the chiral center on J = J1 and J5 to be in the (R)- stereochemistry.

D5 (WO' 999**)** discloses structurally different compounds where the amide carbonyl is attached to the naphthalene ring in a different manner than in the present application, thus teaching away from the claimed invention.

D6 (DK'253) and D7: The compound AFOXOLANER is a structurally different from the claimed compound in that the chiral center and absence of specified (R)-stereochemistry. D6 does not disclose compounds with a 5-position isoxazoline ring substituted with a 4-fluorophenyl group. D6and D7 focus on animal-targeted compounds, while the present invention is aimed at plant protection.

The Applicant has submitted affidavit of Dr. Ming Xu demonstrates that the selection of (R)-stereochemistry is crucial for achieving the desired biological activity,distinguishing the claimed invention from the cited prior art.

The ground of opposition of lack of inventiveness is therefore rejected .

- **GROUND III ON THE NON PATENTABILITY SECTION 3 (d): PATENTABILITY UNDER SECTION 25(1)(f)**
- OPPONENT'S SUBMISSION

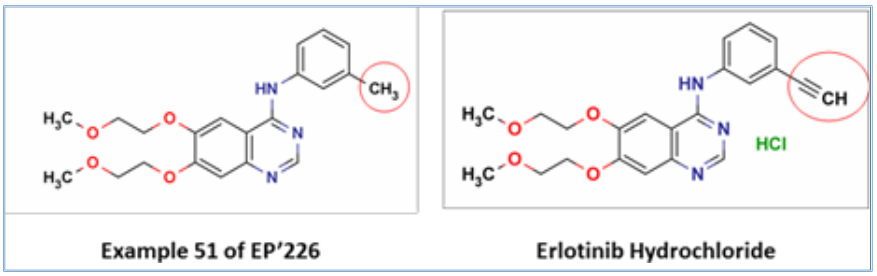
In addition to the arguments made in preceding paragraphs and without prejudice, it is submitted that the composition claimed in the impugned application is not a patentable invention under the Act as it attracts the provisions of Section 3(d) of the Patents Act, 1970.

According to Section 3(d), “the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant”.“Explanation.—For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy”

The Opponent submits that the teachings of prior arts (D1 to D4 and D6) demonstrate that the basic parent structure of the compound remains the same across all disclosures, with changes to the substituents being merely workshop improvements. Such modifications lead to the formation of "derivatives" which are used for the same intended purpose. Therefore, under Section 3(d), Compound of Formula (I) represents the mere discovery of a new form of a known compound - a derivative. Since the modification does not result in an enhancement of efficacy, it is not patentable under Section 3(d).

Additionally, the teachings from prior arts D4 and D7 clearly show that Compound of Formula I is already known for its use in the treatment of pests in crops and animals. The present application claims the use of the same compound for pest control in crops, which constitutes the mere discovery of a new use for an already known substance. According to Section 3(d), such a discovery is non-patentable, as it does not involve any new inventive contribution to the substance or its known use. In light of the above arguments, it is clear that the claimed compound 1, as described in the amended claims, is not patentable under Section 3(d) of the Act. The compound merely represents a derivative of a known substance and does not result in any enhancement of efficacy. Additionally, the discovery of a new use for this compound is insufficient to meet the criteria for patentability. Therefore, the application fails to meet the requirements for patentability and should be rejected on the grounds of non-invention under Section 25(1)(f) of the Act.

- GROUND III – PATENTABILITY UNDER SECTION 25(1)(f)
- APPLICANT’S SUBMISSION The Applicant submits that the instant application is directed at new chemical entities and discloses novel naphthalene isoxazoline compounds that are not known or disclosed in the prior art documents. and are not attracted by section 3(d) of Patents Act 1970. In this regard, just by way of a simple example, even the Division Bench of the Hon’ble Delhi High Court in Roche vs Cipla did not hold Erlotinib, the claimed invention as being a derivative of a prior art compound even when there was a high structural similarity. The court dealt with this issue under “INVENTIVE STEP” and NOT Section 3(d) and treated Erlotinib as a New Chemical entity.



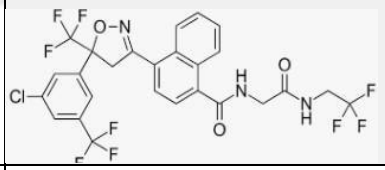
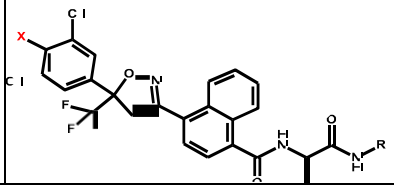
The present invention is better of than the Roche Vs. CIPLA case, as the molecule is significantly different from any of the prior art compounds. Even otherwise, the applicant has provided EC50, CC50 and IC50 values of compounds of present invention in the patent specification also discussed above.

Further, an order for the applicant Gilead Pharmasset, LLC vs Sankalp Rehabilitation Trust before the controller of patent office, Kolkata:

33. The opponents have primarily argued that the claimed invention is mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of the substance. To apply said clause precondition is existence of a known substance with a known efficacy and then one need to show that claimed substance is new form of such known substance. 34. *In the present case, all the opponents have argued that the subject matter of the claims 1-3 falls within the section 3(d) of the Patents Act, 1970 and primarily they have relied on the documents D1, D2, D21, D23 and D27. O1 has identified (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl cytidine as known substance for the claimed compound. As the nucleoside moiety of the claimed compound is structurally different from such known substance hence claimed compound cannot be termed as ester of such known substance. Other opponents have merely referred to D1 without identifying any compound which can be considered as known substance. After going through D1 it is observed that it does not exemplify any compound having uracil base nucleoside which can be considered as a known substance for the claimed compound. The opponents have also cited D2, without referring to any specific compounds as known substance for claimed compounds. D2 discloses Markush structure of formula (I) which encompasses large number of compounds compounds which are useful in treatment of cancer but exemplify compounds include only bromo vinyl uridine (BVU) and gemcytabine (GemCyt) which are referred as similar nucleotides by the opponents. Said exemplify compounds are structurally 40 41 different from the claimed compounds (and also have anti-cancer activity instead of HCV activity) hence such compounds disclosed in D2 cannot be considered as known substance for claimed compound. D21 is referred by the opponents O5, O7, O12 wherein compound 9 of said document is identified as known substance for the claimed compound. Compound 9 (-D-2'-deoxy-2'- fluoro-2'- C-methyl uridine) was found to be inactive for anti-HCV activity and the opponents have failed to show how claimed compound which comprises of phophoramidate moiety (phenoxy phosphoramidate of isopropyl ester of Lalanine amino acid) attached to a nucleoside moiety can be considered as derivatives of such known compound 9. The opponents have referred claimed compound as prodrug of compound 9 of D21 and submitted that prodrugs are not patentable under section 3(d) of the Patents Act (reliance is placed on F. Hoffmann-La Roche Ltd. and Ors. v.*

Cipla Ltd. 2016(65) PTC l(Del)). In this regard it is to note that even if one consider compound 9, having no activity in HCV replicon assay, as known substance for the claimed compound then also the applicant has shown the efficacy for the claimed compound (as compound 25) in HCV replicon assay in table on pages 696-697 of the complete specification. Further D23 is referred by the opponents with PSI-6206 as the closest compound. D23 is not a valid prior art document as it is published after the priority date of the present invention. Prejudice to that even if one consider D23, the markush structure PSI-6206 lack any definition for the substituents hence can not be considered as a known substance for the claimed compound. With reference to D27 the opponent fails to show any known substance. The compound as referred by the opponent for comparsion with claimed compound is a hypothetical compound which is not specifically disclosed in D27. The compound disclosed in D27 are structrally different from the claimed compound and hence same can not be considered as known substance for the claimed compound. Hence claimed invention does not fall within the scope of section 3(d) of the Patents Act.

The claimed compounds are not a derivative, as defined under the principle of ejusdem generis. Further, as demonstrated by the effect of structural changes on activity, bioefficacy tests were conducted on Western Flower Thrips (*Frankliniella accidentalis*) to compare the control efficacy of the compound with those disclosed in D6 and D7.

Compound (2ppM)	Structure	**X**	**R**	**Control on**
1 (D6)		H	H	10%
2 (corresponds to Cmp 3		F	Me	90%

- DISCUSSION AND CONCLUSION : PATENTABILITY UNDER SECTION 25(1)(f)

It is observed that the compounds of the present invention are structurally different from the compounds disclosed in the cited reference. For section 3(d) to apply in the first place, two criteria have to be satisfied: 1) That the claimed invention is a new form of a known substance or a derivative of a known substance; and 2) substance should have known efficacy. The claimed compounds of the present invention are not a salt, ester, ether or polymorph of a

known compound. Further, the claimed compounds are not a derivative.As demonstrated by the effect of structural changes on activity, bioefficacy tests were conducted on Western Flower Thrips to compare the control efficacy of the compound with those disclosed in D6 and D7.The claimed compounds have distinguishable features in their chemical structures and show unexpectedly remarkable antiviral activity against compound AFOXOLANER. Therefore, the claimed compound is not a mere analogue and hence does not fall within the ambit of section 3(d). The ground of non-patentability under Section 25(1)(f) of the Act therefore does not hold valid and is rejected .

- **GROUND IV – LACK OF SUFFICIENCY UNDER SECTION 25(1)(g)**
  - OPPONENTS'S SUBMISSION: states "that the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed".

The opponent submits that the amended claim 6 (referred to as claim 13 in the filed document) of the impugned invention describes a composition consisting of a compound of formula 1 and at least one additional component selected from surfactants, solid diluents, and liquid diluents. This composition may optionally include at least one additional biologically active compound. Moreover, pages 90-92 of the complete specification (Annexure – 1) provide a detailed list of additional biologically active compounds that may be incorporated into the composition.

At the outset, it is submitted that the claim is not supported by any working example in the impugned specification, raising concerns about the scope of the claim and highlighting the insufficient disclosure of the invention. Additionally, the amended claim 6 is overly broad and lacks clarity, as it fails to specify the percentage ranges of the compound of formula 1 and the additional components and the specific additional compound that form the claimed combination.

Pages 102-106 of the complete specification (Annexure-1) present biological examples related to the invention. The Opponent argues that the results are insufficient and unjustifiable, as they fail to provide any data or percentages regarding the amounts of active and inactive components in the composition. Additionally, no information is provided on the types of compositions or the specific names of the surfactants and diluents used.

The specification includes efficacy data for the tested compounds against various pests, claiming their effectiveness. However, the amended claims focus on specific derivatives of formula 1, and the specification does not provide efficacy data for the combination comprising these particular derivatives. Pages 34-62 of the impugned complete specification (Annexure-1) describe a wide range of compounds derived by altering different substituents on the compound of formula 1. Page 73 of the complete specification (Annexure-1) states that the formulations can be in both liquid and solid forms, including emulsifiable concentrates, suspensions, emulsions, dusts, powders, granules, pellets, prills, pastilles, tablets, and filled films. However, it does not specify any particular formulation type that would enable a person skilled in the art to prepare the combination as outlined in amended claim 6.

- GROUND IV – LACK OF SUFFICIENCY [25(1)(g)]

APPLICANT'S SUBMISSION: The Applicant submits that the claims and specification of the present application have been sufficiently disclosed in the patent specification.The applicant also alleges the Opponent of misleading during the hearing that the claims of the present application are not sufficiently described.

- DISCUSSION AND CONCLUSION LACK OF SUFFICIENCY [25(1)(g)] :The complete specification fully and particularly describes the claimed invention. a) General Method of synthesis of the compounds – Preparation scheme 1- 7, Page 26-35 b) Therapeutic applications involving viruses, fungus etc. – Page 36-47 c) Formulations of the compounds – Pages 47-69 d) Specific examples – Pages 69-84 1. Ex 4: Describes the preparation of formula (I) from formula '4' 42 43 2. Ex 3: Describes the preparation of formula '4' from formula '3 3. Ex 2: Describes the preparation of formula '3' from formula '2 4. Ex 1: Describes the preparation of formula '3' from formula '1' e) Specific formulation – Pages 84 f) Biological results along with results – Page 85-97 . The provided examples and data address key aspects necessary for a skilled person to replicate the invention and validate its claims.-Thus, the claimed invention is sufficiently disclosed in the patent specification for a person skilled in the art to perform the same, without undue experimentation. The ground therefore does not hold valid.

❖ **SECTION 14 HEARING AND DISCUSSION:**

The objections were raised under the heading of definitiveness, invention u/s 2(1)(ja) in view of D1-D4,u/s2(1)(j) ,lack of inventiveness u/s 2(1)(ja) in view of D1-D7 , 3(d),3 (e)3(h),scope, insufficient disclosure u/s10(4) ,lack of unity of invention u/s10(5),definitiveness and other requirements. The applicant clearly illustrates the structural and functional differences with respect to cited prior art D1-D4. The claims have been suitably amended, the objection of lack of novelty , clarity and conciseness, scope, definitiveness is therefore waived off. The subject matter of claims falling u/s 3(h) have been waived off as the claims have been deleted. The claim 13 (now claim 6) is dependent on the amended claims and the objection is therefore waived off. The objection regarding lack of novelty u/s2(1)(j) ,lack of inventiveness u/s 2(1)(ja), lack of sufficient disclosure u/s10(4), nonpatentability under section 3(d) have been discussed above under the various grounds of opposition and are not repeated for sake of brevity .The objections are therefore waived off.

❖ **CONCLUSION:**

After thorough and careful consideration of the pre-grant oppositions filed by the Opponent under section 25(1) of the Act, statements and evidences produced by the parties before and at the time of hearing, arguments presented by the parties during hearing, written submissions by the parties filed after hearing and in view of the above analysis and

findings, I found that the grounds under Section25(1)(b),Section 25(1)(e), Section 25(1)(f) and Section 25(1)(g) raised in the pre-grant oppositions are not found valid.

Having considered all the facts and submissions made by the Agent of the Applicant during hearing under section 14 of the Act and the written note of arguments filed by the Applicant after the said hearing as well as in view of all the documents on record and also on the basis of the facts and findings as mentioned in the preceding paragraphs, I am of the opinion that the objection regarding lack of novelty2(1)(j), ,lack of inventive step u/s2(1)(ja),lack of sufficient disclosure under section 10(4), objection under section 10(5),scope ,clarity, definitiveness, claims falling under section 3(d),3(e) and 3(h) of the Patents Act as raised in the hearing notice u/s 14 are waived off.

Hence, in this instant patent application number 202017034452, I hereby proceed with grant of patent in accordance with Section 15 of The Patents Act, 1970 (as amended). The pre-grant opposition as filed under section 25(1) of The Patents Act, 1970 (as amended) and corresponding rule 55 of The Patents Rules, 2003 (as amended) is disposed herewith.

Dated 31 March 2025 **-Sd/-**

SWETA RAJKUMAR
Deputy Controller of Patents & Designs