Abstract:

A manufacturing process for a composition comprising Renofluthrin, glycol ethers as solvent(s), optionally filler solvent(s) / co-solvents to give better safety and compatibility of Renofluthrin for the preparation of insect repellent formulations or ready-to-use (RTU) formulations.
“MANUFACTURE USE PRODUCT FORMULATIONS OF RENOFLUTHRIN”

Technical field:
The present invention relates to intermediary / manufacture use product (MUP) formulation of Renofluthrin; particularly the invention relates to "manufacture use product" composition comprising Renofluthrin; glycol ethers as solvent(s); optionally one or more filler solvents to give better stability, safety and easier handling of Renofluthrin for the preparation of mosquito or insect repellent formulations or ready to use formulations (RTU).

Background and Prior art:
In the recent age, environmental friendly biologically active pesticides, insecticides has drawn increasing attention. Various mosquito and insect repellent products formulations based on pyrethroid compounds are useful in households. Pyrethroids usually can have 2 to 8 optical isomers and biological activity between the isomers varies greatly and therefore need for preparation of highly bioactive insecticides. Some of the optically active insecticides such as Transfluthrin, Prallethrin, Metofluthrin, Meperfluthrin, Dimefluthrin, d-trans allethrin, d-Allethrin are known in the art.

Most commonly used RTU mosquito repellent and other insect repellent formulations, (RTU = Ready to use formulations), consist of hydrocarbon solvent as base or carrier. Most formulations use de-odorized kerosene / aliphatic solvents / de-aromatized fluid solvents / isoparaffin solvents. Liquid evaporators, aerosols sprays, paper mats, paper fumigants and all similar formulations consist of such solvents. These solvents are present either in the end formulation, or are used in the manufacture process of the formulation.

Some formulations like mosquito coils / spirals / incense, use water in the process of manufacture, where the materials used to make the coil mixture are mixed in water and made into dough.

The categories of end formulations can be narrowed down to two:
   i) Organic solvent based formulations using solvents such as aliphatic solvents / isoparaffin solvents / de-aromatized solvents / other hydrocarbon solvents;
   ii) Water based / using water in manufacture process.
Solvents or water, is either present in the final composition of the formulation, or is used in the manufacture process of the formulation.

**Manufacturing Use Product (MP or MUP)** is defined in 40 CFR, Part 152.3 as, "Any pesticide product that is not an end-use product". A product may consist of the technical grade of active ingredient only, or may contain inert ingredients such as stabilizers or solvents (40 CFR § 153(h)). MPs are intended and labeled for formulation and repackaging into other pesticide products.

There are certain prior arts that deal with the Manufacturing Use Product (MUP) insecticidal composition.

**US6482863** discloses an insecticidal composition consisting essentially of an insecticide, and glycol ether solvent, and a co-solvent, wherein said insecticide contains at least one of transfluthrin, tefluthrin, pyranin, pyranin forte, natural pyrethrum, or prallethrin and glycol ether is dipropylene glycol dimethyl ether, wherein at least one co-solvent comprises N-methylpyrrolidone.

**US8658223** discloses Insecticidal compositions, particularly a Manufacturing Use Product (MUP) containing about 20% pyrethrins, which can be diluted further in oils.

Further **US 2013005688** describes composition comprising pyrethrin MUP and mineral oil, wherein the pyrethrin MUP is pyrethrin MUP 20.

**US7018644** discloses non-aqueous, single phase, non-thickened liquid air freshener or insecticidal composition having a flashpoint of greater than about 62° C. is provided. The composition contains: a) a polar solvent (glycol ether); b) 10 wt % of a non-polar aliphatic hydrocarbon solvent; and c) a fragrance or an insecticide.

"Flash point" of a liquid is the lowest temperature at which it can vaporize to form an ignitable mixture in air. Since some end formulations mosquito repellent products require
heating or burning, low flash point solvent systems are not preferred. Higher the flash point of a formulation, safer it is for storage and use.

The efficacy against target insects of any insecticidal composition is based on the dosage of the active ingredient present in the composition.

Recently developed active ingredient 'Renofluthrin' (Application No.4121/MUM/2013) is found to be effective in home insecticide formulations. Renofluthrin is found to be effective and practical for use in existing known formulations types and also has potential to adapt for developing new formulations and delivery systems.

Renofluthrin is an isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate, wherein total trans isomers ranging from 90% to 99.90% and total cis isomers ranging from 0.1% to 10%, having structure:

Renofluthrin is an isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate, wherein the isomers are selected from:

2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (1R,3S)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate;
2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (1S,3R)-3-(2,2-dichlorovinyl)-2,2- dimethyl cyclopropanecarboxylate;
2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (1R,3R)-3-(2,2-dichlorovinyl)-2,2- dimethyl cyclopropanecarboxylate; and
2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (1S,3S)-3-(2,2-dichlorovinyl)-2,2- dimethyl cyclopropanecarboxylate; wherein total trans isomers (1R,3S and 1S,3R) are present in range of 90% to 99.90%, rest being cis isomers (1R,3R and 1S,3S).
Accordingly 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IR,3S)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropane carboxylate; and 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IS,3R)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate are present in range of 90% to 99.90%, and wherein 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IR,3R)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropane carboxylate; and 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IS,3S)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate are present in range of 0.1% to 10%.

Renofluthrin is not soluble in water, also not soluble in most aliphatic solvents such as deodorized kerosene / isoparaffin solvents / de-aromatized solvents.

Renofluthrin is found to be effective, when used as insecticide in the manufacture of mosquito repellent and other household pest repellents.

However, Renofluthrin exhibits limited scope of solubility. It is almost insoluble in water. It is soluble in some hydrocarbon aromatic solvents, but aromatic solvents have strong smell and cannot be used for home application evaporation based insecticides. Even in combinations with other solvents, the smell of aromatic solvent is still dominant, hence cannot be used on regular basis within households. Most mosquito repellent products and formulations are used almost daily in homes.

To overcome the constraints regarding the solubility and odour, an "intermediary" manufacturing use product (MUP) formulation of active ingredient is helpful to give better solubility, stability, safer handling of Renofluthrin. Such intermediate formulation can be used efficiently and conveniently in the manufacture of the end RTU (Ready To Use) formulations such as mosquito repellents.

Formulations of 'Renofluthrin' insecticide having Renofluthrin active ingredient content between 2.5% to 18%, shows effectiveness, when used as intermediate or 'manufacturing use product' (MUP) in the preparations of lower concentration formulations of household mosquito repellents and insect repellents. Range in MUP can be based on the solubility profile of active ingredient Renofluthrin in desired final insecticidal composition. Such
'manufacture use products' (MUP) enable better stability, safety and easier handling of Renofiuthrin to prepare mosquito repellent products.

Such formulations, commonly known as "manufacture use product" (MUP), can then be used to make end product mosquito repellent and insect repellent for household use (RTU formulations). The active ingredient Renofiuthrin has limited solubility, but has good insect repellent effect. MUP formulation provides better compatibility and safety in handling of the active ingredient. The MUP acts as intermediary between the active ingredient and the end use formulation. Some end use formulations are sometimes also referred to as RTU (Ready To Use) formulations.

In view of foregoing, there is need for a formulation and a solvent system to be used as intermediary Manufacturing Use Product (MUP) satisfying the requirements with regard to solubility of Renofiuthrin active ingredient. Efficient MUP to prepare home insecticide formulations, requires higher flash point (preferably more than 50° C) for safety. It also requires wide acceptability of the solvents used in the MUP, safety, low toxicity, odourless to mild acceptable odour, storage stability at various temperatures. It is also necessary for the MUP to have miscibility / solubility / compatibility with De-odorized Kerosene, isoparaffins, de-aromatized solvents, aliphatic solvents etc. It must also be compatible with most packing materials / containers. The MUP mixture should be clear and preferably colourless. It should not impart color or change the color of the end use RTU formulation. All these requirements are important especially for use in liquid vaporizer (LV) or other RTU formulation types, which are visually perceptible to end user consumer.

**Objective of the Invention:**
To comply with the need of effective and safe insecticide, the invention provides "manufacture use product" (MUP) of Renofiuthrin for use in preparations of lower concentration formulations of mosquito repellent and other household pests repellent.

**Summary of the invention:**
In an aspect, the invention provides intermediary formulation or Manufacturing Use Product (MUP) formulation of Renofiuthrin comprising an effective amount of active
ingredient Renofluthrin, one or more glycol ethers as solvent, together with filler solvents for better stability, safety and easier handling of Renofluthrin. Further the said MUP formulations are useful to prepare end use product mosquito repellent and insect repellent for household use (RTU formulations), with better stability and safety in handling of the active ingredient Renofluthrin.

**Brief description of figures:**
Fig 1: depicts Renofluthrin MUP used in the preparation of RTU end products.

**Detailed Description of the Invention:**
The invention will now be described in detail in connection with certain preferred and optional embodiments, so that various aspects thereof may be more fully understood and appreciated.

In a preferred embodiment, the invention provides intermediary Formulation, Manufacturing Use Product (MUP) formulation of Renofluthrin comprising an effective amount of Renofluthrin, one or more solvents from the solvent group of Glycol Ethers, along with filler solvents.

Accordingly, the said intermediate formulation can comprise mixture of Renofluthrin in the range of 4% to 7%, with 96% to 93% glycol ethers respectively.

Further the organic solvents used in current intermediary formulation of Renofluthrin is from solvent group of glycol ethers. Glycol ethers are known organic solvents used in various applications, known for solvency, chemical stability and also mild-odored and miscible with a wide range of organic solvents. They are used in textile, leather and printing applications. They are also used in home cleaning products and specialty formulations for household use.

Some products from glycol ether group have been used for agro-chemicals, herbicides and farm chemicals. Their use in home insect repellents has been limited so far.
The glycol ethers employed in the instant invention are not limited to ethylene glycol monobutyl ether, diethylene glycol monohexyl ether, ethylene glycol monohexyl ether, ethylene glycol monomethyl ether, diethylene glycol monoethyl ether, ethylene glycol monophenyl ether, diethylene glycol monobutyl ether, ethylene glycol monobenzyl ether, diethylene glycol monomethyl ether.

These glycol ethers can be used individually with Renofluthrin, or as mixture of one or more glycol ethers. Preferred glycol ethers are ethylene glycol monobutyl ether, diethylene glycol monomethyl ether, diethylene glycol monobutyl ether, ethylene glycol monohexyl ether, diethylene glycol monomethyl ether.

Renofluthrin is soluble in glycol ethers, the instant MUP is clear solution with high flash point, low toxicity and very mild to none odour.

In another embodiment, the instant MUP formulation is preferably mixture of 5% Renofluthrin (adjusted for purity) in 95% Glycol ethers w/w. Based on purity of active ingredient, the quantity of solvent can be adjusted to make 100% w/w.

Further Renofluthrin 4% to 7%, with 96% to 93% Glycol ethers respectively, is stable at room temperature. At lower temp 5°C to 7°C or lower, over long storage duration, can show slight separation layer. However, when the formulation mixture was heated / or brought back to room temperature / or stirred, gradually it became clear solution again.

In an optional embodiment, to enhance the stability or storage capacity at various temperatures levels, a small percentage of alkylbenzenes like Toluene or Xylene or Ethylbenzene is added to the MUP preparation. By adding small quantity Toluene or Xylene, the instant MUP is made more stable at varied storage temperatures. Even when stored in cold temperatures, it maintained good solubility and clear solution. Toluene is used in the synthesis of Renofluthrin active ingredient, so Toluene is preferred for efficiency and cost advantage.
Therefore, the combination of Glycol ethers along with limited quantity of co-solvent Toluene or Xylene is chosen as final MUP formulation. In the instant formulation, Toluene or Xylene singly would be lesser than 65% of the Renofluthrin content. For example, if Renofluthrin is 5% in the MUP formulation, then Toluene or Xylene content will be less than 3.25%. So it does not have much effect on overall flash point or odour of the MUP.

In another preferred embodiment, the invention provides MUP composition comprising Renofluthrin, glycol ethers as solvents and optionally filler solvent or co-solvent, wherein w/w the Renofluthrin concentration is in the range of 2% to 16%; Glycol ethers (single or mixture) concentration is in the range of 84% to 97%; and optional co-solvent Toluene or Xylene as filler solvent is present not more than 65% of Renofluthrin content in the MUP. Particularly the alkylbenzenes concentration varies from 1-9% with regard to final MUP mixture.

Advantageously, the final MUP mixture 100% w/w is further used in manufacture of wide range of RTU formulations.

Table 1 below gives a few examples to illustrate the Renofluthrin MUP mix combinations:

<p>| Table 1: |</p>
<table>
<thead>
<tr>
<th>Example No.</th>
<th>Renofluthrin %</th>
<th>Glycol Ethers %</th>
<th>Toluene/ Xylene as filler Q.S. %</th>
<th>Final MUP mixture total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5</td>
<td>96</td>
<td>1.5</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>88.50</td>
<td>4.5</td>
<td>100</td>
</tr>
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<tr>
<td>5</td>
<td>5</td>
<td>95</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Note: Q.S. in a formulation refers to balance quantity to make 100% w/w, in the present formulation using co-solvent Toluene. Renofluthrin % adjusted for purity.
According to the invention, Renofluthrin 5% MUP contains Renofluthrin 5% w/w concentration (based on 100% purity) diluted in one or more Glycol Ethers in an amount of 90 to 94% w/w, preferably the glycol ethers are selected from the group consisting of Ethylene Glycol Monobutyl Ether, Diethylene Glycol Monomethyl Ether, Diethylene Glycol Monobutyl Ether, Ethylene Glycol Monoalcohol Ether, Diethylene Glycol Monohexyl Ether and balance % w/w being alkylbenzenes like Toluene or Xylene to make final MUP composition upto 100% w/w.

Similarly Renofluthrin 10% MUP can be prepared by diluting Renofluthrin 10% w/w concentration in one or more Glycol Ethers and balance being Toluene or Xylene. The quantity of Toluene or Xylene being not more than 65% w/w of Renofluthrin content in the MUP (i.e. in Renofluthrin 10% MUP, Toluene or Xylene not more than 6.50% w/w). So the quantity of one or more glycol ethers can be determined accordingly to complete 100% w/w.

Globally Harmonized System of Classification and Labeling of Chemicals (also known as "GHS") is an internationally agreed-upon system. Five GHS categories have been included in the GHS Acute Toxicity. Category 1 is the most severe toxicity category and Category 5 is for chemicals which are of relatively low acute toxicity. Renofluthrin active ingredient has acute oral toxicity in GHS category 3. MUP Mixture of 5% Renofluthrin in Glycol ethers along with filler co-solvent Toluene, lowers the acute oral toxicity to GHS category 5, which is the safest category.

In another embodiment, the intermediate formulation or MUP of Renofluthrin shows more flexibility and compatibility so that it can be used in wide range of RTU formulations for home insecticidal products. Fig 1 depicts some possible uses of Renofluthrin MUP in the preparation of some RTU end products / formulations. Use of MUP is not limited to the formulation types mentioned in this Fig. 1.

This MUP formulation of Renofluthrin in the present invention is more flexible and compatible than other forms of Pesticide formulations like Emulsifiable Concentrate (EC), Soluble Concentrate (SL), Suspension Concentrate (SC).
The "EC" formulations comprise one or more surfactants or emulsifiers. It is a solution of the insecticide/pesticide with emulsifying agents in a water insoluble organic solvent, which forms an emulsion when added to water. Similarly "SL" formulations are a solution of insecticide/pesticide, to be applied after dilution in water. This formulation may contain water-insoluble ingredients. "SC" formulations are stable suspension of insecticide / pesticide in liquid solution usually intended for dilution with water.

In some RTU formulation mosquito repellents, (like Vaporizer paper mat, Liquid vaporizers etc.) water is not required in the manufacture process or in the final composition. In such cases "EC", "SL", "SC" formulations are not required. Some ingredients in "EC", "SL", "SC" type formulations can cause issues or when used in formulations like Liquid vaporizer or some kinds of Aerosol sprays. In any formulations that do not need water (in manufacture process or in end product composition before application), such intermediate formulations (like EC / SL / SC and others) are not advisable. Renofluthrin MUP of the present invention gives the flexibility of use in all types of end product formulations / RTU formulations.

According to the invention Renofluthrin MUP, has the flexibility and compatibility to be used in all known popular RTU formulations used in mosquito repellents. Further the stability and safety of Renofluthrin active is improved by using said MUP.

The instant Renofluthrin MUP can be used in preparation of water based or solvent based RTU of mosquito repellent/insect repellent selected from the group consisting of:

a) Insecticidal incense forms, like mosquito coils/spirals/stick/cylindrical
b) Aerosol sprays
c) Vaporizer mats paper
d) Liquid Vaporizers
e) Fumigants and evaporators including Paper fumigants
f) Other burning heating forms
g) Spraying/diffusion or other non-heating types

In another embodiment, the invention provides process for preparation of RTU end consumer formulations, using Renofluthrin MUP. More specifically in insecticidal
incense / mosquito coil formulation where Renofluthrin MUP can either be added in the mixture dough during preparation or Renofluthrin MUP can be added/sprayed after the incense has been completed and dried, or both.

The insecticidal incense / mosquito coils (RTU) available in market usually contain following ingredients:

- Brown saw Dust, Coconut shell powder, as inert mass.
- Starch, Jiggat, Guar gum, Tamarind seed Powder etc., as Binders for the composition.
- Pottasium Nitrate or similar ingredients as burning agent.
- Sodium Benzoate or similar ingredients as preservative
- Colour, Perfume: For visible color and good smell
- Insecticide active ingredient
- Surfactant / emulsifier, if the active ingredient is not soluble in water and is to be mixed

These are mixed and kneaded to form dough to prepare insecticidal incense of various shapes. Spirals / coil shapes are popular in the market. After drying of this mixture, it is used as insect repellent RTU formulation by heating / burning / smouldering.

Renofluthrin MUP along with equal quantity of surfactant is mixed. Surfactants like 'lauryl alcohol ethoxylate' can be used. This emulsion mixture is subsequently diluted in water, and added in the 'coil dough mixture' / 'insecticidal incense mixture' for kneading.

In another process, Renofluthrin MUP can be added by spraying or dosing, after the incense product is made and dried. Sometimes along with the active ingredient insecticide, perfume can also be dosed or sprayed. In this case, the active ingredient Renofluthrin MUP is not added during the kneading or processing. It is added after the incense is dried and prepared.

"EC'V'SL" type of formulations are not useful when spraying on finished dried incense or coil formulations, because there is no contact with water at this stage. So the ingredients
used in EC / SC / SL etc, to give the insecticide compatibility with water are not necessary or advisable when the insecticide is sprayed on dried incense / dried coils etc. Renofluthrin MUP of the present invention is suitable in both methods of application.

According to the invention, RTU products such as Mosquito coil / incense containing as low as 0.02% Renofluthrin w/w shows good repellent and knock down effect against mosquitoes. The effectiveness / efficacy of mosquito repellent formulation is normally measured in "Knock-down time" (KT) in minutes. i.e. KT50 value in minutes, referring to knock down time of 50% of the test insects quantity.

In Peet Grady chamber study, against mosquito species 'Aedes': Renofluthrin 0.02% coil incense showed KT50 of 20.75 minutes. Against mosquito species 'Culex' Renofluthrin 0.02% coil incense showed KT50 of 22.31 minutes. This confirms that Renofluthrin MUP dosing methods work effectively in mosquito coils / incense. The coils show efficacy results against target insects. The target insects according to the invention include housefly, mosquito, cockroach and other flying and crawling pests.

**Experimental:**

The Solubility experiments for Renofluthrin technical grade active ingredient compound have been conducted to check the compatibility of the same for the preparation of MUP formulations:

**a) Isopropyl myristate (IPM):** It is commonly used solvent in formulations like mosquito repellent mats and aerosol sprays preparations. Renofluthrin 5% was mixed in 95% IPM solvent w/w. At room temperature (ranging between 25 to 32 degrees C) there was initial solubility. But on longer duration storage it started separating out, showing it is incompatible. At lower storage temperatures around (5-7 degrees C), it started forming layers and sedimentation earlier within just 4 to 8 hours.
b) **Isopropyl alcohol (IPA):** It is also a commonly known solvent. IPA is known to be miscible with water. Renofluthrin 5% was mixed in 95% IPA solvent w/w. There was poor solubility and sediments, showing it is incompatible.

c) **Cyclohexane:** Commonly used cycloalkane solvent. Renofluthrin 5% was mixed in 95% Cyclohexane w/w. There was poor solubility showing it is incompatible. Also Cyclohexane has a very low flash point (-20°C) making it unsafe for storage and use in formulations.

d) **Toluene:** Commonly used hydrocarbon organic solvent. It is also used in the synthesis of Renofluthrin active ingredient and has solubility. But Toluene cannot be used as single solvent for dilution and preparing formulations of Renofluthrin. Toluene has mild odour, which may not acceptable in home use formulations. Toluene having flash point of around 4°C, makes it unsafe for use and storage in preparations of RTU formulations.

e) **Xylene:** It is ordinarily used hydrocarbon organic solvent. Renofluthrin has solubility in Xylene. Xylene cannot be used as single solvent for dilution and preparing formulations of Renofluthrin. There are various grades of Xylene. But most Xylenes have flash point between 17 to 29°C. In countries where summer temperatures are easily higher than 30 °C, it is not feasible to use single solvent Xylene formulations. There are also safety and health hazards perceived in use and handling of Xylene.

f) **Aromatic solvents C9 to C18:** Renofluthrin shows good solubility in these solvents. The said solvent flash point ranges between 50 to 80 °C. But these have strong aroma and kerosene like odour and hence not preferred in home use formulations. For RTU formulations like liquid evaporators and aerosols, fragrance of the end consumer formulation plays a very important role in customer acceptance of the product. Also this gives slight yellow or slight brown colour to the mixture.
g) **Iso paraffins / De-aromatized solvent / De-odorized kerosene:** These are commonly used already in various home insecticide RTU formulations already. Renofluthrin was not directly soluble in these.

h) **N-Methylpyrrolidone:** It has high flash point above 90°C. Further it has solubility of Renofluthrin. But it is not commonly used or accepted for use in home insect repellents. Compounds with nitrogen are not preferred in home use products especially those requiring heating or burning. Exposure limits, health and safety issues are also perceived in such solvents with low market acceptance. Hence not suitable for daily or regular home use applications.

i) **Diethyl phthalate / Dibutyl phthalate / Phthalates:** Renofluthrin showed solubility in such phthalates. But phthalates have exposure hazards and limits. They have toxicity concerns. Also these are used as plasticizers hence have compatibility issues with some types of plastic container packing for the RTU formulations. Some phthalates also have compatibility issues with deodorized kerosene / isoparaffins.

The solubility experiments described herein above may be extended in scope with the combination of above solvents. But certain shortfalls found with the individual solvents themselves were causing issues in combination too. Such as IPM and Aromatic solvents in equal proportion, mixed with 5% Renofluthrin w/w was good in flash point and solubility, however it shows odour and smell issues. Solvent mixture 30% de-odorised kerosene and 70% aromatic solvent has issues such as odour, solubility and color change to slight yellow. Therefore, all these tested solvents are not considered by themselves for the preparation of MUP formulation.

j) **Glycol ethers:** Renofluthim is soluble in glycol ethers selected from the group consisting of Ethylene Glycol Monobutyl Ether, Diethylene Glycol Monohexyl Ether, Ethylene Glycol Monohexyl Ether, Ethylene Glycol Monoethyl Ether, Ethylene Glycol Monomethyl Ether, Diethylene Glycol Monoethyl Ether, Ethylene Glycol Monophenyl Ether,
Diethylene Glycol Monobutyl Ether, Ethylene Glycol Monobenzyl Ether, Diethylene Glycol Monomethyl Ether etc.

Further Renofluthrin MUP formulation comprising glycol ether is clear solution with high flash point, low toxicity and very mild to no odour.

Additionally to enhance the stability at various temperatures, alkylbenzenes are added as cosolvent / filler solvents in the Renofluthrin MUP. Solvents like Tolune or Xylene are used in Renofluthrin MUP formulation. When used in low and limited quantity in the MUP, it does not have much effect on odour or flash point of the MUP formulation.

In another preferred embodiment, the intermediate or MUP formulation of Renofluthrin, comprises Renofluthrin as active ingredient in the range of 2.5% to 18%, where Renofluthrin, is isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl) -2,2-dimethylcyclopropane carboxylate, wherein total trans isomers ranging from 90% to 99.90% and total cis isomers ranging from 0.1% to 10%, which is diluted in Glycol Ether solvents that improve the compatibility of active ingredient, increasing safety. Further, the stability of this MUP formulation is increased by using alkylbenzenes as filler solvents / co-solvents.

The invention will now be illustrated with help of examples. The aforementioned embodiments and below mentioned examples are for illustrative purpose and are not meant to limit the scope of the invention. Various modifications of aforementioned embodiments and below mentioned examples are readily apparent to a person skilled in the art.

All such modifications may be construed to fall within the scope and limit of this invention as defined by the appended claims.
Examples:

Example 1: General Procedure For the preparation of Renofluthrin MUP formulation
Renofluthrin ranging from 2% to 18% w/w concentration was diluted in one or more Glycol Ethers and subsequently adding limited quantity of Toluene solvent to make final MUP composition 100% w/w. In this 100% w/w MUP formulation, Toluene not more than 65% w/w of the Renofluthrin active ingredient w/w content, rest of the quantity w/w being one or more Glycol ethers. (as can be seen in examples given in Table 1 herein). Preferably glycol ethers are selected from the group consisting, but not limited to, Ethylene Glycol Monobutyl Ether, Diethylene Glycol Monomethyl Ether, Diethylene Glycol Monobutyl Ether, Ethylene Glycol Monohexyl Ether, Diethylene Glycol Monohexyl Ether.

Example 2: Preparation of 100 grams quantity Renofluthrin 5% MUP:
92% w/w (i.e. 92 grams) of Glycol ether solvent(s), (one, or mixture of more than one Glycol ethers) was taken in a vessel, followed by stirring the liquid. 5% w/w Renofluthrin active ingredient (adjusted for 100% purity) was added gradually to this mixture i.e. for example if the Renofluthrin active ingredient purity is 95%, then 5.26% w/w. The mixture was kept for stirring till it forms clear liquid solution. Then toluene solvent was added to this solution to complete 100 grams w/w and continue stirring further for up to 30 minutes. This gives Renofluthrin 5% MUP formulation liquid which contains w/w Renofluthrin 5.26%, with 92% Glycol Ethers and 2.74% Toluene.

Example 3: RTU Mosquito coil containing 0.02% Renofluthrin w/w,
Quantity 0.4% w/w of Renofluthrin 5% MUP, along with equal quantity of surfactant was mixed. This emulsion mix was then diluted in water, and added in the coil dough mixture for kneading, (i.e. if the insecticidal incense mixture total is 100 grams, Renofluthrin 5% MUP added will be 0.4 grams ) to give Renofluthrin 0.02% w/w mosquito coil.
Example 4: RTU Mosquito coil containing 0.025% Renofluthrin w/w,
Quantity 0.5% w/w of Renofluthrin 5% MUP, along with equal quantity of surfactant was mixed. This emulsion mix was diluted in water, and added in the coil dough mixture for kneading to give Renofluthrin 0.025% mosquito coil.

Example 5: RTU Mosquito coil containing 0.02% Renofluthrin w/w, by spraying on dried incense (mosquito coils after drying)
Incense coils were made and dried. Renofluthrin 5% MUP was added after the complete preparation and drying of the insecticidal incense coil. Quantity 0.4% w/w of Renofluthrin 5% MUP was sprayed or dosed on the dried incense /coil to give coil containing 0.02% Renofluthrin.
(Note: In this method of dosing / spraying active ingredient, given in example 5 and 6, no surfactant / emulsifier was required. The insecticide active ingredient Renofluthrin did not need to be mixed with water in this method.

Example 6: RTU Mosquito coil containing 0.025% Renofluthrin w/w, by spraying on dried incense (mosquito coils after drying) along with perfume
Incense coils were made and dried. Renofluthrin 5% MUP was added after the complete preparation and drying of the insecticidal incense coil. Quantity 0.5% w/w of Renofluthrin 5% MUP was sprayed or dosed on the dried incense / coil to obtain coil containing 0.025% Renofluthrin. Desired % w/w of perfume can be subsequently sprayed on the incense.
Alternatively, the desired % of perfume w/w, can be mixed with Renofluthrin 5% MUP in desired ratio. This mixture can then be sprayed or dosed on the incense.
We claim,

1. A manufacture use product (MUP) formulation of Renofluthrin, comprising Renofluthrin as active ingredient, one or more Glycol Ethers as solvent(s) together with one or more filler solvents or co-solvents.

2. The manufacture use product formulation of Renofluthrin according to claim 1, wherein Renofluthrin is active ingredient insecticide, having isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate,

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \\
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{F} \\
\text{F} \\
\text{F} \\
\text{F}
\end{array}
\]

wherein total trans isomers ranging from 90% to 99.90% and rest being total cis isomers.

3. The manufacture use product formulation of Renofluthrin according to claim 2, wherein the isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane, comprising the isomers selected from the group consisting of;
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl \((lR,3S)\)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate;
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl \((lS,3R)\)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate;
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl \((lR,3R)\)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate; and
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl \((lS,3S)\)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate.

4. The manufacture use product formulation of Renofluthrin, according to claim 1, wherein the concentration of Renofluthrin is present in range of 2.5% to 18%.
5. The manufacture use product formulation of Renofluthrin, according to claim 1, wherein the glycol ethers are selected from the group consisting of ethylene glycol monobutyl ether, diethylene glycol monohexyl ether, ethylene glycol monohexyl ether, ethylene glycol monomethyl ether, diethylene glycol monoethyl ether, ethylene glycol monophenyl ether, diethylene glycol monobutyl ether, ethylene glycol monobenzyl ether, diethylene glycol monomethyl ether or mixtures thereof.

6. The manufacture use product formulation of Renofluthrin, according to claim 1, wherein the filler solvent or co-solvent is selected from the group consisting of Toluene or Xylene.

7. The manufacture use product formulation of Renofluthrin, according to claim 1, wherein Renofluthrin is present in the range of 2.5% to 18% and the rest being one or more Glycol Ethers as solvent(s).

8. The manufacture use product formulation of Renofluthrin, according to claim 1, wherein Renofluthrin is present in range of 2.5% to 18%, diluted in glycol ethers, and filler solvent / co-solvent is selected from the group consisting of Toluene or Xylene.

9. The manufacture use product formulation of Renofluthrin, according to claim 1, wherein the said formulation is used further in preparation of insecticide formulations, insecticidal compositions, insect repellent products, including 'ready to use' (RTU) formulations.

10. The manufacture use product formulation of Renofluthrin, according to claim 9, wherein RTU or further insecticide formulations are selected from the group consisting of Coils, incense, burning forms, evaporation forms smouldering forms, Spirals, Stick, Cylindrical, Aerosols, sprays, Mists, Liquids, Vaporisers, Evaporators, paper, mats, fumigants, paper fumigants, and other burning and heating forms.
11. The manufacture use product formulation of Renofluthrin, according to claim 8, wherein the formulation comprises 5% w/w of Renofluthrin; one or more Glycol Ethers 90% to 95%, and rest being Toluene or Xylene.

12. The manufacture use product formulation of Renofluthrin, according to claim 8, wherein the formulation comprises 10% w/w of Renofluthrin; one or more Glycol Ethers 84% to 90%, and rest being Toluene or Xylene.

13. An insecticidal isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate i.e. Renofluthrin, wherein total trans isomers ranging from 90% to 99.90% and total cis isomers ranging from 0.1% to 10%, having structure:

14. The insecticidal isomeric composition according to claim 13, wherein the isomeric composition of 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane, comprising the isomers selected from the group consisting of:

- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IR,3S)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate;
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IS,3R)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate;
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IR,3R)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate; and
- 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (IS,3S)-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropanecarboxylate.
Figure: 1

Renofluthrin

Renofluthrin MUP

- Incense (coils)
- Mat paper
- Aerosol spray
- Liquid Vaporizers
- Paper fumigants
- Other heating or burning types
- Diffusion /spraying/non-heating types

Water mixing with surfactant
Spraying on dried incense/coils
INTERNATIONAL SEARCH REPORT

PCT/IN2015/000237

A. CLASSIFICATION OF SUBJECT MATTER
A01N53/00, A01N25/02 Version=2015.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

PATSEER, IPO INTERNAL DATABASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>IN 4121/MUM/2013 A; (SHOGUN ORGANICS LIMITED) 31/January/2014. Pages 1-15.</td>
<td>1-14</td>
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<tr>
<td>Y</td>
<td>US 2013/345266 A1; (TANAKA YOSHITO, ; SUMITOMO CHEMICAL COMPANY, LIMITED); 26/December/2013. Page-3; Column-73.</td>
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Further documents are listed in the continuation of Box C.

Date of the actual completion of the international search
04-12-2015

Date of mailing of the international search report
04-12-2015

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