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(54) Title: HIGH CONCENTRATION MULTIACTION TOPICAL INSECTICIDES CONTAINING PYRETHROIDS

(57) Abstract: A topical insecticide preparation is provided which can be safe to use and avoids many common deleterious side effects of conventional topical insecticides. The topical insecticide contains a combination of a first pyrethroid insecticide effective for killing fleas, a second pyrethroid insecticide effective for killing ticks, and an insect growth regulator (IGR). The topical insecticide preparation can be packaged together or packaged so that the first and second pyrethroid insecticides are stored separately prior to administration of the insecticide preparation to the animal. The combination of the first and second pyrethroid insecticides with an insect growth regulator results in an insecticide preparation formulated to have enhanced insecticidal activity against fleas and ticks compared to the effectiveness of the first and second insecticides used alone. Further, the combination of the first and second pyrethroid insecticides with an insect growth regulator produces an insecticide preparation having enhanced insecticidal activity against fleas and ticks while advantageously minimizing the total amount of insecticide needed for its effectiveness.



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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/27023

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8): A01N 43/08( 2006.01),43/40( 2006.01),53/08( 2006.01),57/10( 2006.01),37/00( 2006.01),37/02( 2006.01),37/06( 2006.01)

USPC: 514/471,145,345,357,531,549,552,875,970

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)

U.S. : 514/471, 145, 345, 357, 531, 549, 552, 875, 970

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
Reviewed the file contents of similar cases by applicant: 11/181,344 and 10/910,542.

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

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                    | Relevant to claim No.               |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| Y          | US 6,387,933 A (NAKAMURA et al.) 14 June 2002 (14.06.2002), column 1, last line to column 2, first line; column 3, lines 12-13 and 24-25; column 3, lines 34-38 and 48; column 4, lines 31-40; column 5, lines 46-59. | 1-5, 13-20, 23-34, 37-39, 41        |
| Y          | US 5,286,749 A (KIERNAN et al.) 15 February 1994 (15.02.1994), columns 1-2, Table 1 on column 2, first two compounds; column 3, lines 33-38; Table 1 on column 4.                                                     | 1-5, 13-16, 18, 23-34, 37-39 and 41 |
| Y          | US 5,236,954 A (GLADNEY et al.) 17 August 1993 (17.08.1993), column 1, lines 54-63; column 2, lines 17-46 and 60-63; column 3, lines 60-68; column 4, lines 49-50, 53-57; column 6, lines 10-27, 48-52 and 60-63.     | 1-5, 13-16, 18, 23-34, 37-39, 41    |
| Y          | Database CABA on STN, CAB International, (Oxfordshire, UK), No. 92:112120, NOLAN, J. et al. 'Acaricide resistance in single and multi-host ticks and strategies for control,' abstract, Parassitologia, 1990.         | 1-5, 13-20, 23-34, 37-39, 41        |



Further documents are listed in the continuation of Box C.



See patent family annex.

|                                          |                                                                                                                                                                     |     |                                                                                                                                                                                                                                              |
|------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| * Special categories of cited documents: |                                                                                                                                                                     | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention                                              |
| "A"                                      | document defining the general state of the art which is not considered to be of particular relevance                                                                | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone                                                                     |
| "E"                                      | earlier application or patent published on or after the international filing date                                                                                   | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "L"                                      | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "&" | document member of the same patent family                                                                                                                                                                                                    |
| "O"                                      | document referring to an oral disclosure, use, exhibition or other means                                                                                            |     |                                                                                                                                                                                                                                              |
| "P"                                      | document published prior to the international filing date but later than the priority date claimed                                                                  |     |                                                                                                                                                                                                                                              |

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US06/27023

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                               | Relevant to claim No.        |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Y          | Database CABA on STN, CAB International, (Oxfordshire, UK), No. 79:28333, HASCOET, M.M. et al. 'Synthetic pyrethroids,' abstract, Comptes Rendus des Seances de l'Agriculture de France, 1978.                                                                   | 1-5, 13-20, 23-34, 37-39, 41 |
| Y          | Database CABA on STN, CAB International (Oxfordshire, UK), No. 83:107933, GONG, J. et al. 'Studies on the residues and decomposition of 14C-permethrin in soil,' abstract, Yuanzineng Nongye Yingyong, 1982.                                                     | 1-5, 13-20, 23-34, 37-39, 41 |
| Y          | Database CABA on STN, CAB International (Oxfordshire, UK), No. 89:41108, GARG, R.C. et al. 'Pharmacologic profile of methoprene, an insect growth regulator, in cattle, dogs, and cats,' abstract, Journal of the American Veterinary Medical Association, 1989. | 17, 19                       |
| Y          | BUDAVARI, S. et al. (eds.). The Merck Index. Whitehouse Station (NJ): Merck & Co., Inc. 1996, 12th ed., page 1025, entry no. 6063.                                                                                                                               | 17, 19                       |
| Y          | US 5,437,869 A (KELLEY) 01 August 1995 (01.08.1995), column 1, lines 26-34, 50-57, 59-62; column 3, lines 40-42; Example 8 on column 6; see also Examples 5 to 8.                                                                                                | 20                           |
| Y          | EP 976328 A (SUMITOMO CHEMICAL COMPANY, LIMITED) 02 February 2000 (02.02.2000), paragraphs 1-5, 11-14, 18-19, 24.                                                                                                                                                | 1-12, 21-22, 25-36, 40       |
| Y          | EP 976327 A (SUMITOMO CHEMICAL COMPANY, LIMITED) 02 February 2000 (02.02.2000), claims 1-3; paragraphs 5, 9-12, 13-15, 18, 22.                                                                                                                                   | 1-12, 21-22, 25-36, 40       |
| Y          | US 6,201,017 A (SEMBO et al.) 13 March 2001 (13.03.2001), columns 1-7, in particular column 1, lines 23-31, column 6, lines 63-64, column 7, lines 25-27, Formulation example 3 on column 7; claims 1-5.                                                         | 1-12, 21-22, 25-36, 40       |
| E          | US 7,345,092 A (COTTRELL et al.) 18 March 2008 (18.03.2008), see claims 1-17.                                                                                                                                                                                    | 1-12, 20-22, 25-36, 40       |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/27023

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
  - ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
  - ☐ No protest accompanied the payment of additional search fees.

**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-12, 20-22, 25-36 and 39-40 (in part), drawn to an insecticidal preparation, wherein the "second" insecticide is dinotefuran.

Group II, claims 1-5, 13-21, 23-34, 37-39 and 41, drawn to drawn to an insecticidal preparation, wherein the "second" insecticide is acetamiprid.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Under lack of unity rules, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The "contribution over the prior art" is considered with respect to novelty and inventive step. See PCT Rule 13.1 and 13.2.

Nakamura et al. (US 6,387,933) disclose pesticidal synergism with the combined use of **acetamiprid** and **pyriproxyfen** (column 1, lines 55-64; see also claims 1-8). Ectoparasites of animals (column 1, last line to column 2, first line) such as cat fleas, dog fleas and ticks are controlled (column 3, lines 12-13 and 24-25). Mixtures or separate, i.e. separated, formulations are disclosed (column 3, lines 34-38). Addition of various other insecticides or synergists is disclosed (column 4, lines 31-35), including **permethrin** (column 4, line 37) and **phenothrin** (column 4, line 40). For acetamiprid + pyriproxyfen, the total of these two compounds when treating animals such as cats and dogs is disclosed as 2 mg/kg to 200 mg/kg. (column 5, lines 46-54). CABA abstract 79:28333 discloses that synthetic pyrethroids exhibit rapid decomposition in soil or water. CABA abstract 83:107933 discloses that decomposition of permethrin was positively correlated with soil organic matter content.

Nakamura et al. do not provide an explicit disclosure of a separately packaged preparation of a first insecticide (e.g. permethrin or phenothrin) to kill fleas, a second insecticide to kill ticks (e.g. dinotefuran), and an insect growth regulator (e.g. pyriproxyfen) with either of the separated insecticide, as claimed (see claim 1 for full details). However, there would have been sufficient motivation for one having ordinary skill in the art to have arrived at the claimed invention. The motivation to have the first insecticide composition (e.g. pyrethroids such as permethrin or phenothrin) separately packaged from the second insecticide composition (dinotefuran formulation) arises from the fact that pyrethroids are known to be unstable and decompose in the presence of water and/or organic matter (the two CABA abstracts cited above). Two chambers and a barrier is a routine design for holding two substances that are to be kept separate. One container with two chambers is an obvious design variation in that the product can appear compactly packaged.

Therefore, the claimed invention would have been obvious to a person skilled in the art at the time the invention was made. Consequently, there is no technical relationship among the claimed inventions involving one or more of the same or corresponding special technical feature, which define a contribution that each of the inventions, considered as a whole, makes over the prior art. The inventions as set forth above lack unity of invention for these reasons.