ARGENTINA

Supported by Cuba, Paraguay and Uruguay

ARGENTINA’S PROPOSAL TO INCLUDE ACTIVE INGREDIENTS ON THE LIST OF PRIORITY VETERINARY DRUGS THAT MUST BE EVALUATED OR REEVALUATED BY JECFA.

Argentina appreciates the opportunity to propose the incorporation of active ingredients used in veterinary drugs be included on the list of priorities. We propose the list subsequently be recommended to the JECFA for evaluation or reevaluation and the information be included in the spreadsheet in the Annex in the reference document.

In this regard, Argentina wishes to note that it urges Codex Alimentarius to establish the MRLs for known active ingredients and that these remain an indispensable health tool in our region’s farming practices. These old compounds have been registered largely based on limits or tolerances that have since been discontinued by the agencies that established them. The request that the competent authorities update them and the subsequent lack of new data provided by the original sponsors have been the cause of their suspension. There is no scientific evidence leading to concerns for human health that would merit the suspension of the use of these types of products. However, the lack of benchmark limits has caused problems in international trade.

Based on the foregoing, Argentina would like to recommend that the compounds ethion, fosfomycin (or phosphomycin) and triamcinolone be evaluated by the JECFA, pursuant to the information contained in the attached forms.

JUSTIFICATION: There are no international benchmark MRLs for the abovementioned compounds, except for fosfomycin (Japan has an MRL for fosfomycin for cattle tissue). It is imperative to have MRLs recommended by Codex Alimentarius in order to establish reliable withdrawal times to guarantee the safety of foods derived from animals treated with said compounds and avoid international trade issues.

The profile sheet for each active ingredient is attached as the following annexes:

ANNEX I: ETHION

ANNEX II: FOSFOMYCIN/PHOSPHOMYCIN

ANNEX III: TRIAMCINOLONE
FORMAT FOR GATHERING THE NECESSARY INFORMATION FOR SETTING CCRVDF PRIORITIES

ADMINISTRATIVE INFORMATION

1. Member submitting the request:
   ARGENTINA

2. Names of veterinary drug:
   Ethion

3. Trade names:
   Garrathion, Mosktion F; Mosktion PF; Mosktion Al

4. Chemical names and CAS registry number:
   Phosphorodithioic acid S,S'-methylene O,O,O',O'-tetraethyl ester. - CAS: 563-12-2

5. Names and addresses of the commodities producers:
   OVER SRL
   Meghmmani Organics Limited INDIA

PURPOSE, SCOPE OF APPLICATION, AND JUSTIFICATION

6. Identification of the food safety problem (risk of residue)
   Ethion residues in edible cattle tissues that could create public health concerns and/or international trade issues related to these products.

7. Evaluation of the criteria for inclusion on the list of priorities
   This molecule has been used in veterinary products for decades.
   Products containing ethion are currently used in most of the countries of the regions, primarily as tickicide.
   They were registered according to the tolerance established at that time by the EPA, which has since been discontinued due to the lack of additional information submitted by the sponsor when the EPA conducted its review. No scientific evidence on health concerns has been submitted.
   There is currently an ADI established by CODEX ALIMENTARIUS.

RISK PROFILE ELEMENTS

8. Justification for use
   In Argentina, the emerging problem of B. microplus’s resistance to conventional molecules and the minimal possibility of new developments demand alternative active ingredients that have proven efficacy. In this context, ethion is highly effective against ticks and, given that ticks have not had contact with the chemical compound in years, it is a valuable alternative tool for controlling the common cattle tick (Boophilus microplus).

9. Pattern of veterinary use, including information on approved uses, where available (product labels and other evidence verifying official authorization for use).
   Approved product labels are attached, in addition to use and trade certificates. (see Annex)

10. Products requiring Codex MRLs
   Cattle muscle, liver, kidney, and fat.

RISK ASSESSMENT NEEDS AND QUESTIONS FOR ASSESSORS

11. Specific request for those responsible for the risk assessment
   MRL recommendation for cattle muscle, liver, kidney, and fat, based on the ADI established by CODEX ALIMENTARIUS (ADI: 0.002 mg/kg/day)
AVAILABLE INFORMATION

12. Countries where the veterinary drug is registered
Argentina: Mosktion F 00-162; Mosktion PF Mosktion Al 03-172; Garrathion Max 15-104
Colombia: Mosktion F Reg.I.C.A. N° 6826 MV.
Ecuador: Mosktion PF 3B2-10556-AGROCALIDAD
Nicaragua: Mosktion AI 9771
Paraguay: Mosktion PF 7036; Mosktion AI 8706

13. National or regional MRLs or any other applicable tolerance
MRL (Argentina)
Muscle: 0.020 mg/kg
Kidney: 0.020 mg/kg
Liver: 0.020 mg/kg
Fat: 0.200 mg/kg

14. Lists of available data (pharmacology, toxicology, metabolism, residue depletion, analytical methodologies) (should include a list of the available data with complete study titles)

- NATIONAL RESIDUE SURVEY INFORMATION BULLETIN. Australian Government, Department of Agriculture, Fisheries and Forestry – November 2010. International beef maximum residue limits (MRLs)
- Ethion and cypermethrin residues in cattle treated with Garrathion max.
- Essay on ethion and cypermethrin risk mitigation in baths to remove the product once it has been used. – Validation of analytical techniques to detect ethion and cypermethrin in edible tissues. http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation94/ethion.pdf

TIMELINE

15. Date information may be submitted to JECFA:
September 15, 2016

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1 In preparing the preliminary risk profile, the member(s) should consider the updated data requirements published by JECFA, in order to enable the assessment of the veterinary drug to establish an ADI and the MRLs.
FORMAT FOR GATHERING THE NECESSARY INFORMATION FOR SETTING CCRVDF PRIORITIES

ADMINISTRATIVE INFORMATION
1. Member submitting the request:
ARGENTINA

2. Names of veterinary drugs:
FOSFOMICINA / FOSFOMYCIN / PHOSPHOMYCIN

3. Trade names:
FOSBAC / FOSBAC PLUS T

4. Chemical names and CAS registry number:
(1,2-epoxypropyl)-, (1r,2s)-(r)-phosphonicaci; (2r-cis)-(3-methyloxiranyl)phosphonicacid;(2r-cis)-phosphonicaci; (3-Methyloxiranyl) phosphonicacid; 883a;antibiotic833a; fosfocina; fosfonomycin
CAS # 23155-02-4

5. Names and addresses of the commodities producers:

PURPOSE, SCOPE OF APPLICATION, AND JUSTIFICATION
6. Identification of the food safety problem (risk of residue)
Fosfomycin residues in edible chicken and swine tissues that could create public health concern and/or international trade problems for these products.

7. Evaluation of the criteria for inclusion on the list of priorities
No MRLs have been established for edible poultry or swine tissues for fosfomycin, despite having been used in food producing animals for 30 years.

Given that the product is used in more than 50 countries for food producing animals, it is vital to establish benchmark MRLs and, based on these, withdrawal times to guarantee public health.

RISK PROFILE ELEMENTS
8. Justification of use
Fosfomycin is the only antibiotic of its type, both in structure and in action mechanism. It is not related to other families of antibiotics and has no cross-resistance with other molecules.

The spectrum, action mechanism, lack of toxic effects, and low resistance make it an antibiotic of choice, particularly for intensive production, like poultry and swine.

9. Pattern of veterinary use, including information on approved uses, where available (product labels and other evidence verifying official authorization for use)
Product labels and registration certificates are attached (see Annex).

10. Products requiring Codex MRLs
Chicken and swine muscle, fat, kidney, and liver.
RISK ASSESSMENT NEEDS AND QUESTIONS FOR ASSESSORS

11. Specific request for those responsible for the risk assessment
ADI and MRL must be established for chicken and swine muscle, fat, liver, and kidney.

<table>
<thead>
<tr>
<th>Veterinary Drug Name</th>
<th>Species</th>
<th>Tissues</th>
<th>Additional Comments</th>
<th>Maximum Residues Limits Proposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosfomycin</td>
<td>Poultry</td>
<td>Muscle</td>
<td>ADI Japan: 0.019 mg/kg b.w. per day.</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin and Fat</td>
<td>Dose in Poultry and Pigs: 10 mg/kg b.w. 40 mg/kg b.w.</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td></td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kidney</td>
<td></td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td>Swine</td>
<td>Muscle</td>
<td></td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin and Fat</td>
<td></td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td></td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kidney</td>
<td></td>
<td>500 (μg/kg)</td>
</tr>
</tbody>
</table>

AVAILABLE INFORMATION

12. Countries where the veterinary drug is registered:
Afghanistan, Algeria, Argentina, Armenia, Bangladesh, Bolivia, Chile, Colombia, Costa Rica, Dominican Republic, United Arab Emirates, Ecuador, Egypt, El Salvador, Guatemala, Honduras, Indonesia, Iraq, Jordan, Kenya, Lebanon, the former Yugoslav Republic of Macedonia, Malaysia, Mexico, Morocco, Nicaragua, Oman, Pakistan, Palestine, Panama, Paraguay, Peru, Philippines, Romania, Russia, Saudi Arabia, South Africa, Republic of Korea, Syria, Sri Lanka, Thailand, Tajikistan, Uruguay, Venezuela, Vietnam, Yemen, Zimbabwe.

13. National or regional MRLs or any other applicable tolerance
SENASA Argentina:

<table>
<thead>
<tr>
<th>Veterinary Drug Name</th>
<th>Species</th>
<th>Tissues</th>
<th>Maximum Residues Limits Accepted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosfomycin</td>
<td>Poultry</td>
<td>Muscle</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin and Fat</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kidney</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td>Swine</td>
<td>Muscle</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin and Fat</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td>500 (μg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kidney</td>
<td>500 (μg/kg)</td>
</tr>
</tbody>
</table>

The Japan Food Chemical Research Foundation

Table of MRLs for Agricultural Chemicals

Agricultural Chemical: FOSFOMYCIN

<table>
<thead>
<tr>
<th>Food</th>
<th>MRLs (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle, muscle</td>
<td>0.5</td>
</tr>
<tr>
<td>Cattle, fat</td>
<td>0.5</td>
</tr>
<tr>
<td>Cattle, liver</td>
<td>0.5</td>
</tr>
<tr>
<td>Cattle, kidney</td>
<td>0.5</td>
</tr>
<tr>
<td>Cattle, edible offal</td>
<td>0.5</td>
</tr>
<tr>
<td>Milk</td>
<td>0.05</td>
</tr>
<tr>
<td>Perciformes (such as bonito, horse mackerel, mackerel, sea bass, sea bream and tuna)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

ADI Japan: 0.019 mg/kg b.w. per day.
14. Lists of available data (pharmacology, toxicology, metabolism, residue depletion, analytical methodologies) (should include a list of the available data with complete study titles)

**Birds:**

1) Bedson Technical Department (2010); Setting Maximum Residue Limits for the Antibiotic Fosfomycin, in food producing animals, Bedson S.A.
2) OIE World Organization for Animal Health (2007); OIE List of Antimicrobials of Veterinary Importance; OIE International Committee.
4) Food Safety Commission of Japan (2010); Risk Assessment Report Fosfomycin (veterinary medicines); Food Safety Commission of Japan (FSCJ).
5) FCV-UNCPBA, Serum Disposition of the Fosfomycin Antibiotic in Broilers: Intravenous and Oral Study. Universidad Nacional del Centro de la Provincia de Buenos Aires School of Veterinary Sciences.
6) FCV-UNCPBA, Serum Disposition of the Fosfomycin Antibiotic in Broilers: Intravenous and Intramuscular Study; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
7) FCV-UNCPBA, Tissue concentrations and withdrawal time of Fosfomycin Antibiotic in Broilers: Muscle study – Oral Administration; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
8) FCV-UNCPBA, Tissue Concentration and Withdrawal Time of Fosfomycin Antibiotic in Broilers: Muscle Study- Intramuscular Administration; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
9) FCV-UNCPBA, Tissue concentrations and withdrawal time of the Fosfomycin Antibiotic in broilers: Liver Study – Oral Administration; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
10) FCV-UNCPBA, Tissue Concentrations and Withdrawal Time of the Fosfomycin Antibiotic in Broilers: Liver Study- Intramuscular Administration; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
11) FCV-UNCPBA, Tissue concentrations and withdrawal time of Fosfomycin Antibiotic in Broilers: Kidney Study- Oral administration; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
12) FCV-UNCPBA, Tissue Concentrations and Withdrawal Time of the Fosfomycin Antibiotic in Broilers: Kidney Study- IM Administration: Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.
14) Aramayona J.J, Bregante M.A., Solans C., Rueda S., Fraile L.J., Garcia M.A. (1997); Pharmacokinetics of fosfomycin in chickens after a single intravenous dose and tissue levels following chronic oral administration; Department of Pharmacology and Physiology, Department of Analytical Chemistry, Veterinary Faculty, University of Zaragoza, Spain.
15) Proanálisis S.A (2006); Final Evaluation Report of Oral Toxicity of Single LD 50 of Calcium Fosfomycin in Chickens (Gallus gallus); Proanálisis S.A. Department of Toxicological and Ecotoxicological Studies.
16) Dr. Susana M. Sicardi (1995); Evaluation of mutagenic and/or carcinogenic studies carried out with Fosfomycin; University of Buenos Aires, Faculty of Pharmacy and Biochemistry.
**Swine:**

1) Bedson Technical Department (2010); Establecimiento de límites máximos de residuos del antibiótico Fosfomicina en animales para consumo humano [Establishment of maximum residue levels of the antibiotic fosfomycin in food producing animals]; Bedson S.A.

2) OIE World Organization for Animal Health (2007); OIE List of Antimicrobials of Veterinary Importance; OIE International Committee.

3) Food Safety Commission of Japan (2010); Evaluation of Veterinary Pharmaceutical Products Fosfomicina.

4) Food Safety Commission of Japan (2010); Risk Assessment Report Fosfomycin (veterinary medicines); Food Safety Commission of Japan (FSCJ).

5) FCV-UNCPBA, Serum Disposition of the Fosfomycin Antibiotic in Swine: Intravenous and Oral Study; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.

6) FCV-UNCPBA, Serum Disposition of the Fosfomycin Antibiotic in Broilers: Intravenous and Intramuscular Study; Universidad Nacional del Centro de la Provincia de Buenos Aires, School of Veterinary Sciences.

7) Bedson S.A.; Determinación de residuos de fosfomicina en músculo, hígado, riñón y piel-grasa de cerdos- Administración por vía oral [Determination of fosfomycin residues in swine muscle, liver, kidney and skin/fat – Oral administration]; Bedson S.A.


9) Soraci Alejandro L.; Aportes al conocimiento de la terapia antibiótica racional en producción porcina; Área Toxicología [Contributions to knowledge on the rational antibiotic therapy in swine production; Toxicology Area], FCV-UNCPBA.

10) Aramayona J.J, Bregante M.A., Solans C., Rueda S., Fraile L.J., Garcia M.A. (1997); Pharmacokinetics of fosfomycin in chickens after a single intravenous dose and tissue levels following chronic oral administration; Department of Pharmacology and Physiology, Department of Analytical Chemistry, Veterinary Faculty, University of Zaragoza, Spain.

11) Proanálisis S.A (2006); Informe Final Evaluación de la Toxicidad Oral Letal Media de Dosis Única de Fosfomicina Cálcica en pollos (Gallus gallus) [Final Evaluation Report on the Average Lethal Oral Toxicity of a Single Dose of Calcium Fosfomycin in Chicken (Gallus gallus)]; Proanálisis S.A. Chemical Environmental Bromatological Research.

12) Dr. Susana M. Sicardi (1995); Evaluation of mutagenic and/or carcinogenic studies carried out with Fosfomycin; University of Buenos Aires. Faculty of Pharmacy and Biochemistry.

**TIMELINE**

15. *Date information may be submitted to JECFA:*

The work is available.
FORMAT FOR GATHERING THE NECESSARY INFORMATION FOR SETTING CCRVDF PRIORITIES

ADMINISTRATIVE INFORMATION

1. **Member submitting the request:**
   ARGENTINA

2. **Names of veterinary drug:**
   TRIAMCINOLONA

3. **Trade names:**
   DISTREPBENCIL ET, applied intramuscularly

4. **Chemical names and CAS registry number:**
   (11beta,16alpha)-9-Fluoro-11,16,17,21-tetrahidroxipregna-1,4-dieno-3,20-diona. CAS: 124-04-7

5. **Names and addresses of the commodities producers:**
   NOVARTIS ANIMAL HEALTH
   ELANCO ANIMAL HEALTH.

PURPOSE, SCOPE OF APPLICATION, AND JUSTIFICATION

6. **Identification of the food safety problem (risk of residue):**
   Triamcinolone residues in the edible tissues of cattle, sheep, goats, and swine that could create public health concerns and/or international trade issues related to these products.

7. **Evaluation of the criteria for inclusion on the list of priorities:**
   NO MRL values have been defined for food producing animals.

RISK PROFILE ASPECTS

8. **Justification of use:**
   Triamcinolone is widely used – associated with antibiotics – in the treatment of a variety of food-producing animal infections to relieve inflammation-related symptoms that present themselves as a result and which exacerbate infection conditions.

9. **Pattern of veterinary use, including information on approved uses, where available (product labels and other evidence verifying official authorization for use):**
   Copies of labels and leaflet are attached – application dose for triamcinolone in Distrepbencel ET: 7 mg/300 kg body weight – repeat 3 time/day. (see Annex)

10. **Products requiring Codex MRLs:**
    Triamcinolone - MRL for cattle, sheep, goat, and swine muscle, liver, kidney, and fat.

RISK ASSESSMENT NEEDS AND QUESTIONS FOR ASSESSORS

11. **Specific request for those responsible for the risk assessment:**
    Define an MRL in food-producing animal tissues (cattle-sheep-goat-swine), based on point 10.

AVAILABLE INFORMATION

12. **Countries where the veterinary drug is registered:**
    ARGENTINA - BRAZIL

13. **National or regional MRLs or any other applicable tolerance:**
    For Argentina (and in studies conducted in Brazil to establish the withdrawal time) an MRL was defined at the point of inoculation (muscle, liver, kidney, and fatty tissue). The results of this study indicate that, after two treatments 72 hours apart, the levels of triamcinolone in the muscle were less than 10 mcg/kg. With a 30% safety factor margin, we propose a withdrawal time of 30 days.
14. Lists of available data (pharmacology, toxicology, metabolism, residue depletion, analytical methodologies) (should include a list of the available data with complete study titles)

Report BR 0109-PATSO: “STUDY ON RESIDUE DEPLETION OF PRODUCT “BR00109” IN FAT, LIVER, KIDNEY, AND MUSCLE OF CATTLE SUBJECTED TO INTRAMUSCULAR TREATMENT” (2010).

TIMELINES
15. Date information may be submitted to JECFA:
The work is available.

CHILE

TEMPLATE FOR INFORMATION NECESSARY FOR PRIORITIZATION BY CCRVDF

ADMINISTRATIVE INFORMATION

1. Member(s) submitting the request for inclusion
Chile

2. Veterinary drug names
Lufenuron

3. Trade names
IMVIXA®

4. Chemical names and CAS registry number
1-[2,5-Dichloro-4-[(2R)-1, 1,2,3,3,3-hexafluoropropoxy]phenyl]-3-(2,6-difluorobenzoyl)urea
CAS registry #103055-07-8

5. Names and addresses of basic producers
There are several producers of the active substance.

PURPOSE, SCOPE AND RATIONALE

6. Identification of the food safety issue (residue hazard)
Lufenuron is not acute toxic; it is not a skin or eye irritant, not mutagenic and only a mild skin sensitiser. Studies in rodents and non-rodents show that lufenuron is not teratogenic, not toxic to reproduction and not carcinogenic. Neurological effects seen in subchronic and chronic studies occurred only in high doses after prolonged exposure periods. These effects are related to a saturation of fat compartments with lufenuron and a subsequent increase of the brain levels, which finally triggers the onset of convulsions.

7. Assessment against the criteria for the inclusion on the priority list
This compound meets the criteria for inclusion in the priority list for the following reasons:

- A member is proposing the compound for evaluation (Chile).
- The compound is intended for use in the long-term prevention and control of sea lice infestation with Lepeophtheirus salmonis and Caligus species, on farmed Atlantic salmon (Salmo salar) and Rainbow trout (Oncorhynchus mykiss).
- Salmonid fillet is traded globally but only produced by a few countries.
- There is a Marketing Authorization in Chile since June 17th 2016.
- A Withdrawal Period of 2050 degree days has been approved in Chile in June 17th 2016.

RISK PROFILE ELEMENTS

8. Justification for use
Sea lice are believed to cause the most significant and widespread disease of farmed salmonids, negatively affecting fish welfare and industry productivity. Lice feeding behaviours increase stress and decrease the immune response of the fish, resulting in increased susceptibility to other diseases, reduced growth and increased feed conversion ratio. The skin lesions caused by the parasites may in severe cases result in death of the fish due to osmoregulatory failure or secondary infections.
The effective control of sea lice in Salmonid farms is increasingly difficult due to drug resistance to some marketed products. The need for novel active ingredients providing effective and to some extent long-lasting control of sea lice is urgently needed to ensure the sustainability of the farmed salmonid industry.

Lufenuron is a benzoylphenyl-urea, a well-known class of compounds used in animal health and crop protection; the compound disrupts the formation of chitin, most probably by enzymatic interference, impacting critical stages of formation of new cuticles in sea lice. As such, developmental stages of sea lice fail to molt and ultimately die.

9. Veterinary use pattern, including information on approved uses if available

For the prevention and control of sea lice infestations, *Caligus rogercresseyi* in farmed salmonids. Only for oral administration through the feed prior transfer to sea farming sites. The product use is restricted to freshwater facilities, according to regulatory requirements. Pivotal studies demonstrated the end-use product provides 6-9 months of protection against infestation with sea lice once the fish are transferred to sea cages.

Lufenuron is added to the premix at 10%. Medicated feed is prepared by adding premix to commercial fish feed using top coating or vacuum coating. The medicated feed containing IMVIXA® must be prepared only in the facilities of fish feed companies authorized to manufacture medicated feed, not in farming sites.

Concentration of IMVIXA® in the feed must be proportionally adjusted to the feed rate necessary to reach a dose of 5 mg/kg lufenuron per day for a total dose of 35 mg/kg in treated fish. Sometimes, when the feed rate is less than expected, the feeding period might be extended from 7 days to 14 days maximum to ensure fish receive the complete therapeutic dose of 35 mg/kg.

To warrant the efficacy in preventing and controlling infestations produced by sea lice, it is recommended to use IMVIXA® according to the following considerations:

- Use the product in the absence of any concomitant disease or environmental condition that affects appetite.
- Administer an appropriate amount of feed to ensure complete and homogeneous consumption.
- Ensure administration of correct target dose over a minimum 7 day period.
- Monitor fish feeding during administration.
- Transfer to sea no sooner than 7 days post-treatment.

10. Commodities for which Codex MRLs are required

Fillet (muscle plus overlying skin with scales in natural proportions) for salmon and trout.

RISK ASSESSMENT NEEDS AND QUESTIONS FOR THE RISK ASSESSORS

11. Identify the feasibility that such an evaluation can be carried out in a reasonable framework

12. Specific request to risk assessors

Define an ADI and MRL for lufenuron in salmon and trout.

AVAILABLE INFORMATION

13. Countries where the veterinary drugs are registered

A full Marketing Authorization has been granted in Chile in June 17th, 2016.

14. National/Regional MRLs or any other applicable tolerances

- A European MRL has been established in November 2014 corresponding to the following:

<table>
<thead>
<tr>
<th>Pharmacologically active Substance</th>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)</th>
<th>Therapeutic Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lufenuron (RS-isomers)</td>
<td>Lufenuron</td>
<td>Fin fish</td>
<td>1 350 µg/kg</td>
<td>Muscle and skin in natural proportions</td>
<td>NO ENTRY</td>
<td>Antiparasitic agents (acting) against ectoparasites</td>
</tr>
</tbody>
</table>

- The EU MRL was ratified into the Norwegian legislation in March 2015.
- An MRL has been approved in Japan in March 2015 (1 ppm), which corresponds to the EU MRL because no decimal values are used in Japan.
- A Chilean MRL has been approved in June 29th 2016, which corresponds to the EU MRL (1350 µg/kg).
15. List of data (pharmacology, toxicology, metabolism, residue depletion, analytical methods) available

- Pharmacology package.
- Full toxicological package.
- Metabolism in laboratory animals, lactating goats, laying hens, non-target fish species and in Atlantic salmon.
- Residue depletion in Atlantic salmon and rainbow trout.
- Analytic method for residues in salmon and trout fillet, including validation.

TIMETABLE

16. Date when data could be submitted to JECFA

Data can be submitted from January 2017 onwards.

CUBA

In response to Circular Letter CL 2015/18-RVDF, Cuba supports Argentina’s comments. We would appreciate that our support be recorded.

EUROPEAN UNION

TEMPLATE FOR INFORMATION NECESSARY FOR PRIORITIZATION BY CCRVDF

ADMINISTRATIVE INFORMATION

1. Member(s) submitting the request for inclusion

EUROPEAN UNION

2. Veterinary drug names

Flumethrin

3. Trade names

Bayvarol Strips (3.6 g flumethrin)

4. Chemical names and CAS registry number

- International non-proprietary name: Flumethrin
- IUPAC name: 
  \((\pm)\-\alpha\-\text{Cyano}-4\-\text{fluoro-3-phenoxybenzyl}-3-\text{(}\beta\-4\text{-dichlorostyryl})-2,2\text{-dimethylcyclopropanecarboxylate}\)
- CAS name:
  Cyclopropane carboxylic acid, 3-[2-chloro-2-(4-chlorophenyl) ethenyl]-2,2-dimethyl-, cyano (4-fluoro-3-phenoxyphenyl) methyl ester
- CAS no.:
  69770-45-2

5. Names and addresses of basic producers

Bayer Animal Health GmbH
Kaiser-Wilhelm-Allee 10
Leverkusen
51373
Germany

PURPOSE, SCOPE AND RATIONALE

6. Identification of the food safety issue (residue hazard)

Residues in honey
7. Assessment against the criteria for the inclusion on the priority list
A member has proposed the compound for evaluation (Germany)
A member has established good veterinary practices with regard to the compound
The compound has the potential to cause international trade problems.
The compound is available as a commercial product
There is a commitment that a dossier will be made available.

RISK PROFILE ELEMENTS
8. Justification for use
For the diagnosis and control of flumethrin sensitive *Varroa jacobsoni* in honeybees.

9. Veterinary use pattern, including information on approved uses if available (this should include product labels or other evidence of official use authorization)
Veterinary medicinal product
Please see, accompanying this application, the Summary of Product Characteristics approved in Germany as evidence of official use authorisation, together with an English translation. (see Annex)

10. Commodities for which Codex MRLs are required
Honey

RISK ASSESSMENT NEEDS AND QUESTIONS FOR THE RISK ASSESSORS
11. Specific request to risk assessors
To establish an ADI and MRL for honey that would facilitate international use of the product and trade of honey.

AVAILABLE INFORMATION
12. Countries where the veterinary drugs are registered
Albania, Algeria, Argentina, Azerbaijan, Bulgaria, Chile, Colombia, Croatia, Cyprus, El Salvador, Estonia, Georgia, Germany, Greece, Hungary, Iran, Ireland, Republic of Korea, Latvia, Lithuania, Macedonia, Mexico, Moldavia, Morocco, New Zealand, Nicaragua, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Switzerland, Syria, Thailand, Turkey, Ukraine, United Kingdom

13. National/Regional MRLs or any other applicable tolerances

<table>
<thead>
<tr>
<th></th>
<th>Bees</th>
<th>Honey</th>
<th>No MRL required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine</td>
<td>Muscle</td>
<td>10 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fat</td>
<td>150 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>20 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>10 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Milk</td>
<td>30 μg/kg</td>
<td></td>
</tr>
<tr>
<td>Ovine</td>
<td>Muscle</td>
<td>10 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fat</td>
<td>150 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>20 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>10 μg/kg</td>
<td></td>
</tr>
</tbody>
</table>

Australia MRL

<table>
<thead>
<tr>
<th></th>
<th>Bees</th>
<th>Honey (temporary)</th>
<th>0.005 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine</td>
<td>Edible offal</td>
<td>0.05 mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meat (in the fat)</td>
<td>0.2 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Horse</td>
<td>Edible offal</td>
<td>0.1 mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meat</td>
<td>0.1mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Milk</td>
<td>0.05 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>

Codex MRL (JMPR/CCPR)

<table>
<thead>
<tr>
<th></th>
<th>Cattle</th>
<th>Meat</th>
<th>0.2 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Milk</td>
<td>0.05 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>
## Argentina MRL (Resolución 559/2011 Anexo I)

<table>
<thead>
<tr>
<th>Animal</th>
<th>Organ</th>
<th>MRL (μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bees</td>
<td>Honey</td>
<td>No MRL required</td>
</tr>
<tr>
<td>Cattle</td>
<td>Muscle</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Fat</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Milk</td>
<td>30</td>
</tr>
<tr>
<td>Sheep</td>
<td>Muscle</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Fat</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>10</td>
</tr>
</tbody>
</table>

## Japan MRLs (flumethrin MRLs are currently under revision)

<table>
<thead>
<tr>
<th>Animal</th>
<th>Provisional MRL (current) (ppm)</th>
<th>Final MRL (proposed) (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bees</td>
<td>Honey 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>Cattle/Cow/Calf</td>
<td>Muscle 0.01</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Fat 0.2</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Liver 0.04</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Kidney 0.03</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Other edible parts 0.03</td>
<td>0.05</td>
</tr>
<tr>
<td>Swine/Piglet</td>
<td>Muscle 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Fat 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Liver 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Kidney 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Other edible parts 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>Other land-dwelling animals</td>
<td>Muscle 0.06</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Fat 0.2</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Liver 0.06</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Kidney 0.06</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Other edible parts 0.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Milk</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Muscle 0.03</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Fat (inc skin)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Liver 0.03</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Kidney 0.03</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Other edible parts 0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Chicken</td>
<td>Egg 0.03</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other poultry</td>
<td>Muscle 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Fat (inc skin)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Liver 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Kidney 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Other edible parts 0.005</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Egg 0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* except cattle/cow/calf and swine/piglet

### 14. List of data (pharmacology, toxicology, metabolism, residue depletion, analytical methods) available

(should include a list of the data available with the full study titles)

Complete standard toxicology package and residue package including a validated analytical method.

### TIMETABLE

#### 15. Date when data could be submitted to JECFA

January 2017
NEW ZEALAND

TEMPLATE FOR INFORMATION NECESSARY FOR PRIORITIZATION BY CCRVDF

ADMINISTRATIVE INFORMATION

1. Member(s) submitting the request for inclusion
New Zealand

2. Veterinary drug names
Monepantel

3. Trade names
Zolvix™

4. Chemical names and CAS registry number
   - N-[(1S)-1-Cyano-2-(5-cyano-2-trifluoromethyl-phenoxy)-1-methyl-ethyl]-4-trifluoromethylsulfanyl-benzamide
   - CAS 887148-69-8

5. Names and addresses of basic producers
Elanco Animal Health (A Division of Eli Lilly and Company (NZ) Ltd)(and associated entities in other countries).

PURPOSE, SCOPE AND RATIONALE

6. Identification of the food safety issue (residue hazard)
   A toxicological ADI has been defined by JECFA and is 1200 µg per person. MRLs for sheep are established by CODEX;
   
<table>
<thead>
<tr>
<th>Residue</th>
<th>MRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>fat</td>
<td>13,000 µg/kg</td>
</tr>
<tr>
<td>liver</td>
<td>7,000 µg/kg</td>
</tr>
<tr>
<td>kidney</td>
<td>1,700 µg/kg</td>
</tr>
<tr>
<td>muscle</td>
<td>500 µg/kg</td>
</tr>
</tbody>
</table>

   The product is being extended for use in cattle and hence MRLs are required.

7. Assessment against the criteria for the inclusion on the priority list
   This compound meets the criteria for inclusion in the priority list for the following reasons:
   - A member is proposing the compound for evaluation: New Zealand
   - The compound is available as a commercial product: Yes
   - There is a commitment that a dossier will be made available
   - The compound is intended for use in the control of gastrointestinal nematode infections in cattle.
   - Treatment regimens have been established and there are label recommendations
   - Nematode infections have serious welfare and productivity outcomes for cattle, in particular calves
   - MRLs and withhold periods are necessary to safeguard food safety and facilitate international trade in beef commodities.

RISK PROFILE ELEMENTS

8. Justification for use
   ZOLVIX® is effective against sensitive strains of the following gastrointestinal roundworms of cattle, including those resistant to macrocyclic lactones, benzimidazoles, and levamisole;

   *Haemonchus placei, Haemonchus contortus, Ostertagia ostertagi, Trichostrongylus axei, Cooperia oncophora, Cooperia punctata, Cooperia mcmasteri, Nematodirus helvetianus, Bunostomum phlebotomum.*
9. Veterinary use pattern, including information on approved uses if available (this should include product labels or other evidence of official use authorization)

Sheep: The approved use pattern is 2.5 mg/kg monepantel by oral drench. Based on the dose banding provided on the label, the maximum dose is 3.125 mg/kg monepantel for a 16 kg lamb.

Cattle (proposed): The compound is intended to be applied as an oral drench. The proposed target dose of monepantel is 2.5 mg/kg, but based on the dose banding the highest dose is 3.75 mg/kg for a calf of 100 kg.

For severe infections or re-infections, the treatment may be repeated every 21 days.

10. Commodities for which Codex MRLs are required

Fat, liver, kidney, muscle

RISK ASSESSMENT NEEDS AND QUESTIONS FOR THE RISK ASSESSORS

11. Specific request to risk assessors

No toxicological or pharmacological data will be submitted as an ADI is already defined and no new information has been generated. No metabolic data in toxicological species will be submitted as this has already been evaluated by JECFA and no new information has been generated.

AVAILABLE INFORMATION

12. Countries where the veterinary drugs are registered

New Zealand, Australia, South Africa, European Union, Iceland, Norway, Lichtenstein, Uruguay, Argentina, Switzerland, Chile, and Brazil.

13. National/Regional MRLs or any other applicable tolerances

EU MRLs have been recommended by CVMP in 2016 (EU legislation pending)

<table>
<thead>
<tr>
<th>Residue Tissue</th>
<th>MRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>bovine fat</td>
<td>7,000 µg/kg</td>
</tr>
<tr>
<td>bovine liver</td>
<td>2,000 µg/kg</td>
</tr>
<tr>
<td>bovine kidney</td>
<td>1,000 µg/kg</td>
</tr>
<tr>
<td>bovine muscle</td>
<td>300 µg/kg</td>
</tr>
</tbody>
</table>

14. List of data (pharmacology, toxicology, metabolism, residue depletion, analytical methods) available (this should include a list of the data available with the full study titles)

No toxicological or pharmacological data will be submitted as an ADI is already defined and no new information has been generated. No metabolic data in toxicological species will be submitted as this has already been evaluated by JECFA and no new information has been generated.

<table>
<thead>
<tr>
<th>Metabolism in target species</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Total radioactive residue depletion and metabolism of [14C]-Monepantel following oral administration to beef cattle</td>
</tr>
<tr>
<td>2. Structural investigation of two unknown metabolites observed in liver following oral administration of [14C]-Monepantel to beef cattle</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Residue depletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Depletion of residues of monepantel sulfone in edible tissues of beef cattle following three oral administrations 21 days apart of Zolvix at 3.75 mg monepantel/kg BW</td>
</tr>
<tr>
<td>4. Depletion of residues of monepantel sulfone to limit of quantification in edible tissues of beef cattle following three oral administrations 21 days apart of Zolvix at 3.75 mg monepantel/kg BW</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Analytical methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Validation of an analytical method for the determination of monepantel sulfone in bovine fat, liver, kidney and muscle</td>
</tr>
<tr>
<td>6. Validation of an analytical method for the determination of monepantel and monepantel sulfone in bovine blood by LC-MS/MS</td>
</tr>
</tbody>
</table>

TIMETABLE

15. Date when data could be submitted to JECFA

December 2016
ADMINISTRATIVE INFORMATION

1. Member(s) submitting the request for inclusion
Norway

2. Veterinary drug names
Lufenuron

3. Trade names
To be confirmed

4. Chemical names and CAS registry number
1-[2,5-Dichloro-4-[(2R S)-1, 1,2,3,3,3-hexafluoropropoxy]phenyl]-3-(2,6-difluorobenzoyl)urea
CAS registry #103055-07-8

5. Names and addresses of basic producers
There are several producers of the active substance.

PURPOSE, SCOPE AND RATIONALE

6. Identification of the food safety issue (residue hazard)
Lufenuron is not acute toxic; it is not a skin or eye irritant, not mutagenic and only a mild skin sensitizer. Studies in rodents and non-rodents show that lufenuron is not teratogenic, not toxic to reproduction and not carcinogenic. Neurological effects seen in subchronic and chronic studies occurred only in high doses after prolonged exposure periods. These effects are related to a saturation of fat compartments with lufenuron and a subsequent increase of the brain levels, which finally triggers the onset of convulsions.

7. Assessment against the criteria for the inclusion on the priority list
This compound meets the criteria for inclusion in the priority list for the following reasons:

- A member is proposing the compound for evaluation (Norway).
- For the prevention and control of sea lice (Lepeophtheirus salmonis and Caligus species) infestations on Atlantic salmon (Salmo salar) following treatment in fresh water prior to sea transfer.
- Salmonid fillet is traded globally but only produced by a few countries.
- There is a Marketing Authorization in Chile since June 17th 2016.
- A Withdrawal Period of 2050 degree days has been approved in Chile in June 17th 2016.

RISK PROFILE ELEMENTS

8. Justification for use
Sea lice are believed to cause the most significant and widespread disease of farmed salmonids, negatively affecting fish welfare and industry productivity. Lice feeding behaviours increase stress and decrease the immune response of the fish, resulting in increased susceptibility to other diseases, reduced growth and increased feed conversion ratio. The skin lesions caused by the parasites may in severe cases result in death of the fish due to osmoregulatory failure or secondary infections.

The effective control of sea lice in Salmonid farms is increasingly difficult due to drug resistance to some marketed products. The need for novel active ingredients providing effective and to some extent long-lasting control of sea lice is urgently needed to ensure the sustainability of the farmed salmonid industry.

Lufenuron is a benzoylphenyl-urea, a well-known class of compounds used in animal health and crop protection; the compound disrupts the formation of chitin, most probably by enzymatic interference, impacting critical stages of formation of new cuticles in sea lice. As such, developmental stages of sea lice fail to molt and ultimately die.

9. Veterinary use pattern, including information on approved uses if available
Lufenuron is incorporated into a 10% premix formulation. Medicated feed is prepared through the addition of the premix to commercial fish feeds by top-coating or vacuum coating. Medicated feed is to be prepared only at authorised facilities to produce medicated feed.
The concentration of the premix in feed must be adjusted proportionally to the feeding rate required to achieve the lufenuron dose of 5 mg/kg/day for a total dose of 35 mg/kg in the treated fish. In instances when the expected feeding rate is disrupted, the feeding period may need to be extended from 7 days to a maximum of 14 days to ensure the fish receive the full therapeutic dose.

To ensure the efficacy of the product in preventing and controlling sea lice infestations it is recommended to:

- Use the product in the absence of any concurrent disease or environmental condition affecting appetite.
- Prepare an appropriate amount of medicated feed to ensure complete and homogeneous consumption.
- Ensure administration of correct target dose over a minimum 7 day period.
- Monitor feeding behaviour during administration.
- Transfer to sea no sooner than 7 days post-treatment, taking account of usual hatchery practices.

10. Commodities for which Codex MRLs are required

Fillet (muscle plus overlying skin with scales in natural proportions) for salmon and trout.

RISK ASSESSMENT NEEDS AND QUESTIONS FOR THE RISK ASSESSORS

11. Specific request to risk assessors:

Identify the feasibility that such an evaluation can be carried out in a reasonable framework.

Define an ADI and MRL for lufenuron in salmon and trout.

AVAILABLE INFORMATION

12. Countries where the veterinary drugs are registered

A full Marketing Authorization has been granted in Chile in June 17th, 2016.

13. National/Regional MRLs or any other applicable tolerances

- A European MRL has been established in November 2014 corresponding to the following:

<table>
<thead>
<tr>
<th>Pharmacologically active Substance</th>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)</th>
<th>Therapeutic Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lufenuron (RS-isomers)</td>
<td>Lufenuron (RS-isomers)</td>
<td>Fin fish</td>
<td>1350 µg/kg</td>
<td>Muscle and skin in natural proportions</td>
<td>NO ENTRY</td>
<td>Antiparasitic agents (acting) against ectoparasites</td>
</tr>
</tbody>
</table>

- The EU MRL was ratified into the Norwegian legislation in March 2015.
- An MRL has been approved in Japan in March 2015 (1 ppm), which corresponds to the EU MRL because no decimal values are used in Japan.
- A Chilean MRL has been approved in June 29th 2016, which corresponds to the EU MRL (1350 µg/kg).

14. List of data (pharmacology, toxicology, metabolism, residue depletion, analytical methods) available

- Pharmacology package.
- Full toxicological package.
- Metabolism in laboratory animals, lactating goats, laying hens, non-target fish species and in Atlantic salmon.
- Residue depletion in Atlantic salmon and rainbow trout.
- Analytic method for residues in salmon and trout fillet, including validation.

TIMETABLE

15. Date when data could be submitted to JECFA

Data can be submitted from January 2017 onwards.

PARAGUAY

Paraguay proposes including fosfomycin on the list of priorities for veterinary drug to be evaluated by the JECFA in chicken and swine tissues, given that the presence of these residues could create public health concerns.
ADMINISTRATIVE INFORMATION

1. **Member(s) submitting the request for inclusion**
   United States of America

2. **Veterinary drug names**
   Halquinol 60% in a chalk base

3. **Trade names**
   Quixalud

4. **Chemical names and CAS registry number**
   Halquinol (CAS 8067-69-4) is a mixture of:
   - 57-74% 5,7-dichloro-8-hydroxyquinoline (CAS 773-76-2)
   - 23-40% 5-chloro-8-hydroxyquinoline (CAS 130-16-5)
   - 0-4% 7-chloro-8-hydroxyquinoline (CAS 876-86-8)

5. **Names and addresses of basic producers**
   Elanco Animal Health
   2500 Innovation Way
   Greenfield, IN 46140
   USA
   +1 (317) 276-3000

PURPOSE, SCOPE AND RATIONALE

6. **Identification of the food safety issue (residue hazard)**
   Available toxicological studies for this compound demonstrate that Halquinol is not mutagenic. Studies in rodents and non-rodent animals demonstrate that this compound is not teratogenic, and without effects at the reproductive level. Chronic toxicity studies in rodents and non-rodents will be the basis for the derivation of the ADI.

7. **Assessment against the criteria for the inclusion on the priority list**
   This compound meets the criteria for inclusion in the priority list for the following reasons:
   - A member is proposing the compound for evaluation (United States of America).
   - The compound is available as a commercial product.
   - There is a commitment that a complete dossier will be made available.
   - The compound is intended for use in the treatment and prevention of enteric disease in pigs. Treatment regimens have been established and are label recommendations.
   - Diarrhea caused by enteric pathogens in pigs is a common and life threatening problem in many intensive piggeries.
   - Verified maximum residue limits are necessary to safeguard food safety for domestic use and trade destinations of pig edible tissues.

RISK PROFILE ELEMENTS

8. **Justification for use**
   Halquinol, a halogenated hydroxyquinoline is a mixture of 5,7-dichloro-8-hydroxyquinoline, 5-chloro-8-hydroxyquinoline and 7-chloro-8-hydroxyquinoline and used for the prevention and the treatment of diarrhea infections in pigs. Halquinol acts by combining metallic sites in respiratory enzymes of the cytoplasmic membranes of bacteria and fungi.
9. Veterinary use pattern, including information on approved uses if available

The compound is intended to be applied as medicated feed. The target dose of Halquinol is 8 mg/kg body weight/day for six weeks in pigs and three weeks in poultry.

The feed will be medicated at inclusion rates of 60 to 120 ppm for prevention and treatment of diarrhea infections respectively and in accordance with veterinary prescription. (see Annex)

10. Commodities for which Codex MRLs are required

Pork: Muscle, skin plus fat, liver and kidney

RISK ASSESSMENT NEEDS AND QUESTIONS FOR THE RISK ASSESSORS

11. Specific request to risk assessors

AVAILABLE INFORMATION1

12. Countries where the veterinary drugs are registered

Thailand, Vietnam, Brazil, India, Colombia, Indonesia, Bangladesh, Peru, Philippines, Ecuador, Bolivia, Nepal, Venezuela

13. National/Regional MRLs or any other applicable tolerances

No MRL has been established. A 7 day withhold period is applied prior to slaughter.

14. List of data (pharmacology, toxicology, metabolism, residue depletion, analytical methods) available

Please be advised of the progress of the research program being undertaken by Elanco Animal Health in relation to the identification of maximum residue limits for Halquinol (Quixaalud) in pigs:

Studies completed and status of ongoing studies:

- Genotoxicity
  - In vitro - mammalian gene mutation
  - In vitro - mammalian chromosome aberration
  - Chromosome Aberration in vivo and the Micronucleus Assay in vivo (ICH guideline S2B requires two in vivo tests)
    - MNT in vivo: negative
    - Chromosome Aberration in vivo - negative
  - Metabolites in blood - glucuronic acid and sulfate-metabolites (pathways of phase II biotransformation, detoxifying step) – negative in vitro with Ames and MNT screening tests

- Reproductive toxicity
  - Developmental toxicity in rats
    - Maternal and Embryo-fetal NOAEL: 300 mg/kg/day
  - Developmental toxicity in rabbits
    - Rabbit considered hypersensitive and not a suitable model
  - Developmental toxicity in mice
    - Maternal NOAEL: 30 mg/kg/day (based on clinical signs, death and decreased mean gravid uterus weight from 100 mg/kg/day and increased resorptions at 300 mg/kg/day).
    - Embryo-fetal NOAEL: 100 mg/kg/day (based on decreased fetal body weight associated with marked delays of ossification and increased malformations at 300 mg/kg/day)
  - DRF 2-generation study in rats:
    - NOAEL for parental male toxicity: 600 mg/kg/day
    - NOAEL for parental female toxicity: 200 mg/kg/day (based on decreased body weight/food consumption, microscopic renal findings and increased post-implantation losses at 600 mg/kg/day)
    - NOAEL for reproductive performance: 600 mg/kg/day
• NOAEL for toxic effects on progeny: 200 mg/kg/day (based on dehydration and/or blackish forelimb, and lower body weight observed at 600 mg/kg/day)
• Pivotal 2-generation study in reporting stage

Subchronic toxicity
• 28 days study in rats
  • NOAEL: 150 mg/kg/day in females and 750 mg/kg/day in males
• 90 days study in rats plus 4 week recovery
  • NOAEL: 150 mg/kg/day
• 52 weeks study in rats ongoing
• 28 and 90 days toxicity study in mini-pigs (mini-pigs chosen as second testing species)
• 28 d study - 225 mg/kg/day LOAEL males, NOEL females
• 90 d study ceased due to welfare concerns
• 90 days study in dogs (as alternative second testing species)
  • NOAEL: 60 mg/kg/day
• 39 weeks study in dogs ongoing

Microbiological ADI
• Activity of halquinol and its 4 metabolites against bacterial strains
• Low antimicrobial activity for halquinol, no measurable activity for the metabolites up to the highest tested concentration (256 µg/ml).

Residues
• In Vitro Comparative Metabolism
  • Rates and routes of metabolism of [14C]-5,7-dichloro-8-quinolinol in hepatocytes and hepatic microsomes prepared from male and female Sprague Dawley rat, Beagle dog, Goettingen minipig, Landrace pig and human.
  • [14C]-5,7-dichloro-8-quinolinol was extensively metabolized in all species and genders with the formation of several metabolites being observed. Metabolite identification work was carried out to determine the structural identity of the metabolites formed.
    In hepatocytes from all species the two major metabolites which were common to all samples were a glucose conjugate and a glucuronide conjugate. In hepatic microsomes, hydroxyl-5,7-dichloro-8-quinolinol was identified as the major metabolite and was also common to all species.
    All metabolites identified in human samples were also detected in all the toxicology species.
• Total Residue Study in Swine:
  • All experimental work complete. Currently in reporting stage.
• Residue Depletion in Swine
  • Scheduled to be initiated in October 2016. Projected completion date is April 2017.

15. Date when data could be submitted to JECFA
All data for submission will be available by April 2017.

URUGUAY

Uruguay supports the request sent by Argentina in response to CL 2015/18-RVDF. In Uruguay, there are 41 registries containing the active ingredient ethion. Currently, registration and sale of drugs containing this substance are suspended by Ministerial Resolution.

There are also studies currently being conducted: one on “Residue Depletion of Ethion in Cattle (bath application) and another, “Research Study to Establish the Wait Time Following Three Applications of the Same Product (ethion and cypermethrin).

In both cases, the application is by bath, and the results will be available at the end of the year.
Both studies are being conducted using international protocols approved by the competent authority and under its supervision.
DISTREPENCIL-E-T
ANTIBIÓTICO CERTERIL
5.000.000 U.I.
VENTA BAJO RECETA MÉDICO VETERINARIO

Pentámico G ácido esterina, pentamicina G potásico, pentamicina G benzoato, estrepomicina y novomicina de Garamona.

DISTREPENCIL-E-T es una combinación de tres tipos de penicilina con estreptomicina, y complementado con un corticoesterón: la penicilina de tricíclico.

Esta combinación es efectiva contra una amplia variedad de bacterias Gram positivas y Gram negativas, mientras la administración de tratamiento reduce la respuesta infecciosa de los tejidos, e inhibe una eventual reacción alérgica.

No es necesario que el paciente con antecedentes de alergia a la penicilina, y los pacientes que utilizan corticoesteroides, suelen adquirir reducción de su actividad drempicolica, que se utilizan dependiendo.

Por otra parte, la elevación de penicilinas, secares y productos que la paciente tiene una amplia variedad de penicilinas, y de las indicaciones del clínico, y de la sustracción de la penicilina, y el trastorno de la penicilina.

INDICACIONES
La indicación general, por su amplia actividad drempicolica, se recomienda su uso en el tratamiento de infecciones, en los que se descubre la endometritis endometrial.

No es necesario que el paciente con antecedentes de alergia a la penicilina, utilizan corticoesteroides, suelen adquirir reducción de su actividad drempicolica, que se utilizan dependiendo.

Dosis
- Neumococo bacteriano, sepsis hemorrágica: Infecciones del tracto urinario, abscesos y heridas húmedas, edema post quirúrgico (dr. 1,06), mixtita, piel, ganglio, absceso, eunode o quirúrgico (moqui), en el caso de infecciones de la penicilina, enteritis y leucemia leucémicas de los tejidos.
- Equino: Neumococo bacteriano, sepsis hemorrágica, colitis, abscesos, infecciones de la piel, escocismo y claudicación, mixtita, ganglio, hemorragias del tracto urinario, local o general, formas instauradas del cromocito bacteriano, eunode melógeno y ganglios emplazados.
- Pericarditis: Infecciones bacterianas del tracto gastrointestinal (diarreas de los niños recién nacidos), en las formas instauradas del cromocito bacteriano, sepsis hemorrágica, mixtita, mixtita, abscesos y heridas húmedas.

ADMINISTRACIÓN
Deben utilizarse penicilinas y azúcar, se recomienda el contenido total de la ampolla de solución, que se inyectarán en el frasco ampolla conteniendo la asociación de antibióticos más corticoesterón. Se administrará una inyección de 10 millones de una suspensión absolutamente homogéneas, momento en que estará listo para su uso.

La inyección, en las dosis correspondientes, se aplicará por vía intramuscular profunda, en el buril del estómago o bursáculos, en el paciente de los niños, estrictamente pareja.

La suspensión preparada con DISTREPENCIL-E-T deberá utilizarse inmediatamente después de preparada porque el producto está liofilizado potencialmente. Alérgene bien antes de usar.

PRECAUCIONES
En casos excepcionales, los niños, las mujeres, los niños, la prescripción de antibióticos no son eficaces y la aparición de reacciones adversas, se deben administrar con precaución. En estos casos, la suspensión de la inyección será efectuada.

RECOMENDACIONES
En este caso, se recomienda el tratamiento 14 - 48 horas después que hayan desaparecido los síntomas de la enfermedad, y se haya normalizado la tensión arterial. En cambio, si no se observa mejoría manifieta, dentro de los 3 - 4 días, será prudente revisar el diagnóstico.

RESTRICCIONES DE USO
Los animales tratados no deben sacrificarlos para su consumo durante el tratamiento y hasta 48 horas después de transcurren 15 días desde la última dosis. No utilizar en vacas lecheras en lactación.

Centro Nacional de Investigaciones: 0800-333-0130

FORMULA
- Pauta: Gema frasco ampolla conteniendo penicilina G benzoato 250.000 UI, penicilina G potásica 250.000 UI, penicilina G ácido esterínico 1.000.000 UI, sulbitol de estrepomicina equivalente a 1 g de baso, penicilina de tricíclico 16 mg, cloruro de sodio 0.9%, 37.5 mg.
- Dosis por via intramuscular 15 mg/kg de peso y Lechón 4.4 mg.
- Solvente: Gema frasco conteniendo 15 ml de agua destilada estéril.

PRODUCTOR
NOVARTIS SÁNCHEZ ANIMAL LTDA, São Paulo - Brasil

IMPORTADO Y DISTRIBUIDO POR
NOVARTIS ARGENTINA S.A.
Viaje 8551 (1429) - Buenos Aires - Tel: 4709-7474; Fax: 4709-7474
Tel. 55 4886-9000

DESA DE LA VISTA 1000
Dr. CAPITIEN ARAUJO 340 - BUCARES - Tel: 3362044
Reg. Sanidad. De 0.994-0017045-0/05

USO EN MEDICINA VETERINARIA
Ministerio de Agricultura, Ganadería y Pesca
Servicio Nacional de Sanidad y Calidad Agroalimentaria

CERTIFICASE QUE AL PRODUCTO: “MOSKTON F”

CLASIFICACION: Antiparasitario Externo / Organofosforado.

DESTINADO A: Bovinos.

TITULAR DEL CERTIFICADO: ORGANIZACION VETERINARIA REGIONAL S.R.L.


HABIENDO CUMPLIDO CON TODOS LOS REQUISITOS ESTABLECIDOS POR LA REGLAMENTACION VIGENTE.

LE HA SIDO OTORGADO POR DISPOSICION N° 1493/2011.

EL PERMISO QUE AUTORIZA SU USO Y COMERCIALIZACION.

CERTIFICADO N°: 00-162.

VALIDEZ: Hasta el 16 de Agosto de 2021.

BUENOS AIRES, 24 de Agosto de 2011

La renovación del certificado de uso y comercialización deberá ser solicitada por el titular 120 días antes de la fecha del vencimiento de la validez.

OVER S.R.L.
ORGANIZACION VETERINARIA REGIONAL

SUSANA MEZGER

13/09/11
Ministerio de Agroindustria
Servicio Nacional de Sanidad y Calidad Agroalimentaria

CERTIFICASE QUE AL PRODUCTO: “MOS-K-TION A.L.”

CLASIFICACION: Antiparasitario Externo – Órganososforado - Pirietroide.

DESTINADO A: Bovinos.

TITULAR DEL CERTIFICADO: OVER ORGANIZACIÓN VETERINARIA REGIONAL S.R.L.

EXPEDIENTE N°: 10610/02

HABIENDO CUMPLIDO CON TODOS LOS REQUISITOS ESTABLECIDOS POR LA REGLAMENTACION VIGENTE.

LE HA SIDO OTORGADO POR DISPOSICION N°: 912/03

EL PERMISO QUE AUTORIZA SU USO Y COMERCIALIZACION.

CERTIFICADO N°: 03-172

VALIDEZ: Hasta el 18 Julio de 2023.

BUENOS AIRES, 29 de Febrero de 2016.

La renovación del certificado de uso y comercialización deberá ser solicitada por el titular 120 días antes de la fecha del vencimiento de la validez.
MINISTERIO DE AGRICULTURA, Ganadería y Pesca
Sericio Nacional de Sanidad y Calidad Agroalimentaria

CERTIFICASE QUE AL PRODUCTO: “GARRATHION MAX”

CLASIFICACION: Antiparasitario Externo/ Piretroide/ Órganofosforado.

DESTINADO A: Bovinos.

TITULAR DEL CERTIFICADO: OVER ORGANIZACIÓN VETERINARIA REGIONAL S.R.L.

EXPEDIENTE N°: 323533/12

HABIENDO CUMPLIDO CON TODOS LOS REQUISITOS ESTABLECIDOS POR LA REGLAMENTACION VIGENTE

LE HA SIDO OTORGADO POR DISPOSICION N°: 775/15

EL PERMISO QUE AUTORIZA SU USO Y COMERCIALIZACION

CERTIFICADO N°: 15-104

VALIDEZ: Hasta el 24 de Julio de 2025

BUENOS AIRES, 20 de Octubre de 2015

La renovación del certificado de uso y comercialización deberá ser solicitada por el titular
120 días antes de la fecha del vencimiento de la validez.

[Stamp]
ANNEX

**FOSBAC®**

**COMPLEJO ANTIMIČO ENERGIZANTE DE AMPLIO ESPECTRO POLVO SOLUBLE**

**USO PARA**

Vesícula biliar subíntegra

**FOSBAC® suelto se presenta en una Marca Registada por SECCION® S.A.**

**ANTIBIÓTICO**

**MEDICACIÓN**

En agua de bebé: para asegurar una correcta dilución se recomienda realizar una preparación del producto a diluir en 3 - 10 litros de agua y luego agregar al tanque de agua de bebé. En alimentos: Para asegurar un correcto mascado, se recomienda realizar una preparación con la cantidad de sólidos a diluir en 3 - 10 kg de alimento y luego incorporar a la mezcla final.

**INDICACIONES**

- Infecciones urinarias, infecciones bacterianas, enfermedades digestivas y enfermedades causadas por microorganismos sensibles.
- Enfermedades y enfermedades causadas por microorganismos sensibles: a la Fosfomicina.

**ADMINISTRACIÓN Y DOSIS**

- Administrar por vía oral, mezclado en el agua de bebé o alimento.

**CONTRAINDICACIONES**

- No presenta.

**RECUERDOS DE USO**

- Libere el tratamiento 7 días antes de la faenia en agua y alimento.
- No administrar a ponedoras en producción de huevos destinados al consumo humano.

**CONSERVACIÓN**

- Conservar entre 0º y 25º.

**FECHA DE ELABORACIÓN**

- A medida que se elabore.

**CONTENIDO NETO**

- Se indicará en la etiqueta del producto.
EUROPEAN UNION

Summary of Veterinary Product Characteristics

1. **Name of the veterinary medicinal product:**
   Bayvarol, 6.61 g/strip for honeybees
   Flumethrin

2. **Qualitative and quantitative composition:**
   Each 6.6 g strip contains:
   - **Active ingredient(s):**
     Flumethrin (90 %)  4.00 mg
   - **Other constituents:**
     See section 6.1 for a full list of other constituents

3. **Pharmaceutical form:**
   Strips to be suspended in the corridors between combs.

4. **Clinical data:**
   4.1 **Target animal species:**
   Honeybee
   4.2 **Applications for particular target animal species:**
   To control (treat) varroa mites in honeybees.
   4.3 **Contraindications:**
   Do not apply while bees are foraging or before the honey harvest.
   Do not apply at the same time as other pharmaceutical products intended to combat varroosis.
   Do not apply at the same time as pharmaceutical products intended to combat nosematosis.
   4.4 **Particular warnings for individual target animal species:**
   None.
   4.5 **Particular precautions for use:**
   4.5.1 **Particular precautions for use in animals:**
   Bayvarol is intended for external use as an acaricide and must not be ingested by animals or humans. The active ingredient flumethrin is toxic to fish.
   Propolis from colonies treated with Bayvarol must not be used for human consumption.
   Open the foil pouch immediately before use.
   4.5.2 **Particular precautions for users:**
   Avoid direct contact with the skin, mucous membranes and eyes. If the product accidentally comes into contact with the mucous membranes or eyes, rinse the affected parts with plenty of water.
   Wear protective gloves when suspending the strips.
   Do not eat, drink or smoke while using.
   Wash your hands thoroughly after use.
   4.6 **Adverse events (frequency and severity):**
   None.
   Any adverse events following the use of Bayvarol should be reported to the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit [Federal Office for Consumer Protection and Food Safety], Mauerstr. 39-42, 10117 Berlin or to the marketing authorisation holder.
Report forms can be obtained free of charge from the address given above or by email (uaw@bvl.bund.de).

4.7 Use during gravidity, lactation or while laying:
Not applicable.

4.8 Interactions with other medicinal products and other forms of interaction:
None known.

4.9 Dosage and method of administration:
Four strips for normally developed colonies. Half this dose, i.e. two strips, for weaker colonies, colonies bred in the apiary and new colonies occupying fewer than half the combs.

Strips to be suspended in the corridors between combs.

Bayvarol strips are suspended in the central brood nest area of the combs in such a way that the bees can access them from both sides. To do this, users must bend both the hanging straps at the designated bend points to the same side and suspend the strips above the top bar of the frame. (Fig. 1).

In the case of large colonies occupying several brood spaces, two strips can be joined together at the base so that they can be inserted into and removed from the corridors between the combs without dividing the brood spaces. (Fig. 2).

Strips should be left in place for at least four weeks but not more than six weeks.

4.10 Overdose (symptoms, emergency measures and antidotes), if necessary:
Overdose is unlikely in view of the application form (plastic strips). Bayvarol has not triggered any intolerance in bees even under extreme test conditions.

4.11 Pre-harvest safety interval(s):
0 days.

5. Pharmacological properties:
ATC vet code: QP53AC05
Antiparasitics: Pyrethroid as ectoparasitic for topical application

5.1 Pharmacodynamic properties:
Bayvarol® is an antiparasitic used to control varroa mites in bees and contains the active ingredient flumethrin.

Varroa mites can become resistant to pyrethroids. The active ingredient in Bayvarol is a pyrethroid. Should this be the case, treatment may not be successful. Users should carry out a resistance test before applying Bayvarol in order to ascertain how likely the treatment is to succeed.

Flumethrin is an insecticide in the synthetic pyrethroids group (α-cyano-pyrethroid, type II pyrethroid); these substances affect the activity of the sodium channels in the parasitic nerve cell membrane. Flumethrin has pronounced acaricidal properties.

5.2 Pharmacokinetic data:
No information.

6 Pharmaceutical data:

6.1 List of other constituents:
Low-density polyethylene

6.2 Incompatibilities:
None known.

6.3 Shelf life:
6.3.1 of the veterinary product in sealed container:
60 months.

6.3.2 of the veterinary product once the container has been opened:
No information.
6.3.3 once the preparation has been made up:
Not applicable.

6.4 Special precautions for storage:
Keep away from food, drink and animal feed.

6.5 Nature and contents of container
Folded cardboard box of 5 x 4 strips. Each strip weighs 6.61 g.

6.6 Particular precautions relating to the disposal of unused veterinary products and dealing with waste generated:
Leftover veterinary medicinal products should if possible be disposed of via harmful waste collection services. If the product is disposed of with domestic waste, care must be taken to ensure that the waste cannot be accessed and misused. Veterinary medicinal products must not be disposed of via the drains or waste water system.

7. Marketing authorisation holder:
Bayer Vital GmbH
Animal Health Division
51368 Leverkusen

8. Marketing authorisation number:
MA no.: 26288.00.00

9. Date on which marketing authorisation was first granted / extended:
Marketing authorisation first granted: 21.01.1994 / marketing authorisation most recently extended 03.12.2003

10. This leaflet was last approved in:
September 2008

11. Prohibition on sale, distribution and/or use:
Not applicable.

12. Prescription status / pharmacy obligation:
Available only in pharmacies

Other information
Honey must be thoroughly centrifuged, filtered and skimmed before being put on sale.
Honey in the comb or honey containing pieces of comb must not be put on sale as a foodstuff.

Brief guide to performing the resistance test

A. Mite preparation
1. “Plucking” method

Material
- Recently removed capped brood combs (drone or worker brood)
- Tweezers; paintbrush (size 0-1); binoculars or magnifying glass if available; (plastic) Petri dishes; styropor box (such as Kirchhain breeding box) with a damp cloth (dipped in approximately 50 ml of water) laid on the bottom

Method
- Carefully pluck capped brood stages (pupae) using binoculars or magnifying glass if available
- Use the paintbrush or the tips of the tweezers to place any mites found in empty Petri dishes (10 per dish)
- Keep the dishes in the styropor box until you perform the test (up to three hours maximum)
2. "Powder" method

Material

- Artificial swarm boxes; shallow plastic bath; icing sugar
- (Plastic) Petri dishes with damp filter paper laid on the bottom; paintbrush (size 0-1); tweezers
- Styropor box (such as Kirchhain breeding box), see above.

Method

- Form an artificial swarm (approximately 500 g of bees) from the test colony. Briefly shake the artificial swarm box and powder the bees with approximately one tablespoon of icing sugar.
- Rotate the artificial swarm box over the plastic bath to make sure that the bees are thoroughly covered with icing sugar; leave the box on top of the bath for two to three minutes.
- Look in the icing sugar for mites that have fallen off the bees and transfer them to Petri dishes using damp (not dripping) filter paper ⇒ remove the leftover sugar.
- Keep the dishes in the styropor box until you perform the test (up to three hours maximum).

B. Performing the test

Material

- Test mites (see section A for preparation)
- (Plastic) Petri dishes with bee pupae (one drone per dish, two workers per dish)
- Bayvarol® strips; gloves; stop-watch; paintbrush (size 0-1); base (paper or similar)

Method

- Prepare working area and place pupae in the Petri dishes (label them).
- Prepare the dishes with the test mites; keep paintbrush and stop-watch to hand.
- Put on gloves and have a new Bayvarol® strip to hand.
- Start the stop-watch (60 seconds) and at the same time place five mites on the strip, always moving from left to right.
- Observe the mites and use the paintbrush to stop them leaving the strip.
- After one minute has passed, transfer the mites to the prepared dishes containing the pupae in the same order in which they were placed on the strip ⇒ maintain contact time.
- Repeat the process (contact treatment) with the other five mites in the corresponding test dish.
- Note the time at this point in the test so that you can assess resistance after five hours.
- Setting up the control group: Same procedure as above, except that the mites are not placed on a Bayvarol® strip but are instead transferred to an empty Petri dish.

N.B.: Set up the control groups before the test groups; use different tools and a separate work space.

C. Assessment of condition after five hours

Material

- Either binoculars (40x magnification) or a magnifying glass; paintbrush (size 0-1)

Method – to differentiate between the following mite conditions:

- **Mobile**: when exposed to mechanical stimulus, the animals always continue to move in a coordinated manner.
- **Damaged**: no coordinated movement takes place even when the animals are touched with the paintbrush three times;
  - they may lurch around or may simply have quivering or twitching limbs;
  - most of them will be sitting without moving and quivering (instead of “marching on the spot”) or no longer display any recognisable movement.
D. Assessment

Method
- Count how many control mites are damaged
- The test is only predictive if fewer than 10% of the control mites are damaged
- If at least 90% of the treated mites (hive average) are damaged, then the colony can be treated with Bayvarol®
- If fewer than 90% of the treated mites (hive average) are damaged, the user must assume that the mites are resistant. Bayvarol® should not be administered.