CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 9 **CX/RVDF 16/23/10**

August 2016

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Twenty-third Session

Houston, Texas, United States of America, 17 – 21 October 2016

DRAFT PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION OR RE-EVALUATION BY JECFA

replies to CL 2015/18-RVDF submitted by:

Argentina, Chile, Cuba, European Union, New Zealand, Norway, Paraguay, United States of America, Uruguay

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 *triamciniolone* 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

ANNEX I

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 AI

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

Meghmani 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.

http://www.fao.org/fao-who-codexalimentarius/standards/pestres/pesticide-detail/en/?p_id=34

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[1]

12. Countries where the veterinary drug is registered

Argentina: Mosktion F 00-162; Mosktion PF Mosktion AI 03-172; Garrathion Max 15-104

Colombia: Mosktion F Reg.I.C.A. Nº 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

[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.

ANNEX II

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)-(-)-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:

BEDSON S.A., Las Palmeras 2240. La Lonja. Pilar. Buenos Aires. Argentina.

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.

Veterinary Drug Name	Species	Tissues	Additional Comments	Maximum Residues Limits Proposed
Fosfomycin	Poultry	Muscle	ADI Japan: 0,019 mg/kg b.w. per day. Dose in Poultry and Pigs: 10 mg/kg b.w to 40 mg/kg b.w.	500 (µg/kg)
		Skin and Fat		500 (µg/kg)
		Liver		500 (µg/kg)
		Kidney		500 (µg/kg)
	Swine	Muscle		500 (µg/kg)
		Skin and Fat		500 (µg/kg)
		Liver		500 (µg/kg)
		Kidney		500 (µg/kg)

AVAILABLE INFORMATION[1]

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:

Veterinary Drug Name	Species	Tissues	Maximum Residues Limits Accepted
Fosfomycin	Poultry	Muscle	500 (µg/kg)
		Skin and Fat	500 (µg/kg)
		Liver	500 (µg/kg)
		Kidney	500 (µg/kg)
	Swine	Muscle	500 (µg/kg)
		Skin and Fat	500 (µg/kg)
		Liver	500 (µg/kg)
		Kidney	500 (µg/kg)

The Japan Food Chemical Research Foundation

Table of MRLs for Agricultural Chemicals

Agricultural Chemical: FOSFOMYCIN
Note:

Food	MRLs(ppm)
Cattle, muscle	0.5
Cattle, fat	0.5
Cattle, liver	0.5
Cattle, kidney	0.5
Cattle, edible offal	0.5
Milk	0.05
Perciformes (such as bonito, horse mackerel, mackerel, sea bass, sea bream and tuna)	0.05

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.

3) Food Safety Commission of Japan (2010); Evaluation of a Veterinary Pharmaceutical Product, Fosfomycin.

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.

13) Perez D.S., Tapia M.O. y Soraci A.L. (2014); Fosfomycin: Uses and potentialities in veterinary medicine; Open veterinary Journal, Vol. 4(1): 26-43.

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.

17) D.S.Perez, A.L.Soraci, S.N.Dieguez and M.O.Tapia; Laboratorio de Toxicologia, Universidad Nacional del Centro de la Provincia de Buenos Aires, Tandil, Buenos Aires, Argentina (2011); Determination and withdrawal Time of Fosfomycin in Chicken Muscle, Liver and Kidney; International Journal of Poultry Science 10 (8): 644-655.

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.

8) Perez D.S., Tapia M.O. y Soraci A.L. (2014); Fosfomycin: Uses and potentialities in veterinary medicine; Open veterinary Journal, Vol. 4(1): 26-43.

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.

ANNEX III

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)

Triamciniolone 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

Triamciniolone 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 triamciniolone in Distrepbencil ET: 7 mg/300 kg body weight – repeat 3 time/day. (see Annex)

10. Products requiring Codex MRLs

Triamciniolone - 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[1]

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 triamciniolone 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 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 (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[1]

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:

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

- 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:

(±)-α-Cyano-4-fluoro-3-phenoxybenzyl-3-(β,4-dichlorostyryl)-2,2-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[1]

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

EU MRL (Commission Regulation (EU) No 37/2010)

Bees	Honey	No MRL required
Bovine	Muscle	10 µg/kg
	Fat:	150 µg/kg
	Liver	20 µg/kg
	Kidney	10 µg/kg
	Milk	30 µg/kg
Ovine	Muscle	10 µg/kg
	Fat	150 µg/kg
	Liver	20 µg/kg
	Kidney	10 µg/kg

Australia MRL

Bees	Honey (temporary)	0.005 mg/kg
Bovine	Edible offal	0.05 mg/kg
	Meat (in the fat)	0.2 mg/kg
Horse	Edible offal	0.1 mg/kg
	Meat	0.1mg/kg
Milks		0.05 mg/kg

Codex MRL (JMPR/CCPR)

Cattle	Meat	0.2 mg/kg
	Milk	0.05 mg/kg

Argentina MRL (Resolución 559/2011 Anexo I)

Bees	Honey	No MRL required
Cattle	Muscle	10 µg/kg
	Fat	150 µg/kg
	Liver	20 µg/kg
	Kidney	10 µg/kg
	Milk	30 µg/kg
Sheep	Muscle	10 µg/kg
	Fat	150 µg/kg
	Liver	20 µg/kg
	Kidney	10 µg/kg

Japan MRLs (flumethrin MRLs are currently under revision)

		Provisional MRL (current) (ppm)	Final MRL (proposed) (ppm)
Bees	Honey	0.005	0.005
Cattle/Cow/Calf	Muscle	0.01	0.2
	Fat	0.2	0.2
	Liver	0.04	0.05
	Kidney	0.03	0.05
	Other edible parts	0.03	0.05
Swine/Piglet	Muscle	0.005	0.005
	Fat	0.005	0.005
	Liver	0.005	0.005
	Kidney	0.005	0.005
	Other edible parts	0.005	0.005
Other land-dwelling animals	Muscle	0.06	0.01
	Fat	0.2	0.2
	Liver	0.06	0.02
	Kidney	0.06	0.01
	Other edible parts	0.1	0.02
Milk		0.05	0.05
Chicken	Muscle	0.03	0.01
	Fat (inc skin)	0.03	0.6
	Liver	0.03	0.01
	Kidney	0.03	0.01
	Other edible parts	0.03	0.01
	Egg	0.03	0.03
Other poultry	Muscle	0.005	0.005
	Fat (inc skin)	0.005	0.005
	Liver	0.005	0.005
	Kidney	0.005	0.005
	Other edible parts	0.005	0.005
	Egg	0.03	0.03
Fish		0.005	0.005

* except cattle/ cow/ calf and swine/piglet

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)*

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;

13,000 µg/kg	fat
7,000 µg/kg	liver
1,700 µg/kg	kidney
500 µg/kg	muscle

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 gastro-intestinal 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[1]

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)

7,000 µg/kg	bovine fat
2,000 µg/kg	bovine liver
1,000 µg/kg	bovine kidney
300 µg/kg	bovine muscle

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.

Metabolism in target species	
1	Total radioactive residue depletion and metabolism of [^{14}C]-Monepantel following oral administration to beef cattle
2	Structural investigation of two unknown metabolites observed in liver following oral administration of [^{14}C]-Monepantel to beef cattle
Residue depletion	
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
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
Analytical methods	
5	Validation of an analytical method for the determination of monepantel sulfone in bovine fat, liver, kidney and muscle
6	Validation of an analytical method for the determination of monepantel and monepantel sulfone in bovine blood by LC-MS/MS

TIMETABLE

15. Date when data could be submitted to JECFA

December 2016

NORWAY

TEMPLATE FOR INFORMATION NECESSARY FOR PRIORITIZATION BY CCRVDF

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[1]

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:

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

- 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.

UNITED STATES

TEMPLATE FOR INFORMATION NECESSARY FOR PRIORITIZATION BY CCRVDF

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 INFORMATION[1]

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 (Quixalud) 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.

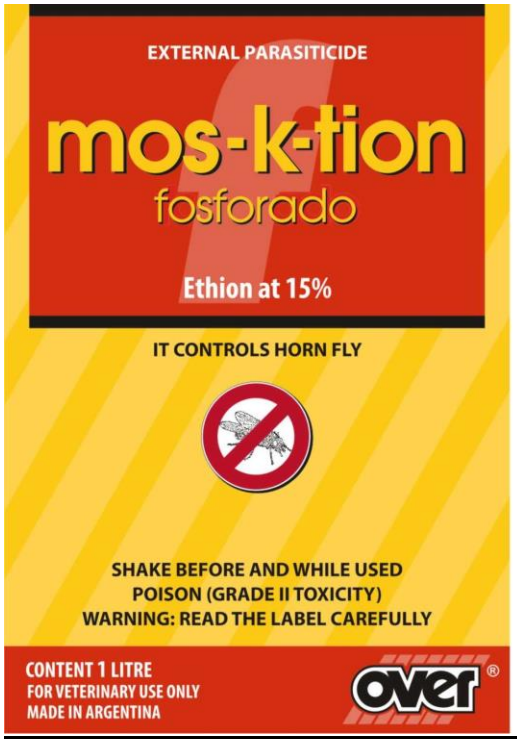
Both studies are being conducted using international protocols approved by the competent authority and under its supervision.

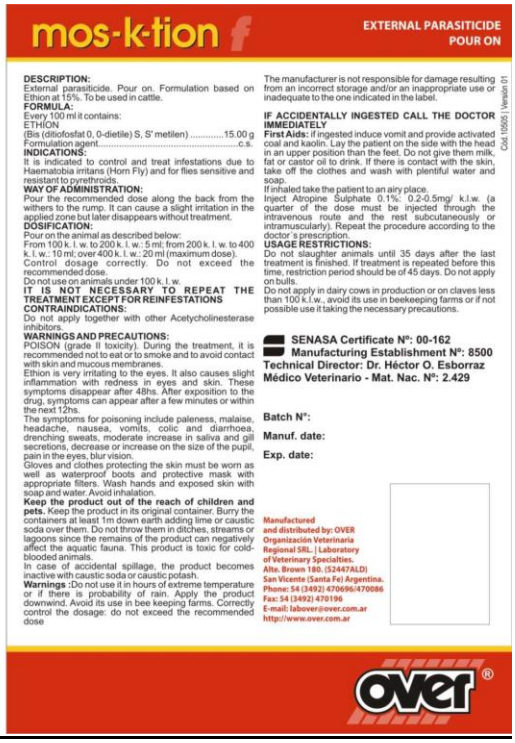
Supporting Documentation Submitted by:

Argentina, European Union, United States

ARGENTINA

ANNEX





ANNEX

ANNEX

CÓDIGO DE BARRAS: **7798156463024**

ANNEX

DISTREPBENCIL-E-T

NOVARTIS ANIMAL HEALTH

ANTIBIOTICO ESTERIL
5.000.000 U.I.

VENTA BAJO RECETA MEDICO VETERINARIO

Penicilina G sódica cristalina, penicilina G procaínica, penicilina G benzatina, estreptomicina y acetonida de triamcinolona.
Sólo para uso intramuscular en animales domésticos.
DISTREPBENCIL-E-T, es una combinación de tres tipos de penicilina con estreptomicina, y complementado con un corticoesteroide: la acetonida de triamcinolona.
Esta combinación es eficaz contra una amplia variedad de bacterias Gram positivas y Gram negativas, mientras la acetonida de triamcinolona reduce la respuesta inflamatoria de los tejidos, e inhibe una eventual reacción alérgica.
No por conocida, es oportuno destacar la acción sinérgica de la penicilina y de la estreptomicina, antibióticos que utilizados conjuntamente, superan ampliamente su actividad terapéutica, que si se utilizaran separadamente.
Por otra parte, la asociación de penicilinas, asegura rápidas y prolongadas concentraciones sanguíneas, que se mantienen durante 6 - 9 días en los bovinos, 4 - 6 días en los equinos, 5 - 7 días en los ovinos y 4 - 7 días en los porcinos.

INDICACIONES

En general, por su amplio alcance terapéutico, se recomienda su uso en el tratamiento de infecciones, en las que se desconoce el verdadero agente causal. No es menos aconsejable su utilización profiláctica, antes y después de las intervenciones quirúrgicas, realizadas por profesionales, o en relación con las habituales tareas de castración, descole, señalada, etc.
Bovinos - Neumonía bacteriana, septicemia hemorrágica, infecciones del tracto urinario, abscesos y heridas infectadas, úlcera podal (foot rot, pietín), metritis, pielonefritis, peritonitis, actinomicosis, actinobacilosis, fases iniciales del carbunclo bacteridiano sintomático y gangrena gaseosa, queratoconjuntivitis, difteria, neumoenteritis, diarreas infecciosas y leptospirosis de los terneros.
Equinos - Neumonía bacteriana, septicemia hemorrágica, abscesos y heridas infectadas, infecciones del tracto urinario, metritis, peritonitis, adenitis equina (moquillo), mal de cruz y mal de nuca (sin perjuicio del tratamiento quirúrgico), infección de las bolsas guturales, influenza, fases iniciales del tétano y carbunclo bacteridiano, conjuntivitis, queratitis, onfaloflebitis, poliartritis y diarrea blanca de los potrillos.
Ovinos y caprinos - Neumonía bacteriana, septicemia hemorrágica, colibacilosis, diarreas bacterianas, abscesos, infecciones tras la esquila, descole y castración, mastitis, metritis, infecciones del tracto urinario, foot-rot o pietín, fases iniciales del carbunclo sintomático bacteridiano, edema maligno y gangrena enfisematosa.
Porcinos - Infecciones bacterianas del tracto gastrointestinal (diarrea de los recién nacidos, de los lechones y necroenteritis), neumonía bacteriana, septicemia hemorrágica, metritis, mastitis, abscesos y heridas infectadas.

ADMINISTRACION

Deben utilizarse jeringas y agujas estériles, se extraerá el contenido total de la ampolla de solvente, que se inyectará en el frasco ampolla conteniendo la asociación de antibióticos más corticoesteroide. Se agitará vigorosamente hasta que se forme una suspensión absolutamente homogénea, momento en que estará listo para su uso.
La inyección, en las dosis correspondientes, se aplicará por vía intramuscular profunda, en la tabla del cuello o grupa de bovinos y equinos, y en el muslo de los ovinos, caprinos y porcinos.
La suspensión preparada con **DISTREPBENCIL-E-T** deberá utilizarse inmediatamente después de preparada porque el producto diluído pierde potencia. Agítese bien antes de usar.

DOSIFICACION

Bovinos, equinos, ovinos, caprinos y porcinos, 1 ml cada 24 - 33 kg. de peso vivo. La dosificación puede ajustarse, en más o menos, según criterio profesional, y si fuera necesario, puede repetirse cada 3 - 5 días.

RECOMENDACIONES

Como norma es conveniente continuar el tratamiento 24 - 48 horas después que hayan desaparecido los síntomas de la enfermedad, y se haya normalizado la temperatura. En cambio, si no ocurre mejoría manifiesta, dentro de los 3 - 4 días, será prudente rever el diagnóstico.

PRECAUCIONES

En raras ocasiones pueden ocurrir en los animales reacciones de sensibilidad a la penicilina y estreptomicina. Si se presentan tales reacciones, cuya prevención está dada por la adición de acetonida de triamcinolona, administrar de inmediato la terapia apropiada a base de epinefrina o antihistamínicos, o ambos.
Mantener fuera del alcance de los niños.

RESTRICCIONES DE USO

Los animales tratados no deben sacrificarse para su consumo durante el tratamiento y hasta después de transcurridos 30 días de la última dosis. No utilizar en vacas lecheras en lactación.

Centro Nacional de Intoxicaciones: 0800-333-0160

FORMULA

Polvo: Cada frasco ampolla contiene, penicilina G benzatina 2.500.000 U, penicilina G procaínica 1.250.000 U, penicilina G sódica cristalina 1.250.000 U, sulfato de estreptomicina equivalente a 2g de base, acetonida de triamcinolona 10 mg, citrato de sodio anhidro 37,5 mg,
Carboximetilcelulosa sódica 25 mg y Lecitina aprox. 34 mg
Solvente: Cada ampolla contiene 15 ml de agua destilada estéril.

PROPIETARIO
NOVARTIS SAÚDE ANIMAL LTDA., São Paulo - Brasil

IMPORTADO Y DISTRIBUIDO POR
NOVARTIS ARGENTINA S.A.
Ramallo 1851 (1429) - Buenos Aires - Tel.: 4703-7474; Fax: 4703-7014
Director Técnico: Dr. Pedro E. Steffan, Med. Vet. Matr. 3771 CPMV
Reg. SENASA N° 90524
AGRO IMPORT COLUMBIA SRL
Av. Capitán Arrien 140 - Santa Cruz - Bolivia - Tel.: 3362644
Resp. Técnico: Dr. Elith Guerrero Iturbe
Reg. SENASAG PUV-F N° 001029/05

Cód. 6214062-A

USO EN MEDICINA VETERINARIA

ANNEX

"2011 – Año del Trabajo Decente, la Salud y Seguridad de los Trabajadores"

Ministerio de Agricultura, Ganadería y Pesca

Servicio Nacional de Sanidad y Calidad Agroalimentaria

CERTIFICASE QUE AL PRODUCTO: "MOSKTION F" ----------

CLASIFICACION: Antiparasitario Externo / Organofosforado. ----------

DESTINADO A: Bovinos. ----------

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

EXPEDIENTE N°: 1474/2000. ----------

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 ----------

DNAPV y A
go
946

REPUBLICA ARGENTINA

Dr. HUGO ALBERTO QUEVEDO
COORDINACION DE PRODUCTOS FARMACOLOGICOS, VETERINARIOS Y ALIMENTOS PARA ANIMALES

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

ANNEX

"2016 – Año del Bicentenario de la Declaración de la Independencia Nacional"

Ministerio de Agroindustria

Servicio Nacional de Sanidad y Calidad Agroalimentaria

CERTIFICASE QUE AL PRODUCTO: "MOS-K-TION A.I."----------

CLASIFICACION: Antiparasitario Externo – Órganofosforado - Piretroide.----------

DESTINADO A: Bovinos----------

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

EXPEDIENTE Nº: 10610/02----------

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

LE HA SIDO OTORGADO POR DISPOSICION Nº: 912/03----------

DNAPV y A
MSM

EL PERMISO QUE AUTORIZA SU USO Y COMERCIALIZACION----------

CERTIFICADO Nº: 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.----------

OVER S.R.L.
ORGANIZACIÓN VETERINARIA REGIONAL

ANNEX

"2015 – Año del Bicentenario del Congreso de los Pueblos Libres"

Ministerio de Agricultura, Ganadería y Pesca

Servicio 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 Nº: 323533/12----------

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

LE HA SIDO OTORGADO POR DISPOSICION Nº: 775/15----------

EL PERMISO QUE AUTORIZA SU USO Y COMERCIALIZACION----------

CERTIFICADO Nº: 15-104----------

VALIDEZ: Hasta el 24 de Julio de 2025----------

BUENOS AIRES, 20 de Octubre de 2015----------

DNAPV y A
MSM

REPUBLICA ARGENTINA
SERVICIO NACIONAL DE SANIDAD Y CALIDAD AGROALIMENTARIA
MINISTERIO DE AGRICULTURA GANADERIA Y PESCA

Dr. HUGO ALBERTO QUEVEDO
COORDINACIÓN DE PRODUCTOS FARMACOLÓGICOS, VETERINARIOS Y ALIMENTOS PARA ANIMALES

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. ----------

ANNEX

COMPOSICIÓN
Cada 100 g contiene:

Fosfomicina Cálcica	25 g
Excipientes c.s.p.	100 g

DESCRIPCIÓN
Fosbac® contiene Fosfomicina, un antibiótico derivado del ácido fosfónico, que tiene un amplio espectro de actividad contra bacterias Gram positivas y Gram negativas.

INDICACIONES
Fosbac® es apropiado para usar en Aves Gallináceas, Pollos de engorde, Recrías livianas y pesadas para el Tratamiento de: Colibacilosis, Enfermedad respiratoria crónica, Coriza, Tifosis, Cólera aviar, Listeriosis, Infecciones estafilocócicas y enfermedades causadas por microorganismos sensibles a la fosfomicina.
Fosbac® es apropiado para usar en Cerdos para el tratamiento de: Colibacilosis, Salmonelosis, Enteritis Necrótica, Rinitis Atrófica, Streptococosis, Neumonía por *Pasteurella*, Pleuroneumonía por *Actinobacillus*, Artritis Bacteriana, Erisipelas, Cistitis, Pielonefritis, Complejo M.M.A., Disentería y otras enfermedades causadas por microorganismos sensibles a la Fosfomicina.

ADMINISTRACIÓN Y DOSIS
Administrar por vía oral, mezclado en el agua de bebida o alimento.
Aves: La dosis recomendada es: 160 mg de Fosbac® por kilogramo de peso vivo vía oral, mezclado con el agua de bebida o alimento durante 3 a 7 días, según el criterio del médico veterinario actuante.
Cerdos: De 120 a 160 mg de Fosbac® por kg de peso vivo vía oral; mezclado con el agua de bebida o alimento durante 3 a 7 días, equivalente a 3,5 - 4,5 kilogramos de Fosbac® por tonelada de alimento y a 2 - 2,8 kg de Fosbac® por cada 1000 litros de agua de bebida. Según el criterio del Veterinario actuante.

CONTRAINDICACIONES
No posee.

FOSBAC®

COMPLEJO
ANTIBIÓTICO ENERGIZANTE
DE AMPLIO ESPECTRO
POLVO SOLUBLE

Sólo Para Uso Veterinario
Venta bajo receta
FOSBAC®
es una Marca Registrada
de BEDSON® S.A.

ANTIBIOTICO

Industria Argentina

bedson

MODO DE USO
En agua de bebida: para asegurar una correcta dilución se recomienda realizar una predilución del producto a dosificar en 5 - 10 litros de agua y luego agregar al tanque de agua de bebida. En alimento: Para asegurar un correcto mezclado, se recomienda realizar una premezcla con la cantidad de producto a dosificar en 5 - 10 Kg. de alimento y luego incorporar a la mezcla final.

PRECAUCIONES
Mantener fuera del alcance de los niños.
Utilizar dentro de las 72 horas de preparadas la dilución en el agua de bebida.

RESTRICCIONES DE USO
Suspender el tratamiento 7 días antes de la faena en aves y cerdos. No administrar a ponedoras en producción de huevos destinados al consumo humano.

CONDICIONES DE ALMACENAMIENTO
Conservar entre 0° y 30°C.

LOTE N°:

FECHA DE ELABORACIÓN:

FECHA DE VENCIMIENTO:
24 meses después de la fecha de elaboración.

CONTENIDO NETO:

SENASA Cert. N° 95.399
Establecimiento Elaborador N° 8416
Centro Nacional de Intoxicaciones (Argentina): 0800-333-0160

ELABORADO Y DISTRIBUIDO POR:
BEDSON® S.A.
Director Técnico: Dr. Roberto O. Harkes. Veterinario;
Matrícula Profesional N° 7034
Ruta 8 Km. 47, La Lonja (B1635DIK) Pilar, Bs. As., Argentina.
Teléfonos: desde exterior (54) 230-4470249 / 4470250
Local: 0230-4470249 / 4470250 Fax: (54) 230-4470453
bedson@bedson.com
www.bedson.com

CÓDIGO: EA001ARG/2

EUROPEAN UNION

ANNEX

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 ectoparasiticide 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

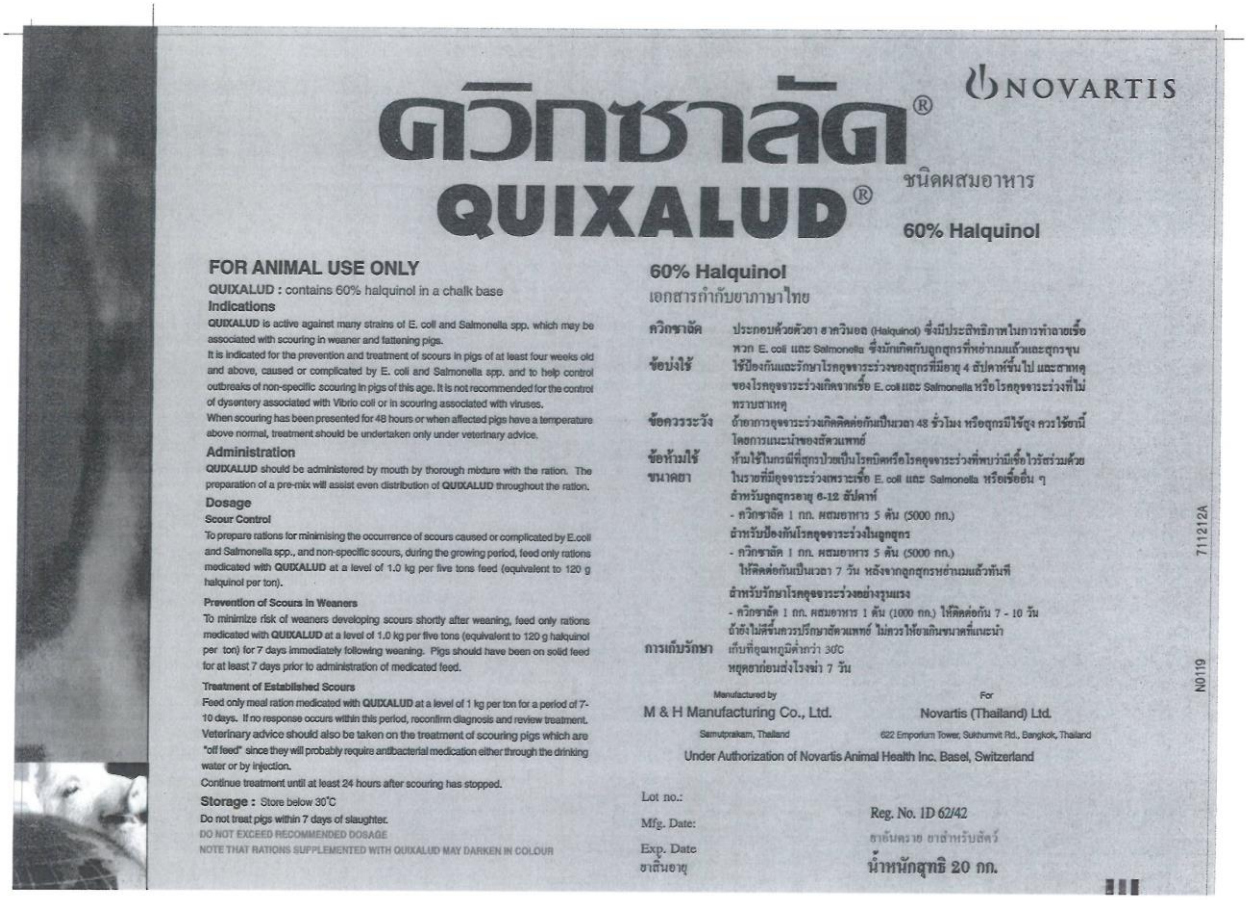
D. Assessment

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.

UNITED STATES OF AMERICA

ANNEX



ควิกซาลัด®
QUIXALUD®
NOVARTIS
ชนิดผสมอาหาร
60% Halquinol

FOR ANIMAL USE ONLY

QUIXALUD : contains 60% halquinol in a chalk base

Indications

QUIXALUD is active against many strains of E. coli and Salmonella spp. which may be associated with scouring in weaner and fattening pigs.
It is indicated for the prevention and treatment of scours in pigs of at least four weeks old and above, caused or complicated by E. coli and Salmonella spp. and to help control outbreaks of non-specific scouring in pigs of this age. It is not recommended for the control of dysentery associated with Vibrio coli or in scouring associated with viruses.
When scouring has been presented for 48 hours or when affected pigs have a temperature above normal, treatment should be undertaken only under veterinary advice.

Administration

QUIXALUD should be administered by mouth by thorough mixture with the ration. The preparation of a pre-mix will assist even distribution of **QUIXALUD** throughout the ration.

Dosage

Scour Control

To prepare rations for minimising the occurrence of scours caused or complicated by E.coli and Salmonella spp., and non-specific scours, during the growing period, feed only rations medicated with **QUIXALUD** at a level of 1.0 kg per five tons feed (equivalent to 120 g halquinol per ton).

Prevention of Scours in Weaners

To minimize risk of weaners developing scours shortly after weaning, feed only rations medicated with **QUIXALUD** at a level of 1.0 kg per five tons (equivalent to 120 g halquinol per ton) for 7 days immediately following weaning. Pigs should have been on solid feed for at least 7 days prior to administration of medicated feed.

Treatment of Established Scours

Feed only meal ration medicated with **QUIXALUD** at a level of 1 kg per ton for a period of 7-10 days. If no response occurs within this period, reconfirm diagnosis and review treatment. Veterinary advice should also be taken on the treatment of scouring pigs which are "off feed" since they will probably require antibacterial medication either through the drinking water or by injection.

Continue treatment until at least 24 hours after scouring has stopped.

Storage : Store below 30°C

Do not treat pigs within 7 days of slaughter.

DO NOT EXCEED RECOMMENDED DOSAGE

NOTE THAT RATIONS SUPPLEMENTED WITH QUIXALUD MAY DARKEN IN COLOUR

60% Halquinol

เอกสารกำกับยาภาษาไทย

ควิกซาลัด	ประกอบด้วยตัวยา ฮาลวินอล (Halquinol) ซึ่งมีประสิทธิภาพในการทำลายเชื้อ พวก E. coli และ Salmonella ซึ่งมักเกิดกับลูกสุกรที่หย่านมแล้วและสุกรขุน
ข้อบ่งใช้	ใช้ป้องกันและรักษาโรคอุจจาระร่วงของสุกรที่มีอายุ 4 สัปดาห์ขึ้นไป และสาเหตุของโรคอุจจาระร่วงเกิดจากเชื้อ E. coli และ Salmonella หรือโรคอุจจาระร่วงที่ไม่ทราบสาเหตุ
ข้อควรระวัง	ถ้าอาการอุจจาระร่วงเกิดติดต่อกันเป็นเวลา 48 ชั่วโมง หรือสุกรมีไข้สูง ควรใช้ยานี้โดยการแนะนำของสัตวแพทย์
ข้อห้ามใช้	ห้ามใช้ในกรณีที่สุกรป่วยเป็นโรคบิดหรือโรคอุจจาระร่วงที่พบว่ามีเชื้อไวรัสร่วมด้วย
ขนาดยา	ในรายที่มีอุจจาระร่วงเพราะเชื้อ E. coli และ Salmonella หรือเชื้ออื่น ๆ สำหรับลูกสุกรอายุ 6-12 สัปดาห์ - ควิกซาลัด 1 กก. ผสมอาหาร 5 ตัน (5000 กก.) สำหรับป้องกันโรคอุจจาระร่วงในลูกสุกร - ควิกซาลัด 1 กก. ผสมอาหาร 5 ตัน (5000 กก.) ให้ติดต่อกันเป็นเวลา 7 วัน หลังจากลูกสุกรหย่านมแล้วทันที สำหรับรักษาโรคอุจจาระร่วงอย่างรุนแรง - ควิกซาลัด 1 กก. ผสมอาหาร 1 ตัน (1000 กก.) ให้ติดต่อกัน 7 - 10 วัน ถ้ายังไม่ดีขึ้นควรปรึกษาสัตวแพทย์ ไม่ควรให้ยาผสมอาหารพื้นหย่า
การเก็บรักษา	เก็บที่อุณหภูมิต่ำกว่า 30°C หยุดยาก่อนส่งโรงฆ่า 7 วัน

Manufactured by
M & H Manufacturing Co., Ltd.
Samutprakarn, Thailand

For
Novartis (Thailand) Ltd.
622 Emporium Tower, Sukhumvit Rd., Bangkok, Thailand

Under Authorization of Novartis Animal Health Inc. Basel, Switzerland

Lot no.:
Mfg. Date:
Exp. Date
ยาสิ้นอายุ

Reg. No. 1D 62/42
ยาสัตวราย ยาสำหรับสัตว์
น้ำหนักสุทธิ 20 กก.

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