Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

**PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



[IODIGUARD]

Product type [3]

[Iodine (including PVP-iodine) as included in the Union list of approved active substances]

Case Number in R4BP: [BC-FA019472-65]

Evaluating Competent Authority: [FR]

Date: [19/07/2018]

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# CONCLUSION

**Conclusion on physico-chemical properties**

The formulation IODIGUARD is an Another Liquid (AL) formulation, ready-to-use preparation. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable. The appearance of the product is that of brown liquid. It is not explosive and has no oxidizing properties. The product is not considered as flammable.

The stability of IODIGUARD was not demonstrated after 8 weeks at 40°C. However, a mitigation measure is proposed by applicant: do not store above 25°C.

A shelf life study of 1 year is proposed by the applicant. However, the total iodine content decreased strongly after 1 year (-34%). Therefore, to set a shelf life, data on efficacy and degradation substance must be available.

Efficacy is demonstrated at 0.075% (equivalent to a degradation of 50% of AS), however explanations on the fate of iodine over time in the biocidal product are not available.

These explanations (or tests of all form of iodine on the batch after storage) are expecting in post authorisation in a 3 months delay.

Its technical characteristics are acceptable for an AL formulation.

Analytical method for the determination of the active substance in the biocidal product was provided and validated.

**Conclusion on efficacy**

The product IODIGUARD, as a ready to use concentrate used after milking, by dipping, with a contact time of 5 minutes, has shown a sufficient efficacy in phase 2, step 1 tests against bacteria and yeasts.

Taking into account European discussions at WG III2017, in the frame of early WG discussion on Union authorisation applications based on iodine/PVP-iodine, field study submitted showed statistically the efficacy of the product IODIGUARD with regards to a formulation without iodine. Moreover according to the literature review, the iodine level of the product IODIGUARD supports a sufficient efficacy for teats disinfection.

The authorization holder has to report any observed resistance incidents to the Competent Authorities (CA) or other appointed bodies involved in resistance management.

**Conclusion on human health**

The risk during mixing and cleaning is acceptable with gloves during cleaning of teats and equipment for professionals for primary exposure. Secondary exposure is covered by primary exposure.

**Conclusion on indirect exposure via residues in food**

Considering the intended use of IODIGUARD and based on overall available information, a risk via food cannot be excluded for children. The estimation of iodine contamination in milk is performed considering the worst case situation. Human health risk is acceptable for all milking applications based on estimated intakes, except for toddlers, where total daily intake considerably exceeds the UL. Iodine from toddler dietary intake, arising from every other source except from iodine containing teat disinfection product residues, takes up almost the whole fraction of the UL if current EU data is used. It highlights the importance to obtain more reliable information on iodine background levels in food items in the EU, and consequently to update the data supporting the current UL. Iodine exposure pathways that are not a consequence of biocidal use are outside the remit of the BPC. Where unacceptable risks are identified as a result of consideration of total dietary intake of iodine in addition to exposure arising from biocidal use, a risk management decision cannot be taken in isolation with respect to the biocides use only. It would be advisable that this issue is addressed at European level in order to ensure that all relevant regulatory bodies can be involved in agreeing a way forward. So for the background levels, all sources of iodine, and not just those arising from teat treatments would need to be taken into consideration. Therefore a wider approach to the consumer risk assessments encompassing different regulatory areas would need to be considered.

**Conclusion on ecotoxicology and environment**

The levels of exposure to iodine for the non-target organisms of the aquatic (STP and surface water) and terrestrial compartments following the use of the product IODIGUARD on teats are lower than the threshold values or still in the range of the background level for each compartment under the use conditions provided in the SPC.

The predicted concentrations of iodine in groundwater are higher than the threshold values of 0.1 µg/L provided in the Drinking Water Directive 98/83/EC, but still in the range of the background level of iodine considered acceptable under the use conditions provided in the SPC.

**General conclusion**

FR CA considers that the product shall be authorised against bacteria and yeasts, by professional users by manual non-medical teat disinfection for cows, ewes and goats in post-milking.

# ASSESSMENT REPORT

## Summary of the product assessment

### Administrative information

#### Identifier of the product

| **Identifier[[1]](#footnote-1)** | **Country (if relevant)** |
| --- | --- |
| IODIGUARD |  |

#### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | Centre Technique d’hygiène |
| **Address** | 128 avenue chateau fleury  26104 Romans sur Isère  France |
| **Authorisation number** | **FR-2018-0056** | |
| **Date of the authorisation** | **20/08/2018** | |
| **Expiry date of the authorisation** | **19/08/2028** | |

#### Manufacturer of the product

|  |  |
| --- | --- |
| **Name of manufacturer** | Centre technique d'hygiène |
| **Address of manufacturer** | 128 avenue chateau fleury  26100 Romans sur Isère  France |
| **Location of manufacturing sites** | Zone des chasses  26100 Romans sur Isère  France |

#### Manufacturers of the active substance

|  |  |
| --- | --- |
| **Active substance** | PVPI solution 10% |

|  |  |
| --- | --- |
| **Name of the manufacturer 1** | Ashland Services BV |
| **Address of the manufacturer** | Algorta Norte,  Av. El Golf 99 Of 703, Santiago, Las Condes, Chile (Algorta Mine, Chile) |
| **Location of manufacturing sites:** | Algorta Norte, Av El Golf 99 Of  703 Las Condes, Santiago, Chile |

Algorta Norte is a manufacturer of owner data Ashland Services BV in Technical Equivalence (T.E. asset num. EU-0012442-0000) and Ashland Services BV is in Article 95 List.

|  |  |
| --- | --- |
| **Name of the manufacturer 2** | SQM Europe N.V. Belgium |
| **Address of the manufacturer** | Bladgen Speciality Chemicals Ltd  Osprey House  Black Eagle Square  Westerham  TN16 1 PA Kent  United-Kingdom |
| **Location of manufacturing sites:** | Los militares 4290,  Las Condes Santiago,  Chile |

SQM Europe N.V. Belgium is in Article 95 List.

|  |  |
| --- | --- |
| **Name of the manufacturer 3** | Alcoholes Montplet, S.A |
| **Address of the manufacturer** | American Iodine Company Inc.  3120 Golden Springs Drive  Plano TX 75025  USA |
| **Location of manufacturing sites 1:** | Cosayach S.A. Compania de Salitre y Yodo –  Amunategui 178,  Santiago,  Chile |
| **Location of manufacturing sites 2:** | ACF Minera SA,  Serrano 498,  Iquique,  Chile |

|  |  |
| --- | --- |
| **Name of the manufacturer 4** | Alcoholes Montplet, S.A |
| **Address of the manufacturer** | Norkem Limited  Bexton Lane, Knutsford  Cheshire, WA 16 9FB  United-Kingdom |
| **Location of manufacturing sites 1:** | Cosayach S.A. Compania de Salitre y Yodo –  Amunategui 178,  Santiago,  Chile |
| **Location of manufacturing sites 2:** | ACF Minera SA,  Serrano 498,  Iquique,  Chile |

|  |  |
| --- | --- |
| **Name of the manufacturer 5** | Alcoholes Montplet, S.A |
| **Address of the manufacturer** | Pantheon European Office  Norkem Limited  Julianalaan 11  3708 BA Zeist  The Netherlands |
| **Location of manufacturing sites 1:** | Cosayach S.A. Compania de Salitre y Yodo –  Amunategui 178,  Santiago,  Chile |
| **Location of manufacturing sites 2:** | ACF Minera SA,  Serrano 498,  Iquique,  Chile |

|  |  |
| --- | --- |
| **Name of the manufacturer 6** | Alcoholes Montplet, S.A |
| **Address of the manufacturer** | Independent Iodine Company NV  Hortensiadreef 40  2920 Kalmthout  Belgium |
| **Location of manufacturing sites 1:** | Cosayach S.A. Compania de Salitre y Yodo –  Amunategui 178,  Santiago,  Chile |
| **Location of manufacturing sites 2:** | ACF Minera SA,  Serrano 498,  Iquique,  Chile |

Manufacturers from 3 to 6, is not clear for each one the location of manufacturing site, but the owner data is Alcoholes Montplet, SA who is included in Article 95 List.

### Product composition and formulation

NB: the full composition of the product according to Annex III Title 1 should be provided in the confidential annex.

Does the product have the same identity and composition as the product evaluated in connection with the approval for listing of the active substance(s) on the Union list of approved active substances under Regulation No. 528/2012?

Yes

No

#### Identity of the active substance

|  |  |
| --- | --- |
| **Main constituent(s)** | |
| **ISO name** | PVP-Iodine |
| **IUPAC or EC name** | 2-Pyrrolidinone, 1-ethenyl-, homopolymer, compd. with iodine |
| **EC number** |  |
| **CAS number** | PVP-iodine used as carrier for iodine in biocidal formulations: 25655-41-8 |
| **Index number in Annex VI of CLP** |  |
| **Minimum purity / content** | 10% v/v  (995g/kg for iodine) |
| **Structural formula** |  |

#### Candidate(s) for substitution

The active substance contained in the biocidal product is not candidate for substitution in accordance with Article 10 of BPR.

#### Qualitative and quantitative information on the composition of the biocidal product

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| --- | --- | --- | --- | --- | --- |
| PVP iodine\* | PVP iodine | *Active substance* | 25655-41-8 | Not assigned | 1.50 |
| *Min. Iodine technical* | Iodine |  | *7553-56-2* | *231-442-4* | *0.137* |

*\* Concept of pure /technical is not applicable to PVP iodine as it is a mixture.*

#### Information on technical equivalence

*Not relevant.*

#### Information on the substance(s) of concern

One co-formulant, benzene sulfonic acid, is classified H412. Hence, it shall be considered whether it is a substance of concern in the formulation.

According to the appendix 1 of the Transitional Guidance on mixture toxicity assessment for biocidal products for the environment, the calculation of the relative toxic units of compounds shows that the toxicity of product is principally linked (more than 95%) to the toxicity of iodine compounds. So, the benzene sulfonic acid is not considered as substance of concern in this formulation.

#### Type of formulation

|  |
| --- |
| Another Liquid (AL) formulation, ready-to-use preparation |

### Hazard and precautionary statements

**Classification and labelling of the product according to the Regulation (EC) 1272/2008**

|  |  |
| --- | --- |
| **Classification** | |
| Hazard category | Aquatic chronic cat 3 |
| Hazard statement | H412: Harmful to aquatic life with long-lasting effects |
|  | |
| **Labelling** | |
| Signal words | - |
| Hazard statements | H412: Harmful to aquatic life with long-lasting effects |
| Precautionary statements | P273: Avoid release to the environment  P501: Dispose of contents/container in accordance with local/ regional/national/international regulation (to be specified). |
|  | |
| Note | **-** |

### Authorised use(s)

#### Use description

Table 1. Use # 1 – Teat disinfection

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfection in post milking |
| **Target organism (including development stage)** | Bacteria and Yeasts |
| **Field of use** | Indoor |
| **Application method(s)** | Manual non-medical teat disinfection for cows, ewes and goats in post-milking.  Dip treatment |
| **Application rate(s) and frequency** | Ready to use  2 mL per teat  2 x/day, each day  Contact time : 5 minutes |
| **Category(ies) of users** | Professional users |
| **Pack sizes and packaging material** | The product IODIGUARD is packaged in jerry cans HDPE containers of 20 L and HDPE barrels of 60 L and 220 L. |

#### Use-specific instructions for use

|  |
| --- |
| * Wear gloves during the cleaning of the teats and equipment. |

#### Use-specific risk mitigation measures

|  |
| --- |
| - |

#### Where specific to the use, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| - |

#### Where specific to the use, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| - |

#### Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| - |

### General directions for use

#### Instructions for use

|  |
| --- |
| * Always read the label or leaflet before use and follow all the instructions provided. * Respect the conditions of use of the product (concentration, contact time, temperature, pH, etc.) * The product must be brought to a temperature above 20°C before use. * Leave the product until next milking. Keep the cows standing until the product has dried (at least 5 minutes). * Inform the registration holder if the treatment is ineffective. |

#### Risk mitigation measures

|  |
| --- |
| - |

#### Particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| * Eye contact: Immediately flush with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses if easy to do. Continue to rinse with warm water for at least 10 minutes. Get medical attention if irritation or vision impairment occurs. * Skin contact: Remove contaminated clothing and shoes. Wash contaminated skin with soap and water. Contact poison treatment specialist if symptoms occur. * Ingestion: Wash out mouth with water. Contact poison treatment specialist. Seek medical advice immediately if symptoms occur and/or large quantities have been ingested. * Inhalation: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Seek medical advice immediately if symptoms occur and/or large quantities have been inhaled. * In case of impaired consciousness place in recovery position and seek medical advice immediately. Do not give fluids or induce vomiting. * Keep the container or label available. |

#### Instructions for safe disposal of the product and its packaging

|  |
| --- |
| * Do not discharge unused product on the ground, into water courses, into pipes (sink, toilets…) nor down the drains. Do not discharge unused product in fields, nor outdoor environment. * Dispose of unused product, its packaging and all other waste in accordance with local regulations. |

#### Conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| * Protect from frost. * Store in a dry, cool and ventilated place. * Do not store at a temperature above 25°C. * Do not store more than 12 months. * Protect the product form direct sunlight. |

### Other information

|  |
| --- |
| * The product contains pyrrolidones derivatives. Do not use in case of known hypersensitivity. * Explanation on the fate of iodine in the biocidal product during storage (or test of all forms of iodine on the batch after storage) is requested in post authorization in a 3 months delay. |

### Packaging of the biocidal product

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of packaging** | **Size/volume of the packaging** | **Material of the packaging** | **Type and material of closure(s)** | **Intended user (e.g. professional, non-professional)** | **Compatibility of the product with the proposed packaging materials (Yes/No)** |
| Cans | 20 L | Opaque HDPE | Hermetically closed | Professional | Yes |
| Barrels | 60 L  220 L | Opaque HDPE | Hermetically closed | Professional | Yes |

### Documentation

#### Data submitted in relation to product application

**Identity, physicochemical and analytical method data**

Physico-chemical properties studies and analytical methods on the biocidal product IODIGUARD were provided by *Centre Technique d’Hygiène*. See the annex 3.1.

**Efficacy data**

Efficacy studies on the biocidal product were provided:

* For bacteria :
* Laboratory studies according to EN 1656 standard (phase 2, step 1)
* Field test according to the methodology of EN 1499 standard (phase 2, step 2)
* For yeasts:
* Laboratory study according to EN 1657 standard (phase 2, step 1).

See the annex 3.1

**Toxicology data**

Bovine Corneal Opacity and Permeability (BCOP) Assay was conducted for the product IODIGUARD for eye irritation properties. See the annex 3.1.

**Residues data**

No specific residue data were submitted in the context of this dossier.

**Ecotoxicology data**

No ecotoxicology studies were submitted in the context of this dossier.

#### Access to documentation

*Centre Technique d’Hygiène* has access to analytical methods on the active substance Iodine with a Letter of Access of *Alcoholes Montplet, one of applicants of the active substance iodine*.

## Assessment of the biocidal product

### Intended use(s) as applied for by the applicant

Table 1. Intended use # 1 – Teat disinfection

|  |  |
| --- | --- |
| Product Type(s) | 3 |
| Where relevant, an exact description of the authorised use |  |
| Target organism (including development stage) | Bacteria and yeasts. |
| Field of use | Indoor |
| Application method(s) | Manual non-medical teat disinfection for cows, ewe and goats.  Dip treatment |
| Application rate(s) and frequency | 2 ml per teat  2 x/day, each day |
| Category(ies) of user(s) | Professional users |
| Pack sizes and packaging material | The product IODIGUARD is packaged in jerry cans HDPE containers of 20 L, 60 L and 220 L. |

### Physical, chemical and technical properties

The biocidal product is a ready-to-use formulation.

The product does not contain hydrocarbons or H304 co-formulant content ≥10%.

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **GLP** | **Reference** | **Comments** |
| --- | --- | --- | --- | --- | --- | --- |
| Physical state at 20 °C and 101.3 kPa | Visual method | IODIGUARD  Batch 26230415001 | Viscous brown opaque liquid | Y | A.J. Wooley, 2015  Report N°41500716 | Acceptable |
| Colour at 20 °C and 101.3 kPa |
| Acidity / alkalinity and pH | CIPAC MT 75 | IODIGUARD  Batch 26230415001 | pH at 25°C (1% aqueous dispersion) : 4.32  Neat pH at 25°C : 4.02 | Y | A.J. Wooley, 2015  Report N°41500716 | Acceptable |
| Relative density / bulk density | EC A3 | IODIGUARD  Batch 26230415001 | D420 = 1.03 | Y | A.J. Wooley, 2015  Report N°41500717 | Acceptable |
| Storage stability test – **accelerated storage** | CIPAC MT 75  OECD 114  EC A5  Titrimetric quantification of total iodine: « dosage de l’iode actif” | IODIGUARD  Batch 26230415001 | |  |  |  | | --- | --- | --- | |  | **Initial** | **8 weeks at 40°C in glass bottle** | | **Active ingredient content** (total active iodine) | 0.132% w/w | 0.071% w/w  (-46%) | | **Appearance** | Brown opaque liquid.  250 mL amber glass bottle with a white, opaque, plastic screw on lid with an orange plastic tamper proof seal. No signs of corrosion or degradation.  0.006% of weight packaging gain | | | **pH at 25°C**  Neat  1% aqueous dilution | 4.02  4.32 | 3.71  4.04 | | **Acidity/Alkalinity** (%H2SO4) | - | 0.127% w/w | | **Viscosity at 20°C (mPa.s)**  Shear rate:  0.102 s-1  0.238 s-1  0.510 s-1  1.02 s-1  2.55 s-1 | 3.18 x 104  1.72 x 104  9.96 x 103  6.10 x 103  3.29 x 103 | 3.69 x 104  1.97 x 104  1.09 x 104  6.36 x 103  3.13 x 103 | | **Viscosity at 40°C (mPa.s)**  Shear rate:  2.55 s-1  5.10 s-1  10.2 s-1  25.5 s-1  51.0 s-1 | 379  288  238  197  182 | 444  315  244  199  182 | | **Surface tension (1g/L)** | 63.7 to 64.0 mN/m | 64.1 to 64.2 mN/m | | Y | A.J. Wooley, 2015  Report N°41500716 | The stability of Iodiguard was not demonstrated after 8 weeks at 40°C.  However, a mitigation measure is proposed by applicant: do not store above 25°C.  As a shelf life study is available, no more data required. |
| Storage stability test – **long term storage at ambient temperature** | CIPAC MT 75  OECD 114  EC A5  EC A3  Titrimetric quantification of total iodine: « dosage de l’iode actif” | IODIGUARD  Batch 26230415001 | |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | **Initial** | **After 6 months** | **After 1 year in opaque HDPE** | **After 18 months in opaque HDPE** | | **Active ingredient content** (total active iodine) | 0.132% w/w | 0.106% w/w (-20%) | 0.087% w/w  (-34%) | 0.0053 % w/w (-96%) | | **Appearance** | Brown opaque liquid.  20 kg black, opaque, plastic (HDPE) with an opaque orange screw on lid and an opaque orange plastic tamper proof seal. The container has two large manufacturers’ labels on. No signs of corrosion, degradation or seepage. <0.06% of weight packaging change | | | | | **D420** | 1.03 |  | - |  | | **pH at 25°C**  Neat  1% aqueous dilution | 4.02  4.32 | 3.90  4.26 | 3.90  4.41 | 3.67  4.21 | | **Acidity/Alkalinity** (%H2SO4) | - | 0.109 w/w | 0.109% w/w | 0.134% | | Y | A.J. Wooley, 2015  Report N°41500717 | A shelf life study of 1 year is proposed by the applicant.  The total iodine content decreased strongly after 1 year (-34%). Therefore, to set a shelf life, data on efficacy and degradation substance must be available.  Efficacy isdemonstrated at 0.075% (equivalent to a degradation of 50% of AS), however explanations on the fate of iodine over time in the biocidal product are not available. These explanations (or tests of all form of iodine on the batch after storage) are expecting in post authorisation in a 3 months delay. |
| Storage stability test – **low temperature stability test for liquids** |  |  |  |  |  | This study is not needed because mention is made on the label not to store under 0°C (see the label attached in the IUCLID file). |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** |  |  | The active substance is light sensitive but the packaging is an opaque HDPE can. |  |  | Protect from direct sunlight |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** |  |  | Not required |  |  |  |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** |  |  | See ”Storage stability test – **long term storage at ambient temperature”** |  |  |  |
| Wettability |  |  | Not relevant |  |  |  |
| Suspensibility, spontaneity and dispersion stability |  |  | Not relevant |  |  |  |
| Wet sieve analysis and dry sieve test |  |  | Not relevant |  |  |  |
| Emulsifiability, re-emulsifiability and emulsion stability |  |  | Not relevant |  |  |  |
| Disintegration time |  |  | Not relevant |  |  |  |
| Particle size distribution, content of dust/fines, attrition, friability |  |  | Not relevant |  |  |  |
| Persistent foaming |  |  | Not relevant |  |  |  |
| Flowability/Pourability/Dustability |  |  | Not relevant |  |  |  |
| Burning rate — smoke generators |  |  | Not relevant |  |  |  |
| Burning completeness — smoke generators |  |  | Not relevant |  |  |  |
| Composition of smoke — smoke generators |  |  | Not relevant |  |  |  |
| Spraying pattern — aerosols |  |  | Not relevant |  |  |  |
| Physical compatibility |  |  | Not relevant |  |  |  |
| Chemical compatibility |  |  | Not relevant |  |  |  |
| Degree of dissolution and dilution stability |  |  | Not relevant |  |  |  |
| Surface tension | EC A5 | IODIGUARD  Batch 26230415001 | 63.7 to 64.0 mN/m (1g/L) | Y | A.J. Wooley, 2015  Report N°41500716 | Acceptable  Not surface active product. |
| Viscosity | OECD 114 | IODIGUARD  Batch 26230415001 | |  |  | | --- | --- | | **Viscosity at 20°C (mPa.s)**  Shear rate:  0.102 s-1  0.238 s-1  0.510 s-1  1.02 s-1  2.55 s-1 | 3.18 x 104  1.72 x 104  9.96 x 103  6.10 x 103  3.29 x 103 | | **Viscosity at 40°C (mPa.s)**  Shear rate:  2.55 s-1  5.10 s-1  10.2 s-1  25.5 s-1  51.0 s-1 | 379  288  238  197  182 | | Y | A.J. Wooley, 2015  Report N°41500716 | Acceptable |

### Physical hazards and respective characteristics

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **GLP** | **Reference** | **Comments** |
| --- | --- | --- | --- | --- | --- | --- |
| Explosives |  |  | Waived on the basis of the classification (see justification and manual classification according to annex I of CLP in sections 12 and 13). See details in confidential part. |  |  | Acceptable |
| Flammable gases |  |  | Not relevant |  |  |  |
| Flammable aerosols |  |  | Not relevant |  |  |  |
| Oxidising gases |  |  | Not relevant |  |  |  |
| Gases under pressure |  |  | Not relevant |  |  |  |
| Flammable liquids |  |  | Waived on the basis of the classification (see justification and manual classification according to annex I of CLP in sections 12 and 13). See details in confidential part. |  |  | Acceptable |
| Flammable solids |  |  | Not relevant |  |  |  |
| Self-reactive substances and mixtures |  |  | Waived on the basis of the classification (see justification and manual classification according to annex I of CLP in sections 12 and 13). See details in confidential part. |  |  | Acceptable |
| Pyrophoric liquids |  |  | Not relevant |  |  |  |
| Pyrophoric solids |  |  | Not relevant |  |  |  |
| Self-heating substances and mixtures |  |  | Not relevant |  |  |  |
| Substances and mixtures which in contact with water emit flammable gases |  |  | Not relevant |  |  |  |
| Oxidising liquids |  |  | Waived on the basis of the classification (see justification and manual classification according to annex I of CLP in sections 12 and 13). See details in confidential part. |  |  | Acceptable |
| Oxidising solids |  |  | Not relevant |  |  |  |
| Organic peroxides |  |  | Not relevant |  |  |  |
| Corrosive to metals | Section 37.4 of UN-MTC according to CLP regulation | IODIGUARD - LOT 16001693 | Mass loss of specimens after 7 days exposure times for aluminum specimen: 0,4% (<13.7%)  Mass loss of specimens after 7 days exposure times for steel specimen: 1,1% (<13.7%) | N | Conte E., 2016 | Acceptable  The product is not classified H290 cat 1 metal corrosive according to CLP regulation. |
| Auto-ignition temperatures of products (liquids and gases) |  |  | Waived on the basis of the classification (see justification and manual classification according to annex I of CLP in sections 12 and 13). See details in confidential part. |  |  | Acceptable |
| Relative self-ignition temperature for solids |  |  | Not relevant |  |  |  |
| Dust explosion hazard |  |  | Not relevant |  |  |  |

|  |
| --- |
| **Conclusion on the physical hazards and respective characteristics of the product** |
| The formulation IODIGUARD is an Another Liquid (AL) formulation, ready-to-use preparation. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable. The appearance of the product is that of brown liquid. It is not explosive and has no oxidizing properties. The product is not considered as flammable.  The stability of IODIGUARD was not demonstrated after 8 weeks at 40°C. However, a mitigation measure is proposed by applicant: do not store above 25°C.  A shelf life study of 1 year is proposed by the applicant. However, The total iodine content decreased strongly after 1 year (-34%). Therefore, to set a shelf life, data on efficacy and degradation substance must be available.  Efficacy isdemonstrated at 0.075% (equivalent to a degradation of 50% of AS), however explanations on the fate of iodine over time in the biocidal product are not available.  These explanations (or tests of all form of iodine on the batch after storage) are expecting in post authorisation in a 3 months delay..  Its technical characteristics are acceptable for an AL formulation.  **Implication concerning labelling for the product:**  Protect from frost.  Do not store at a temperature above 25°C.  Store in a dry, cool and ventilated place.  Do not store more than 12 months.  Protect from direct sunlight. |

### Methods for detection and identification

**Physico-chemical properties and Analytical method for determination of active ingredient and impurities in the technical active ingredient**

Physical and chemical properties of the active substance and analytical methods for determination of active ingredient in the technical active ingredient have already been evaluated at EU level and are presented in the CAR of the active substance iodine (2013). The applicant Centre Technique d’Hygiène of the biocidal product IODIGUARD is not the applicant of the active substance and that supported the annex I inclusion dossier of the active substance but has a letter of access to these data.

**This analytical method is based on European Pharmacopoeia and provided in the CAR of the active substance for determining the active substance (total available Iodine) and relevant component in the biocidal product.**

|  |  |
| --- | --- |
| **Report:** | Morel A., 2015 |
| Title: | Dosage de l’iode actif |
| Document No | - |
| Test facility | Laboratoire Solutio  BP 147 – Les Chasses – 26104 Romans - FRANCE |
| Guidelines: | - |
| GLP | No |

**According to European Pharmacopoeia, the active iodine is defined as the total of iodine substance (I2), free and complexed with the PVP.**

**Preparation of accuracy samples:**

Weight 10g of IODIGUARD solution in a beaker. Added 100mL of distilled water and a magnet bar.

The determination of iodine is performed by a redox titration with sodium thiosulfate. The equation is:

**I2 (aq) + 2 S2O32- (aq) = S4O62- (aq) + 2 I- (aq)**

**Validation of the analytical method:**

|  |  |  |
| --- | --- | --- |
| Specificity | To demonstrate that the quantification of iodine is not affected by other co-formulants present in the biocidal product, a blank (product without iodine) was quantify.  No interference was found in the blank sample. | |
| Linearity | 11 samples were injected, covered the range from 0.00 to 20.0 g/L of PVPi (corresponding to 0.00 to 2020 ppm of active iodine)  R²=0.9959, Y=104.32X-41.136 | |
| Precision | Repeatability was evaluated with 10 independent determinations of the formulated product, no outlier. | |
| Compound | Repeatability (RSD) |
| Iodine | RSD = 0.6% < 3.63% (RSD calculated with modified equation of Horwitz) |
| Accuracy | Accuracy was determined by analysis of 10 independent determinations in which known amounts of the reference substance were added to a blank formulation. The accuracy results are expressed as the recovery rate. | |
| Compound | Accuracy (recovery ) |
| Iodine | 100.0% |

**Analytical methods for determining relevant components and/or residues in different matrices**

| **Matrix** | **Test substance** | | **Analytical method** | **Fortification range / Number of measurements** | **Linearity** | **Specificity** | **Recovery rate (%)** | | | | **Limit of quantification / detection (LOQ / LOD)** | **LOQ required** | **Acceptance** | **Reference** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Range | Mean | | St. dev. |
| Soil | iodide and iodate are determined as a sum value, which is reported as iodine equivalents | | ICP-MS | Not reported | 200 – 500 µg/L | Yes | Not reported | | | | Quoted LOD = 0.01µg I /L (relates to the water extract of the soil) | 0.05 mg/kg\* | Not acceptable as no supporitng validation data is provided. No method required due to low PECs in comparison to natural background levels | J. Popke et al. (1997), Doc. No. 492-009; A4.2a/01  P. Schramel (1997), Doc. No. 492-008; A4.2a/02 |
| iodine | | Sandel-Kolthoff methodology  Photometric determination | 5 – 1000 mg/kg moist soil / 5 replicates for natural soil, 3 replicates for artifical soil | 0.1 – 0.5 µg iodine | Yes | Natural soil:  72.9 – 100%  Artificial soil:  74.5 – 93% | | Natural soil: 86.3%  Artificial soil: 86.2% | Natural soil:  5.9 - 10.0%  Artificial soil:  3.1 and 7.5% | LOD = 5 mg /kg dry soil | 0.05 mg/kg\* | Not acceptable for monitoring due to the use of carcinogenic substance (As2O3)  No method required due to low PECs in comparison to natural background levels | Knoch, E. (2009), Doc. No. 434-001, A4.2a/03 |
| iodide and iodate are determined as a sum value, which is reported as iodine | | ICP-MS | 22.4-36.2 mg/kg of iodine, 2 soils 2 replicates  5 replicate analyses of 4 soils with certified iodine content (1.9-19.3 mg/kg) | 5-50 µg iodine/L (iodine/indium ratio of 0.05-0.5) | Yes | 92-105% for fortified samples. Good agreement with certified levels | | - | 0-2.7% | LOD = 0.02 µg/L (refers to the water extract)  LOQ at least 0.7 mg/kg | 0.05 mg/kg\* | Not fully acceptable (some missing information)  No method required due to low PECs in comparison to natural background levels | H. Yamada et al (1996), Doc. No. 492-017, A4.2a/04 |
| Air | iodine | | In air sampling tubes, I2 is partially but stoichiometrically converted to iodide. Iodide is determined by IC-PED. | Air at concentration of 0.05, 0.1 and 0.2 ppm and relative humidities of 25%, 50%, and 80% were sampled.  6 measurements per concentration / relative humidity combination (only 5 in one case). | Calibration range: 0.1 – 5.0 µg iodide/mL | Yes | Overall  62.7 – 103%  25% r.H:  95 – 103  50% r.H:  94.2 – 99.4  80% r.H.:  62.7 – 86.8 | | 90.7  98.2  97.2   76.5 | 12.6  4.2  2.7  12.4 | LOD = 0.0004 ppm (2.5 L air sample)  LOQ = 0.001 ppm (2.5 L air sample) | 0.1 mg/m3\*\* | Acceptable | OSHA, (1994), Doc. No. 592-036; A4.2b/01 |
| In case of high air humidity, air sampled using impingers containing an alkaline collection solution and iodide is determined by IC-PED. The use of bubblers is expected to enhance the recovery due to increased dispersion. | Air at concentration of 0.05, 0.1 and 0.2 ppm and relative humidities of 80% were sampled.  3 measurements per concentration | See above | See above | Overall range:  86.3 – 95.1% | | 95.1 at 0.05 ppm  94.8 at 0.1 ppm  86.3 at 0.2 ppm | Range:  0.002 – 0.005 | See above |  |
| Water  (synthetic drinking water, industrial and domestic sewage) | iodide | | Ion chromatographic separation (IC) and conductivity or UV detection | No fortification and determination of recovery rates performed. | Working range: 0.1 – 50 mg I/L | Organic acids, such as mono- and dicarboxylic acids, can interfere as well as sulphate In case of UV-detection, organic agents may interfere. | Not reported. An interlaboratory trial was performed which proved the validity of the method (not generally required as no work up except filtering is performed) | | | | LOQ = 0.1 mg/L | 0.59 mg/L\*\*\* | Acceptable  No method required due to low PECs in comparison to natural background levels | DIN-ISO 10304‑3, Doc. No. 492-004; A4.2c/01 |
| Water | Reference is made to the method described for the determination of iodide in soil. This method is also applicable for the determination of iodide in water. The digestion step of the soil sample can be omitted (see above). | | | | | | | | | | | - | Not acceptable due to missing supporting data  No method required due to low PECs in comparison to natural background levels | -- |
| Water | iodide | GC-ECD | | For the determination of the recovery, mineral waters were fortified with with KI solutions. | Not reported | Yes | 80 – 110% | | 92% | Not reported | LOQ: 2.9 µg/L to 3,6 µg/L  LOD: 1,7 µg/L to 1,1 µg/L | 0.59 mg/L\*\*\* | Not acceptable for monitoring due to the use of carcinogenic substance (ethylene oxide)  No method required due to low PECs in comparison to natural background levels | S. Kirchner et al. (1996); Doc. No. 492-006; A4.2c/04 |
| Water (rain water, brine solution, soil solution) | Total iodine, iodide and iodate (separately) | IC-ICP-MS | | Not tested | Not reported | Yes | - | | - | - | Quoted LOD: 0.05 µg/L total iodine  LOD for iodide and iodate range from 0.1 to 1 µg/L. | 0.59 mg/L\*\*\* | Not acceptable due to missing supporting data  No method required due to low PECs in comparison to natural background levels | S. Yoshida et al (2007); Doc. No. 492-018; A4.2c/05 |
| Water (Milli Q, tap water, surface water) | Iodide and iodate (separately) | IC-ICP-MS | | 5 µg/L, 5 samples | Calibration range 1-10 µg/L | Yes | Not reported | | I-: 95-100%  IO3-: 94-100% (for all waters) | I-: 0.9-1.8 %RSD  IO3-: 1.1-1.9% RSD (for all waters) | LOQ: At least 5 µg/L (validated)  Calculated: 0.77µg/L for I-, 0.48 µg/L for IO3- | 0.59 mg/L\*\*\* | Acceptable  No method required due to low PECs in comparison to natural background levels | Sacher et al (2005): Doc. No. 492-021; A4.2c/06 |
| Water (drinking) | Iodide and iodate (separately) | IC-ICP-MS | | 6.4-17.5 µg/L (1 fortifcation level per specie, 3 samples per level and 2 different water samples) | I-: 0.06-640 µg/L  IO3-: 0.09-874 µg/L | Yes | Not reported | | I-: 92-95%  IO3-: 94-97% | I-: 0.5-1.4 %RSD  IO3-: 0.3-0.8-% RSD | LOQ: At least 6.4 and 8.8 µg/L for I- and IO3- respectively (validated) | 0.59 mg/L\*\*\* | Acceptable  No method required due to low PECs in comparison to natural background levels | Liu et al (2010); Doc. No. 492-022; A4.2c/07 |
| Milk and milk powder | iodide | HPLC with electrochemical detector | | Accuracy/precision data generated in the approximate range 0.6-4.3 µg/g and 270-310 µg/L for milk powders and liquid milk respectively. Each sample analysed in blind duplicates over two days. 6-9 laboratories participated (interlaboratory tested). | The correlation coefficient should be > 0.99. Applicability range of method quoted as 0.03 -1 µg/g and 0.3-10.0 µg/g for whole milk and milk powders respectively (no further supporting data) | Yes | 75-106% and 87.8% for milk powders (mp) and whole milk (wm) respectively | | 90.8% (mp) 87.8% (wm) | Precision:  7-24%RSD (mp)  5-12%RSD (wm) | LOQ can be taken from applicability range: 0.03 µg/g (wm)  0.3 µg/g (mp) | ≥90 µg/L (0.09 µg/g)\*\*\*\* | Acceptable (internationally agreed std method).  Further data may be required pending on conclusions of a full dietary risk assessment | 1. ISO 14378, Doc. No. 492-013; A4.3/01  2. D. Sertl and W. Malone (1993) |
| Milk and bovine liver | Total iodine | ICP-MS of digested samples | | Standard material (milk powder and bovine liver) with certified iodine content in the range 0.1-5.4 mg/kg ( | Not reported (internal standardisation with129I- enriched iodate) | Yes | Not tested (good agreement with certified content) | | - | 0.8-8.8% | LOQ: At least 0.3 mg/kg (validated for milk powder)) | ≥90 µg/L (milk) \*\*\*\* | Not fully acceptable (some missing information) | Rädlinger and Heumann (1998); Doc. No. 492-019; A4.3/02 |

\*: General requirement for soil according to TNsG on Analytical methods

\*\*: Based on the occupational exposure limit (OEL) / MAK value of 0.1 mg/m3 established for iodine in most European countries

\*\*\*: Lowest concentration having an effect on aquatic organisms (based on EC50 for Daphnia Magna). The general pesticide limit of 0.1 µg/L in drinking water according to Council Directive 98/83/EC does not apply to a non-xenobiotic substance like iodine

\*\*\*\*: The approximate level of natural background concentration of iodine in milk

|  |
| --- |
| **Conclusion on the methods for detection and identification of the product** |
| This analytical method for the determination of total active iodine (I2) by titration was available in European Pharmacopoeia and validated in the CAR of active substance.  It can be used in the biocidal product IODIGUARD. |

|  |
| --- |
| **Conclusion on the methods for detection and identification of residues of active substance for monitoring** |
| Analytical methods were provided and validated at EU level for the determination of iodine residue in animal products (milk) with a LOQ = 0.3 mg/kg.  Analytical methods were provided and validated at EU level for the determination of iodine residue in soil (ICP-MS), water (IC-ICP-MS) and air (ICP-PED) with respectively LOQ = 0.05 mg/kg, 0.1 mg/L and 0.1 mg/ m3.  Iodine is not toxic (T) or very toxic (T+) active substance. Therefore, an analytical method in biological matrices is not required. |

### Efficacy against target organisms

#### Function and field of use

MG 01: Disinfectants

PT3: Veterinary hygiene

The product IODIGUARD is a ready to use disinfectant, for teat disinfection.

The product is used by professional users.

After the milking, teats of dairy cows, ewes or goats are treated with IODIGUARD by dipping of the teats into the top of the dip.

The top of the dip contains approximately 8 mL of IODIGUARD and these 8 mL are enough to treat the four teats of a cow. Once the teats are dipped, the operator slightly moves the teats to allow the formation of a droplet on the sphincter at the basis of the teat. This place is the crucial place to be protected since it is the entry point of the contaminants. Before the next milking, the potential remaining product is washed with a foaming soap and wipes in order to have disappeared for the next milking.

The frequency of application is 2 applications per day.

#### Organisms to be controlled and products, organisms or objects to be protected

The product IODIGUARD is used to disinfect the teats of the udders of dairy animals, such as dairy cows, ewes and goats, after milking. It irreversibly inactivates vegetative bacteria and yeasts.

The product is used for the purpose of the protection of human and animal health (to prevent spoilage of milk and to prevent the transmission of disease causing microorganisms for animals).

#### Effects on target organisms, including unacceptable suffering

The product is intended to produce a reduction in the number of viable bacterial cells (bactericidal activity), and yeast cells (yeasticidal activity) of relevant test organisms under defined conditions.

#### Mode of action, including time delay

The mode of action of iodine is non-selective and is based on the following mechanisms:

- Iodine rapidly penetrates into microorganisms showing a high affinity pattern of adsorption.

- Iodine combines with protein substances in the bacterial cell; these could be peptidoglycans in the cell walls or enzymes in the cytoplasm. This results in irreversible coagulation of the protein and consequent loss of function.

- Iodine is known to act on thiol groups in the cell; if a thiol enzyme is part of a metabolic chain then metabolic inhibition will result.

- Iodine reacts with key groups of proteins, in particular the free-sulphur amino acids cysteine and methionine, nucleotides and fatty acids.

- Iodine interferes at the level of the respiratory chain of the aerobic microorganisms by blocking the transport of electrons through electrophilic reactions with the enzymes of the respiratory chain.

The rapid penetration of iodine into microorganisms and its mode of action indicate that the time-delay i.e. contact time required for sufficient efficacy depends on the tolerance of the organism to iodine and the concentration of iodine used for treatment.

Contact times for the different activities claimed are determined in the efficacy tests (see table below).

#### Efficacy data

Laboratory and field studies were conducted with the product IODIGUARD according to EN 14885:2006 standard and according to discussions/conclusions at Efficacy WG meeting in order to establish efficacy criteria to be achieved, summarised in the minute of Efficacy WG V 2015. The results are summarized in the table below.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Bactericide | Teat disinfection | DESINFECTANT D017.A75 (IODIGUARD 1.5 % w/w PVPI) | Bacteria  *E.coli*  *S.aureus*  *S.uberis* | EN 1656 : 2010 | Phase 2 step 1 test (suspension test)  Concentration tested: 20 % v/v /60 % v/v /80 % v/v  Temperature: 30°C  Contact time: 5 min  Additional conditions: 10 g/L skimmed milk  Criteria: at least a 5 log reduction | Bactericidal activity demonstrated at 20 % v/v | Study A-11-103/A  R.I: 1 |
| Bactericide | Teat disinfection | IODIGUARD (0.75 % w/w iodine free) | Bacteria  *E.coli*  *S.aureus*  *S.uberis* | EN 1656 : 2010 | Phase 2 step 1 test (suspension test)  Concentration tested: 20 % v/v /40 % v/v / 60 % v/v /80 % v/v  Temperature: 30°C  Contact time: 5 min  Additional conditions: 10 g/L skimmed milk  Criteria: at least a 5 log reduction | Bactericidal activity demonstrated at 40 % v/v | Laboratoire Solutio, August 2015  R.I: 1 |
| Yeasticide | Teat disinfection | IODIGUARD (1.5 % w/w PVPI) | Yeasts  *C.albicans* | EN 1657:2007 | Phase 2 step 1 test (suspension test)  Concentration tested: 20 % v/v /40 % v/v / 60 % v/v  Temperature: 30°C  Contact time: 5 min  Additional conditions: 10 g/L skimmed milk  Criteria: at least a 4 log reduction | Yeasticidal activity demonstrated at 20 % v/v | Laboratoire Solutio, July 2014  R.I: 1 |
| Bactericide | Teat disinfection | IODIGUARD 1,5 % w/w PVPI) | Bacteria  *E.coli K12* | Field test according to the modified methodology of EN 1499 standard | 8 cows (2 teats treated with the product and 2 tests treated with a formulation without iodine, after milking)  Concentration tested :100 % v/v  Contact time: 5 min  Criteria: 4 log reduction (difference between the number of test organisms released from teats before (VI) and after the teat disinfection (VF) significantly different) | The formulation without iodine showed no efficacy (no significant difference with Wilcoxon test between VI and VF : p-value=0.77)  For the tested product: VF is significantly different from VI with Wilcoxon test  Mean log reduction with the product = 1.73±0.83 | Laboratoire Solutio, March 2016  R.I: 2 |
| Bactericide | Teat disinfection | Various Iodine based formulations | *S.aureus*  *S.agalactiae* | NMC protocols:  -Protocol B :  Determination of the ability of a teat dip to prevent new IMI under experimental challenge conditions -Protocol C:  Standardized procedures for conducting a control study based on natural infection under field conditions. | Summary of efficacy data for iodophor teat dips | Protocol B: Efficacy consistently has averaged over 50% for both pathogens Studies on specific concentrations of iodine indicated good efficacy with formulation containing from .05 to 1% titratable iodine  Protocol C: Under natural exposure to mastiffs pathogens, efficacy of iodophor products  ranged from a 40% increase to 90% reduction in incidence of IMI | Pankey et al, 1984  R.I: 2 |
| Bactericide | Teat disinfection | Various Iodine based formulations | *S.aureus*  *S.agalactiae* | NMC - SUMMARY OF PEER-REVIEWED PUBLICATIONS ON EFFICACY OF PREMILKING AND POSTMILKING TEAT DISINFECTANTS PUBLISHED SINCE 1980 (Updated January 2004) | Summary of peer-reviewed research on efficacy of iodine post-milking teat disinfectants published since 1980 | According to NMC protocol, The results expressed as a reduction of infection probability, showed that a large variety of formulations within 0.05-1% iodine were significantly efficient against the main cow mastitis pathogens | <http://www.cfsph.iastate.edu/Infection_Control/Species/Teatbibliography.pdf>  R.I: 2 |

* **Results of laboratory tests (EN 1656 and EN 1657):**
* Phase 2, step 1 tests have been performed for bactericidal activity (EN 1656) and yeasticidal activity (EN 1657), according to the requirements of the norms for teat disinfection, at 30°C with a contact time of 5 minutes, showing the efficacy of the product IODIGUARD applied as a ready to use.
* Moreover, regarding the loss in iodine after the accelerated storage stability test (-46% of total iodine after storage at 40 °C during 8 weeks) and long term storage (-34% of total iodine after 12 months at ambient temperature), a test according to EN 1656 standard has been performed in order to demonstrate that even with a loss of half iodine content (750 mg/L instead of 1500 mg/L of free iodine), the product IODIGUARD remains efficient, at 30°C with a contact time of 5 minutes.
* **Test design and results of field test:**

Several discussions took place in Efficacy WG in 2015 pointing out that phase 2 step 1 tests are insufficient to prove the efficacy of teat disinfectant. Then it was asked to the applicants to complete the efficacy demonstration with tests against bacteria simulating the conditions of use. In the frame of this dossier, a field test has been proposed by the applicant and the protocol is described below.

Test design:

A field test according to the modified methodology of EN 1499 standard (phase 2, step 2 test) has been conducted in order to demonstrate in field conditions the efficacy of the product IODIGUARD: the principle of this trial is to artificially contaminate the teats of cows with bacteria (K12 strain of *E.coli*). The number of test organisms released from teats into sampling fluids is assessed before and after the teat disinfection. The ratio of the two resulting values represents a measure for the antimicrobial activity of the product tested. The necessary precision is achieved by repeating the tests on 8 cows.

No reference hygienic handwash product has been tested following the principles of EN 1499 standard but a formulation without active substance was applied on the same cows (2 others udders), on the same day and under comparable environmental conditions. Indeed, the application conditions of a reference soap would be different (less quantity of water for rinsing, problem of dripping and no film-forming effect) and the formulation without iodine will allow to compensate extraneous influences if need be. The efficacy of the product IODIGUARD should be evaluated with a statistical comparison of the number of test organisms released from teats into sampling fluids assessed before and after the teat disinfection.

The test procedure was conducted with the following steps:

1. After milking, the 4 teats of a cow are washed with running tap water with a soap, then rinsed and dried;
2. The 4 teats are immersed in the contamination fluid (K12 strain of *E.coli*) and dried in the air;
3. The 4 teats are dipped in TSB as sampling fluid in order to assess the release of test organisms before treatments of the cows (initial content of micro-organisms, prevalues VI) (sampling of 4 VI per cow, i.e 32 prevalues VI, i.e 16 VIR for the formulation without iodine and 16 VIP for the product);
4. Repeat the steps 1 and 2 (washing, rinsing, drying and immersion in the contamination fluid);
5. 2 teats are dipped into the product fluid and the 2 other teats in the formulation without active substance during several seconds to allow the formation of a droplet on the sphincter at the basis of the teat. Contact time is 5 minutes, then rinsing with running tap water;
6. The 4 teats are dipped in TSB + neutraliser as sampling fluid in order to assess the release of test organisms after treatments of the cows (sampling of 2 postvalues VFP per cow for the product and 2 postvalues VFR per cow for the formulation without active substance).

Verification of the methodology – test validation:

- The absence of effect from soap (control A) and neutraliser (control B) and the validation of the method (control C), are validated according to acceptance basic limits of EN 1499 standard.

- Acceptance criteria for test results are those defined in EN 1499 standard.

* The applicant submitted a Wilcoxon test comparing VFR values from formulation without iodine to VFP values from the tested product.
* Moreover, as no reference product is defined for teats disinfection, the number of test organisms released from teats into sampling fluids assessed before (values VIP) and after (values VFP) the teat disinfection shall be significantly different for the tested product. A mean log reduction should be also calculated to assess the effect of the product IODIGUARD.

Results:

* Basic limits and acceptance criteria fulfilled the requirements of EN 1499 standard.
* According to Wilcoxon test, the product IODIGUARD is significantly more efficient than the formulation without iodine.
* According to Wilcoxon test, the number of test organisms released from teats into sampling fluids assessed before (prevalues VIP) and after (postvalues VFP) is significantly different for the tested product, and then the product IODIGUARD can be considered as active. A mean log reduction of 1.73±0.83 is obtained.

Taking into account European discussions at WG III2017, in the frame of early WG discussion on Union authorisation applications based on iodine/PVP-iodine, the EFF WG agreed that results of this field study was accepted as demonstrating the efficacy of the product IODIGUARD, but justification should be added e.g. by referring to literature studies, experiences of products being on the market, or other appropriate information. This one is presented below:

Argumentation provided:

After intensive bibliography researches including veterinary theses, commercial brochures, agricultural good practice documents, scientific articles and this in European but also non-European sources, no direct criterion could be found concerning a minimal in vivo bacterial count reduction applicable to field studies for post-milking teat antisepsis products.

Nevertheless, Pankey et al, 1984[[2]](#footnote-2) have summarized field efficacy data for iodophor products from a range of independent studies. The review indicates that “Post-milking teat antisepsis is regarded as the single most effective practice for prevention of intra-mammary infections(IMI) of lactating dairy cows”. It also showed that, among 36 studies on formulations with 0.05-1% iodine:

* Iodophor teat dips have provided effective control of new IMI by *S.aureus* and *S.agalactiae*, the most frequently isolated mastitis pathogens
* One of these field studies was on a PVPI-based formulation at 0.35% w/w and was very efficient with percent reductions of 78 and 67%, for *Staphylococcus* *aureus* and *Streptococcus* *agalactiae*, respectively. This formulation may be compared with Iodiguard, with 1.5 % w/w PVPI (i.e 0.13 % iodine).
* These results (% reduction related to the PVPI concentration) do not show any specific trend between iodine concentration and efficacy, probably due to numerous confounding factors involved. Overall, it shows that globally efficacy ranges 40-100% whatever the iodine concentration and it has to be noted that a common value appearing in literature is a reduction of at least 50% of mastitis cases with iodine treatment.

Moreover, National Mastitis Council’s review in 2014[[3]](#footnote-3) lists peer-reviewed published efficacy data of iodine post-milking teat disinfectants on various bacterial strains, expressed as a reduction probability. The results show also that a large variety of formulations within 0.05-1% iodine were significantly efficient against the main cow mastitis pathogens.

|  |
| --- |
| **Conclusion on the efficacy of the product** |
| French competent authorities (FR CA) assessed that the product IODIGUARD, as a ready to use concentrate used after milking, by dipping, with a contact time of 5 minutes, has shown a sufficient efficacy in phase 2, step 1 tests against bacteria and yeasts.  Taking into account European discussions at WG III2017, in the frame of early WG discussion on Union authorisation applications based on iodine/PVP-iodine, field study submitted showed statistically the efficacy of the product IODIGUARD with regards to a formulation without iodine. Moreover according to the literature review, the iodine level of the product IODIGUARD supports a sufficient efficacy for teat disinfection. |

#### Occurrence of resistance and resistance management

No reduction in efficacy was reported in the literature for such applications indicating that no development of resistant microorganisms has occurred.

The authorization holder has to report any observed incidents related to the efficacy to the Competent Authorities (CA).

To ensure a satisfactory level of efficacy and avoid the development of resistance, the recommendations proposed in the SPC have to be implemented.

#### Known limitations

None

#### Evaluation of the label claims

French competent authorities (FR CA) assessed that the product IODIGUARD, as a ready to use concentrate showed a sufficient efficacy, for teat disinfection (bacteria and yeasts) in post milking, with a contact time of 5 minutes.

#### Relevant information if the product is intended to be authorised for use with other biocidal product(s)

The product IODIGUARD is not intended to be used with another biocidal product.

### Risk assessment for human health

Please refer to iodine CAR.

The following data on active substance issued from CAR will be used for human health risk assessment:

|  |  |
| --- | --- |
| Endpoint | Values |
| AEL | 0.01 mg/kg/d |
| AEC inhalation | 1 mg/m3 ou 0.1 ppm |
| Vapour Pressure (Pa) at 25°C | 40.7 Pa at 25°C |
| Molecular weight (g/mol) | 253.81 g/mol |

The product type 3 (veterinary hygiene biocidal products) was already assessed in iodine CAR as manual or automatic non-medical teat disinfection and udder washes, and as surface disinfection in animal houses.

Iodine is a natural and essential compound:

* Iodine is an essential dietary trace element for mammals. It is required for the synthesis of the thyroid hormones, which control metabolism and play an important role in reproduction, growth and development.
* Background values between 0.5 and 20 mg iodine/kg are found in soil, whereas in groundwater a mean concentration of 1 μg/L is reported. The background values in surface water (0.5 to 20 μg iodine/L) are considerably lower than in marine water (45 to 60 μg iodine/L). The levels in rain water (0.1 to 15 μg/L) are comparable to those of surface water (Iodine Assessment Report, SE, September 2013).

The reduction of iodine background concentrations in soil by leaching has an impact on the iodine level in crops and animals, and consequently in human food. For this reason, recommendations for the daily intake for humans were established. e.g. by the World Health Organisation (WHO) at 150 – 200 μg/day and the fortification of table salt with iodine has become a mean to prevent a deficiency for this essential dietary trace element.

#### Assessment of effects on Human Health

***Skin corrosion and irritation***

In order to avoid unnecessary animal experiment, no skin irritation/corrosion study was conducted. Classification is determined by calculation according to the CLP Regulation (Regulation (EC) No.1272/2008) based on the available data on each component.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin corrosion and irritation** | |
| Value/conclusion | According to the composition, none of the component is toxicologically relevant for skin irritation or corrosion. |
| Classification of the product according to CLP | Not classified |

***Eye irritation***

Bovine Corneal Opacity and Permeability (BCOP) Assay was conducted for the product Iodiguard:

| **Summary table of in vitro studies on serious eye damage and eye irritation** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline,**  **GLP status, Reliability** | **Test substance, Doses** | **Relevant information about the study** | **Results**  *(In vitro Irritancy score)* | **Remarks** | **Reference** |
| OECD 437  GLP | Iodiguard  0.75 mL | Negative control: 0.9% w/w sodium chloride  Positive control: neat ethanol | Test Item: 1.6  Negative control: 1.4  Positive control: 39.7 | None | N. Warren, 2015 |

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | *In vitro* irritancy score of the test item: 1.6. |
| Classification of the product according to CLP | An *in vitro* assay was provided by applicant. No classification is needed for this endpoint. |

***Respiratory tract irritation***

In order to avoid unnecessary animal experiment, no study of respiratory tract irritation is available. Classification is determined by calculation according to the CLP Regulation (Regulation (EC) No.1272/2008) based on the available data on each component.

|  |  |
| --- | --- |
| **Conclusion used in the Risk Assessment – Respiratory tract irritation** | |
| Classification of the product according to CLP | Not classified |

***Skin sensitization***

In order to avoid unnecessary animal experiment, skin sensitization study was not conducted. Classification is determined by calculation according to the CLP Regulation (Regulation (EC) No.1272/2008) based on the available data on each component.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin sensitisation** | |
| Value/conclusion | According to the composition, none of the component is toxicologically relevant for skin sensitisation. |
| Classification of the product according to CLP | Not classified |

***Respiratory sensitization (ADS)***

Sensitisation is available. Classification is determined by calculation according to the CLP Regulation (Regulation (EC) No.1272/2008) based on the available data on each component.

|  |  |
| --- | --- |
| **Conclusion** **used in Risk Assessment – Respiratory sensitisation** | |
| Value/conclusion | According to the composition, none of the component is toxicologically relevant for respiratory sensitisation. |
| Classification of the product according to CLP | Not classified |

***Acute toxicity***

In order to avoid unnecessary animal experiment, no acute toxicity studies were conducted. Classification is determined by calculation (oral, inhalation and dermal route) according to the CLP Regulation (Regulation (EC) No.1272/2008) based on the available data on each component.

*Acute toxicity by oral route*

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute oral toxicity** | |
| Classification of the product according to CLP | Not classified |

*Acute toxicity by inhalation*

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute inhalation toxicity** | |
| Classification of the product according to CLP | Not classified |

*Acute toxicity by dermal route*

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute dermal toxicity** | |
| Classification of the product according to CLP | Not classified |

The sentence “The product contains pyrrolidones derivatives. Do not use in case of known hypersensitivity.” should be mentioned.

***Information on dermal absorption***

No dermal absorption study was provided on the product IODIGARD. However, a read across with the value available in the CAR (12%) is proposed and accepted by eCA considering the two formulations are very similar.

|  |  |
| --- | --- |
| **Value(s) used in the Risk Assessment – Dermal absorption** | |
| Substance | Iodine |
| Value(s) | 12 % |
| Justification for the selected value(s) | CAR value |

***Available toxicological data relating to non active substance(s) (i.e. substance(s) of concern)***

No substance of concern is identified.

#### Exposure assessment

IODIGUARD is ready-to-use product packaged in jerry cans of 20 L, 60 L and 220 L black HDPE.

It is intended to be used by professionals to disinfect teats of cows, ewe and goats after the milking (PT3). Teat dips are filled in with 500 mL of IODIGUARD, the top of the dip is screwed. Method of application is dipping into teat dips and the application dose is 2 mL/teat/event resulting in 16 mL/animal/day (8 mL for treating the four teats of a cow two times a day).

In IODIGUARD formulation there are two sources of I2/I-:

* total iodine from PVP at a content of 0.255% considering it represents 17%[[4]](#footnote-4) of PVPI and
* I- from KI at a content of 0.038%.

Thus, the quantity of the various forms of iodine in IODIGUARD is: 0.255 + 0.038 = 0.29% (m/m) for the human risk assessment.

**Identification of main paths of human exposure towards active substance(s) and substances of concern from its use in biocidal product**

| **Summary table: relevant paths of human exposure** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | | | **Secondary (indirect) exposure** | | |
| **Industrial use** | **Professional use** | **Non-professional use** | **Industrial use** | **Professional use** | **General public** |
| Inhalation | n.a. | No | n.a. | n.a. | No | n.a. |
| Dermal | n.a. | Yes | n.a. | n.a. | Yes | n.a. |
| Oral | n.a. | No | n.a. | n.a. | No | n.a. |

n.a.: not applicable

Inhalation exposure of iodine from this type of product (teat disinfectant) was a point of discussion at the WG IV-2017, and it was concluded that inhalation exposure to vapours could be considered as negligible for this type of formulation and therefore inhalation exposure to vapours does not need to be assessed.

Therefore only dermal exposure is considered for the following phases:

**Primary exposure:**

IODIGUARD was designed as viscous solution for two purposes:

* + to adhere to the teats and stay on it (the total drying time is approximately 50 minutes);
  + to avoid any spill during manipulation by the operator.

Furthermore, a qualitative test showed that IODIGUARD does not drip during its application.

**Mixing/loading phase:**

The jerry cans of product are sold with a tap to facilitate loading of the teat dip.

**Dermal exposure:**

Based on the properties of IODIGUARD avoiding spills and drops from the product and the use of a tap, exposure will be limited.

In the HeadHoc recommendation 13 (2017)[[5]](#footnote-5), two approaches are presented: mixing and model 4 or the layer approach. To take into consideration reduction of exposure by using a tap, the ConsExpo cleaning product factsheet equivalent to mixing and loading model 4 was chosen as a reasonable worst-case scenario as it leads to the lower exposure than the layer approach.



**Application phase:**

**Dermal exposure:**

Teat of animals will be dipped in the cup of the upper part of the teat dip. Due to the nature of the product, very few drips are expected and exposure should be lower than mixing and loading.

So application by dipping is covered by the mixing and loading step for dermal exposure.

**Cleaning phase:**

**Dermal exposure:**

Before the next milking, the potential remaining product must be washed with a gentle foaming soap and wipes. Workers may be directly exposed to the remaining product on teat skin.

After application, a small amount of diluted product will remain in the application equipment; however this will be highly diluted by the wash-water.

**Secondary exposure:**

Exposure of the general public is not relevant.

***List of scenarios***

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario** | **Primary or secondary exposure**  **Description of scenario** | **Exposed group** |
| 1. | Mixing/loading | **Primary exposure – dermal route**  Exposure to droplets direct to the skin is considered during loading. | Professionals |
| 2. | Application by dipping | **Primary exposure – dermal route**  Worker can be exposed to some drip on the hands.  Application by dipping is covered by the mixing and loading step for dermal exposure. | Professionals |
| 3. | Cleaning of teats, removal of applied product post-milking | **Primary exposure – dermal route**  Direct skin exposure during cleaning of remaining product on teat skin. | Professionals |
| 4. | Cleaning of equipment | **Primary exposure – dermal route**  Cleaning of teats by wiping with a dry cloth before milking is only relevant if the cows have received a post-milking treatment.  After disinfection the entire dip is cleaned. | Professionals |

***Industrial exposure***

No industrial exposure is foreseen. The product IODIGUARD is a bactericide and yeasticide used as teat disinfectant by professionals. Therefore the assessment of industrial exposure is not relevant.

***Professional exposure***

*Scenario [1] loading of the product in teat dip tank*

| **Description of Scenario [1] – Mixing and loading - Dermal exposure** | | | |
| --- | --- | --- | --- |
| The ConsExpo cleaning product factsheet equivalent to mixing and loading model 4 as proposed in HeadHoc recommendation 13 was chosen as a reasonable worst-case scenario as it leads to the lower exposure than the layer approach.  Exposure is assessed using instant application mode from the consumer exposure model ConsExpoWeb.  To assess the product amount on skin, the cleaning and product factsheet on page 24 propose the same approach as mixing and model 4:   * + 0.01 ml of product will land on the skin after the transfer of less than 1L to a receiving vessel. | | | |
|  | Parameters | Value | Reference |
| Tier1 | Frequency (per day) | 2 | Applicant data |
| Weight fraction compound (%) | 0.29 | Applicant data |
| Product amount (milligram) | 10.3 | Density of Iodiguard = 1.03;  Contamination for any closure, < 1L container = 0.01 mL/operation  For mixing and loading, default value for dermal exposure is set at 0.01 ml or 0.01 g (when density 1 g/cm3).  Cleaning Products Fact Sheet, 2006 |
| Body weight (kg) | 60 | HEEG opinion No. 17, 2013 |
| Dermal absorption (%) | 12 | CAR of the active substance |

**Calculations for Scenarios [1] loading of the product in teat dip tank**

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg/d)** | **Estimated dermal uptake (mg/kg/d)** | **Estimated oral uptake (mg/kg/d)** | **Estimated total uptake (mg/kg/d)** |
| Scenario [1]  Loading of the teat dip tank | 1 | n.a. | 1.2 × 10⁻4 | n.a. | 1.2 × 10⁻4 |

*Scenario [2] Application by dipping*

Application by dipping is covered by the mixing and loading step for dermal exposure and inhalation exposure is covered by the cleaning step.

As dermal and inhalation exposure are covered by other tasks no scenarios will be presented for application.

*Scenario [3] Cleaning of teats, removal of applied product post-milking*

| **Description of Scenario [3] – Cleaning of animals teats - dermal exposure** | | | |
| --- | --- | --- | --- |
| As proposed on headhoc recommendation 13 and the Disinfectant Products Fact Sheet (RIVM report 320005003/2006), as a worst-case scenario it is consider that 0.1% of the amount of biocidal product applied on animal teats will transfer on worker skin during cleaning. This approach is applied because no information is given about the duration to wait before the next milking and as the product is film forming and will last longer than non-forming film.  Dermal exposure per animal cleaning is calculated according to the following formula:  Where:  AR: Application rate (mL/animal/d)  C: Weight fraction substance (%)  d: Density  DA: Dermal absorption (%)  AP: Amount of product considered (0.1%)  BW : body weight (kg)  The total exposure takes into account a number of 82 cows/day. | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Frequency (per day) | 2 | Applicant data |
| Product amount (%) | 0.1 | Disinfectant Products Fact Sheet (RIVM report 320005003/2006) |
| Application rate (mL/animal/d) | 16 | Applicant data (2ml per teat, 4 teat per cow and 2 applications per day) |
| Weight fraction substance (%) | 0.29 | Applicant data |
| Density | 1.03 | Properties of Iodiguard |
| Number of cows | 82 | HEAdhoc recommendation No. 13, 2017 |
| Body weight (kg) | 60 | HEEG opinion No. 17, 2013 |
| Dermal absorption (%) | 12 | CAR of the active substance |
| Tier 2 | Penetration factor (gloves) | 10% |  |

**Calculations for Scenarios [3] cleaning of animals teats**

| **Summary table: estimated exposure from professional uses** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | | **Tier/PPE** | **Estimated inhalation uptake (mg/kg/d)** | **Estimated dermal uptake (mg/kg/d)** | **Estimated oral uptake (mg/kg/d)** | **Estimated total uptake (mg/kg/d)** |
| Scenario [3] Cleaning of animals teats | 1 | | n.a. | 7.84 × 10⁻3 | n.a. | 7.84 × 10⁻3 |
| Scenario [3] Cleaning of animals teats | 2 /gloves | | n.a. | 7.84 × 10⁻4 | n.a. | 7.84 × 10⁻4 |

*Scenario [4] Cleaning of equipment*

| **Description of Scenario [4] – Cleaning of equipment - dermal exposure** | | | |
| --- | --- | --- | --- |
| As proposed on headhoc recommendation 13 and the Disinfectant Products Fact Sheet (RIVM report 320005003/2006), for cleaning of equipment, RISKOFDERM ‘Loading liquid, automated or semi-automated’ for the cleaning phase of different equipment (dipping cup, spraying nozzle etc.) is used. The indicative value is 0.92 mg/min and a duration of is 5 minutes is considered. | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Weight fraction substance (%) | 0.29 | Applicant data |
| Density | 1.03 | Properties of Iodiguard |
| Indicative value (mg/min) | 0.92 | RISKOFDERM ‘Loading liquid, automated or semi-automated’ |
| Exposure duration (minutes) | 5 |  |
| Body weight (kg) | 60 | HEEG opinion No. 17, 2013 |
| Dermal absorption (%) | 12 | CAR of the active substance |
| Tier 2 | Penetration factor (gloves) | 10% |  |

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg/d)** | **Estimated dermal uptake (mg/kg/d)** | **Estimated oral uptake (mg/kg/d)** | **Estimated total uptake (mg/kg/d)** |
| Scenario [4] Cleaning of equipment | 1 | n.a. | 1.60 × 10⁻3 | n.a. | 1.60 × 10⁻3 |
| Scenario [4] Cleaning of equipment | 2 /gloves | n.a. | 1.60 × 10⁻4 | n.a. | 1.60 × 10⁻4 |

*Scenario [5] Secondary exposure*

Not relevant.

**Further information and considerations on scenarios**

None.

***Non-professional exposure***

No non-professional exposure is foreseen. The product IODIGUARD is a bactericide and yeasticide used as teat disinfectant by professionals. Therefore the assessment of non-professional exposure is not relevant.

***Exposure of the general public***

No general public exposure is foreseen. The product IODIGUARD is a bactericide and yeasticide used as teat disinfectant by professionals. Therefore the assessment of exposure of general public is not relevant.

***Monitoring data***

None.

***Dietary exposure***

Considering intended uses of the product IODIGUARD, livestock can be exposed to the active substance iodine. Residue of iodine can be found in food and products from animal origin. As a consequence, the human dietary assessment needs to be performed in this dossier.

*Residue definitions*

In water, iodide (I-) and iodate (IO3-) are the predominant species. In addition a natural background level of methyl iodide might also be found in water. At pH values between 4 and 9, iodide is the predominant specie. In alkaline and well oxidized waters iodate is the predominant specie.

The livestock is expected to be exposed to the active substance iodine (I2). When absorbed, iodine is quickly reduced to iodide by nonenzymatic reactions. Iodide is readily and (almost) completely absorbed. The bioavailability after oral administration is > 90%.

The residue of iodine expected in food and products from animal origin is iodide (I-).

*List of scenarios*

In place of residue data to determine residues of iodine in milk following use of IODIGUARD, the consumer exposure followed the harmonized approach developed at EU level (WG TOX II-III-IV 2017, and Webex post WG tox IV 2017 meetings).

The applicant (Centre Technique d’Hygiène) has also provided dietary risk assessment in framework of this dossier. Nevertheless, considering the recent EU discussions, the decisions made in the WG TOX and WebEx meetings have been implemented.

Based on the details below the following three theoretical intakes has been calculated and evaluated:

* Iodine intakes resulting from only the proposed teat treatment.
* Iodine intakes from milk (sum of the proposed teat treatment + background levels in milk (200 µg/L)).
* Iodine intakes from all dietary sources (sum of the proposed teat treatment + background levels in milk (200 µg/L) + mean intake associated with other dietary sources (adult = 185 µg/day, infant = 96 µg/day)).

| **Summary table of main representative dietary exposure scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Type of use** | **Description of scenario** | **Subject of exposure** |
| 1. | Professional users - indoor | Manual non-medical teat disinfection for cows, ewe and goats.  Dip treatment post-milking  2 ml per teat  2 x/day, each day | Livestock (dairy cows, ewes and goats) |

The active substance iodine is not considered as a cumulative substance:

* no log Pow is defined,
* no data suggests a potential bioaccumulation of iodine/iodide in the body under normal circumstances,
* iodide in excess of physiological requirement is excreted mainly via the urine, and in smaller quantities via faeces, saliva, milk, sweat, tears, bile, other secretions and exhaled air.

Therefore no bioaccumulation of iodine is expected.

*Information of non-biocidal use of the active substance*

According to Regulation (EU) No. 2015/861, several iodine-containing compounds are authorized as feed additives, and also as antiseptics and sanitisers in veterinary medicine.

| **Summary table of other (non-biocidal) uses** | | | |
| --- | --- | --- | --- |
|  | **Sector of use** | **Intended use** | **Reference value(s)** |
| 1. | Feed additive  Iodine as  - Potassium iodide,  - Calcium iodate anhydrous,  - Coated Granulated calcium iodate anhydrous | The recommended maximum content of total iodine in complete feed for:  - equines is 3 mg/kg feed/d  - dogs is 4 mg/kg feed/d  - cats is 5 mg/kg feed/d  - ruminants for milk production is 2 mg/kg (0.080 mg/kg bw/d)  - laying hens is 3 mg/kg feed/d (0.205 mg/kg bw/d) | These values were recommended by the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP Panel) in 2013[[6]](#footnote-6) to bring the exposure of adult consumers below the Upper Intake Level. |
| 2. | Veterinary medicine  Iodine and iodine  inorganic compounds  including:  - Sodium/potassium-iodide  - Sodium/potassium-iodate  - Iodophors including polyvinylpyrrolidoneiodine (PVP-iodine) and iodoform | All food producing species:  Various iodine-containing compounds are used in veterinary medicine as antiseptics and sanitisers.  Iodine compounds are used in teat dips for the prevention and control of mastitis in cattle and in topical preparations for prevention of infections in wounds. Preparations for oral and parenteral administration are also available for the treatment of iodine-deficiency. | Regulation (EU) No.37/2010  The Committee for Veterinary Medicinal Products (CVMP) decided in 1996 that it would be **inappropriate to elaborate MRLs for iodine**. Therefore, iodine was included in Annex II of Council Regulation (EEC) No. 2377/90[[7]](#footnote-7) and later, in Annex of Commission Regulation (EU) No.37/2010[[8]](#footnote-8) . |

The Committee for Veterinary Medicinal Products (CVMP) has reviewed iodine for the use in veterinary medicine as antiseptic, sanitiser, teat dip for prevention and control of the mastitis, topical preparation for preventing wounds infections. CVMP reported that “only small increases in serum iodine concentration were found after teat dipping indicating that the procedure had a negligible effect on tissue iodine concentrations”, and it was concluded that no MRL is required for any food-producing species (see Commission Regulation (EU) No 37/2010). Considering the EC document ”interim approach for the establishment of maximum residue limits for residues of active substances contained in biocidal products for food and feed and specific migration limits in food contact materials” adopted during Competent Authorities meeting of 17 March 2017, it was stated at the Competent Authorities meetings of 17 March and 17 May 2017, that no biocide MRL are necessary for iodine in line with CVMP assessment for iodine.

**Estimated iodine residues in milk resulting from iodine PT3 biocidal product use**

In line with the EU iodine PT3 decision, bibliographic data are used to present an approach based on linear extrapolation of iodine residues in milk from the CAR data across different in-use concentrations of iodine and numbers of product applications per day.

A comparison of the use patterns and resulting worst case iodine residues in milk considered within the CAR (studies considered sufficiently detailed) was realized. The studies summarised below are considered relevant to the proposed use patterns of iodine.

**Table 1 - Residues of iodine in milk reported in iodine PT3 CAR studies**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| CAR Study | Iodine  (%) | Applications | Mean treated residue (µg/L) [range] | Mean control residue (µg/L) [range] | Difference (additional iodine residues in milk)  (µg/L) [mean] |
| *Falkenberg*  *2002* | 0.27 | 2x pre-milking | 243.7  [160 - 374] | 212.7  [124 - 300] | 31  (+14.6%) |
| *Iwarsson (A)*  *1974* | 0.50 | 1x post-milking  2x post-milking | 85.5  [46 - 125]  226.3  [135 - 334] | 64 [10 - 186] | 21.5  (+33.6%)  162.3 (+253.6%) |
| *Iwarsson (B)*  *1974* | 0.50 | 2x post-milking | 244  [74 - 392] | 70  [16 - 171] | 174  (+248.6 %) |
| *Iwarsson (C)*  *1974* | 0.25  0.50 | 2x post-milking | 187, 176  301, 334 | N/A - a decrease of approx. 50 % in total iodine residues was observed when halving product iodine content | |

Access to the O’Brien study is not possible in the framework of this dossier. So the data from *Iwarsson (B)* in the table above has been used to support an approximately linear extrapolation of the iodine content in milk based on the concentration of iodine in a teat disinfectant solution.

IODIGUARD contains an in-use concentration of iodine (0.255 %, considering 17% from PVPI) and potassium iodide (0.038 %). Even though it is noted that both iodine forms are equally relevant for dietary exposure (total iodine), as the bibliographic data are based on available iodine (0.5 % in *Iwarsson 1974)* the maximum available iodine content has been considered in the dietary risk assessment (0.255 %).

**Estimated iodine residues in milk considering background**

It is noted that values reported by EFSA in monitoring studies conducted within the EU indicate mean levels of iodine in milk of 100 - 200 µg/L (EFSA 2005 and EFSA 2013). The most appropriate background level to use in the risk assessment was discussed and agreed in the WebEx meeting (October 2017), where it was concluded that the value of 200 μg/L iodine in milk was considered appropriate as an EU harmonised value.

Based on the assumed linear relationship between iodine concentration and iodine residues in milk, and the agreed background level in milk of 200 µg/L, the estimated residues of iodine in milk have been derived and presented in Table 2.

**Table 2 - Estimated residues of iodine in milk based on extrapolation of O’Brien 2013 data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Product | Iodine  (%) | Applications | Estimated mean residues of iodine in milk (µg/L) | |
| Proposed teat treatment | TOTAL milk  (+ 200) |
| *Iwarsson 1974* | 0.500 | 2x post-milking | 174 | 374 |
| *IODIGUARD* | 0.255 | 2x post-milking | 89 | 289 |

*Calculation for 2x post-milking:*

*For 2 milkings at 0.255 % iodine intended treatment = 174 µg/L x (0.255/0.5) = 89 µg/L*

*For 2 milkings at 0.255 % iodine total = 89 µg/L + 200 µg/L = 289 µg/L*

**Intake values (milk consumption) for dietary risk assessment**

There are several sources of milk consumption data available to undertake the consumer intake assessment. This point was discussed during 2017 WG TOX meetings and it was concluded that the values from EFSA PRIMo rev 2 are relevant.

According to the ‘EFSA model for chronic and acute risk assessment’ (PRIMo rev.2), the consumption of milk and milk products from sheep, goats and other animals (such as buffaloes) is in the range of 0.002 - 0.12 g/kg bw/day for both adults and children leading to an uptake of milk and milk products well below 10 g/day for each of the animals. Even if the milk from these animals had considerably higher iodine residues than milk from dairy cows, these would not contribute significantly to the iodine supply. Thus, a detailed risk assessment of the residues in milk from these animals is considered to be not relevant.

As only a chronic risk assessment (see section ‘Toxicological reference values for iodine’) is being undertaken, the intake values from the EFSA PRIMo rev 2 (**0.45 L adult and 0.46 L toddler**) have been used to estimate the dietary exposure of adults and toddlers to iodine. These values have been agreed at WG TOX IV 2017. The estimated dietary exposure results are presented in Table 3.

**Table 3 – Iodine daily exposure from milk**

|  |  |  |  |
| --- | --- | --- | --- |
| **Consumer group** | Estimated mean residues of iodine in milk (µg/L) | **L per day/person**  (Density of whole milk 1030 g/L) | **Daily exposure (µg/d/pers)** |
| Adult | 289 | 0.45 | 130 |
| Toddler | 289 | 0.46 | 133 |

**Intake values (from food except milk consumption) for dietary risk assessment**

Iodine dietary intake for sources other than milk was included in the third calculation.

The iodine exposure via food was measured in different dietary commodities in framework of EU countries surveys. The monitoring values are subjected to a large variability depending principally of the diets and the geographical localizations. This point was discussed during 2017 WG TOX meetings and it was concluded that the values from the UK survey are adequate to represent the EU iodine dietary intake from sources other than milk: 185 µg/day for adults and 96 µg/day for toddler.

**Conclusion for dietary exposure assessment**

The dietary exposure has been discussed in various WG TOX and WebEx meetings for iodine-based union authorisations. This EU iodine PT3 approach considered the following default values / decisions for the determination of the worst-case consumer exposure estimate (WCCE):

* 2 manual milkings per day where the product may be used either pre- or post milking
* total daily milk intake of 0.45 l for adults and 0.46 l for toddlers
* background iodine concentration in milk of 200 µg/l
* intake of iodine from dietary sources other than milk : 185 µg/day for adults and 96 µg/day for toddlers

**Table 3 – Iodine daily exposure from food**

|  |  |  |
| --- | --- | --- |
|  | **Adults (0.45 L/day)** | **Toddler (0.46 L/day)** |
|  | **Estimated daily intake (µg/day)** | **Estimated daily intake (µg/day)** |
| **2x post-milking teat disinfection (0.255% available iodine)** | | |
| Intake from milk due to teat treatment1 | 40 | 41 |
| Total milk intake2 | 130 | 133 |
| Total dietary intake3 | 315 | 229 |

1 Iodine intake from milk due to teat treatment is derived from BP specific residue values (based on Iwarsson 1974).

2 Total milk intake is the sum of the estimated additional iodine intake resulting from the transfer into milk following teat disinfection and the iodine background in milk of 200 µg/l.

3 Total dietary intake is the sum of the estimated additional iodine intake resulting from the transfer into milk following teat disinfection, the iodine background in milk of 200 µg/l and iodine from other sources, i.e. 185 µg/day for adults or 96 µg/day for toddlers.

#### Risk characterisation for human health

**Reference values to be used in Risk Characterisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF** | **Correction for oral absorption** | **Value** |
| AELshort-term | Upper intake level deduced by Scientific committee on food | 600 µg/d | - | - | 0.01 mg/kg bw/d |
| AELmedium-term |
| AELlong-term |
| AEC |  |  | - | - | 1 mg/m3 (0.1 ppm) |
| ARfD | n.a. | - | - | - | - |
| ADI | n.a. | - | - | - | - |

**Maximum residue limits or equivalent**

Residue definitions

|  |  |  |  |
| --- | --- | --- | --- |
| **MRLs or other relevant reference values** | **Reference** | **Relevant commodities** | **Value** |
| AEL = UL  (Upper Intake Level) | Iodine CAR | food | Europe: 600 μg/day for adult  (0.01 mg/kg bw/d.), 200 µg/day for infant, toddler and child (1-3 years old), 250 µg/day for child of 4-6 years old8.  USA: 1200 μg/day,  0.02 mg/kg bw/d. |
| ARfD | Iodine CAR | - | Not applicable. Substance is not acute toxic or harmful. |
| Drinking water limit | Iodine CAR | water | No drinking water limit is established.  30 μg/L is a threshold proposed and calculated is based on 10% Upper Intake Level and a daily intake of 2 L drinking water |
| MRL | Competent Authorities meetings of 17 March and 17 May 2017 | Food of animal origin | No MRL required. |

The Scientific Committee on Food (SCF) based the iodine tolerable upper intake (UL) on studies of short term duration and in a small number of subjects (n=10-32). For iodine intakes about 1700-1800 μg/day, the studies showed an increased serum thyroid-stimulating hormone (TSH) and thyrotropin-releasing hormone (TRH), but these changes were considered marginal and not associated with any clinical adverse effects. The results were supported by a five years study where, for approximately similar iodine intakes, no clinical thyroid pathology occurred. An uncertainty factor of 3 was selected to derive the UL for adults. The ULs for toddlers and children were derived by adjustment of the adult UL on the basis of metabolic weight, since there is no evidence of increased susceptibility in children. The SCF adopted the value of 600 μg/day as a UL for adults including pregnant and lactating women (2002)[[9]](#footnote-9). The UL for toddlers was set at 200 µg/day.

Nevertheless, in the iodine CAR, it is reported that a healthy adult can tolerate iodine intake of more than 1000 µg/day without any adverse effects.

As indicated by the SCF, the tolerable upper intake levels ULs are not a safety threshold. Indeed, the SCF indicated that the UL “may be exceeded for short periods without appreciable risk to the health of the individuals concerned”.

Furthermore, besides the exposure due to the treatment the user is also exposed by dietary exposure. An assessment for dietary exposure is included. User is exposed to iodine through background in milk (due to natural sources and feed supplementation) and by other dietary sources. This exposure represents between 25% and 46% of the UL considering respectively the recommended dietary intake of iodine (approach proposed in the CAR) or the dietary intake values discussed recently for iodine union authorisations at the European level.

***Risk for industrial users***

No exposure is foreseen.

**Systemic effects**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake due to biocidal use**  **mg/kg bw/d** | **Estimated uptake/ AEL due to biocidal use**  **(%)** | **Biocidal use:**  **Acceptable**  **(yes/no)** | **Estimated uptake/ AEL due to biocidal use**  **+ dietary intake 46% UL (%)** | **Estimated uptake/ AEL due to biocidal use**  **+ dietary intake 25% UL (%)** |
| Scenario 1 Mixing/loading | 1 | 0.01 | 1.20 × 10⁻4 | 1.2 | Yes | 47.2 | 26.2 |
| Scenario 3  Cleaning phase | 1 | 0.01 | 7.84 × 10⁻3 | 78.4 | Yes | 124.4 | 103.4 |
| Scenario 3  Cleaning phase | 2 | 0.01 | 7.84 × 10⁻4 | 7.8 | Yes | 53.8 | 32.8 |
| Scenario 4 Cleaning phase | 1 | 0.01 | 1.60 × 10⁻3 | 16.0 | Yes | 62.0 | 41.0 |
| Scenario 4 Cleaning phase | 2 | 0.01 | 1.60 × 10⁻4 | 1.6 | Yes | 47.6 | 26.6 |

**Combined scenarios**

| **Summary table: combined systemic exposure from professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Estimated inhalation uptake (mg/kg/d)** | **Estimated dermal uptake (mg/kg/d)** | **Estimated oral uptake (mg/kg/d)** | **Estimated total uptake (mg/kg/d)** |
| Scenarios  [1, 3 & 4]  Tier 1 | n.a. | 9.56 × 10⁻3 | n.a. | 9.56 × 10⁻3 |
| Scenarios  [1, 3 & 4]  Tier 2 | n.a. | 1.06 × 10⁻3 | n.a. | 1.06 × 10⁻3 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenarios combined** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake due to biocidal use**  **mg/kg bw/d** | **Estimated uptake/ AEL due to biocidal use**  **(%)** | **Biocidal use:**  **Acceptable**  **(yes/no)** | **Estimated uptake/ AEL due to biocidal use**  **+ dietary intake 46% UL (%)** | **Estimated uptake/ AEL due to biocidal use**  **+ dietary intake 25% UL (%)** |
| Mixing/ loading and cleaning phases  Scenarios [1, 3 & 4] | 1 | 0.01 | 9.56× 10⁻3 | 95.6 | Yes | **141.6** | 120.6 |
| Mixing/ loading and cleaning phases  Scenarios [1, 3 & 4] | 2 | 0.01 | 1.06 × 10⁻3 | 10.6 | Yes | **56.6** | 35.6 |

**Local effects**

Iodine has irritant property on respiratory tract, a local risk assessment should be presented in the risk assessment part. However, as no inhalation exposure is expected for this type of formulation, no assessment is performed.

Local effects by inhalation are considered, taking into account the AEC of 1 mg/m3 (0.1 ppm) from the CAR.

**Conclusion**

The risk due to biocidal use is acceptable for professionals with gloves during the cleaning of teats and equipment.

Considering the addition of the exposure due to the dietary intake, the total exposure to iodine is inferior to the upper limit intake proposed by Scientific Committee on Food of the European Commission (SCF).

As the background value has been recently discussed (between 25% of 46% of UL) in the framework of Union authorisations, both risk assessment have been performed in this report.  
Nevertheless, the 25% value is the one agreed in the CAR.

Hence the conclusion from FRCA will be based on the agreed 25% value.

***Risk for non-professional users***

No exposure is foreseen.

***Risk for the general public***

No exposure is foreseen.

***Risk for consumers via residues in food***

The estimated dietary intakes of iodine have been compared to the relevant UL for adults (600 µg/d) and infants/toddlers (200 µg/d) and presented in the table below.

Considering the above mentioned decisions, estimated daily iodine intakes were calculated for the IODIGUARD biocide product (0.255% available iodine). Intakes which exceed the respective UL are highlighted in red text.

**Table 4 – Iodine Dietary risk assessment estimations**

|  |  |  |
| --- | --- | --- |
|  | **Adults (0.45 L/day)** | **Toddler (0.46 L/day)** |
|  | **Estimated daily intake (µg/day)**  [% of UL] | **Estimated daily intake (µg/day)**  [% of UL] |
| **2x post-milking teat disinfection (0.255% available iodine)** | | |
| Intake from milk due to teat treatment1 | 40 [6.7 % UL] | 41 [20.5 % UL] |
| Total milk intake2 | 130 [21.7 % UL] | 133 [66.5 % UL] |
| Total dietary intake3 | 315 [52.5 % UL] | 229 [114.5 % UL] |

1 Iodine intake from milk due to teat treatment is derived from BP specific residue values (based on Iwarsson 1974).

2 Total milk intake is the sum of the estimated additional iodine intake resulting from the transfer into milk following teat disinfection and the iodine background in milk of 200 µg/l.

3 Total dietary intake is the sum of the estimated additional iodine intake resulting from the transfer into milk following teat disinfection, the iodine background in milk of 200 µg/l and iodine from other sources, i.e. 185 µg/day for adults or 96 µg/day for toddlers.

*Calculation for 2x post-milking applications:*

*Percentage UL for adult= (40/600) = 6.7 % or (130/600) = 21.7 % or (315/600) = 52.5 %*

*Percentage UL for children= (41/200) = 20.5 % or (133/200) = 66.5 % or (229/200) = 114.5 %*

An exceedance of the Upper Intake Level (UL) for infant, toddler and children cannot be excluded based on the available data. At this stage, no additional refinement can be realised without any measurements of iodine residue in milk.

The Upper Intake Level (UL) is a reference value considered to compare the exposure via food estimated for the uses of IODIGUARD. As stated above, the UL is an indicative upper value exposure, but does not represent a threshold directly linked to a toxicological risk.

**Conclusion**

The estimation of iodine contamination in milk is performed considering the worst case situation. Human health risk is acceptable for all milking applications based on estimated intakes, except for toddlers, where total daily intake considerably exceeds the UL. Iodine from toddler dietary intake, arising from every other source except from iodine containing teat disinfection product residues, takes up almost the whole fraction of the UL if current EU data is used. It highlights the importance to obtain more reliable information on iodine background levels in food items in the EU, and consequently to update the data supporting the current UL.

### Risk assessment for animal health

As no guidance is currently available to assess animal health, the eCA did not perform assessment for animal health.

The Committee for Veterinary Medicinal Products (CVMP) has reviewed iodine for the use in veterinary medicine as antiseptic, sanitiser, teat dip for prevention and control of the mastitis, topical preparation for preventing wounds infections.

CVMP reported that “only small increases in serum iodine concentration were found after teat dipping indicating that the procedure had a negligible effect on tissue iodine concentrations”.

As teat dipping does not increase significantly the iodine concentration in animal tissues, it could be concluded that the use of iodine in teat disinfection does not raise systemic concerns for animal health.

### Risk assessment for the environment

|  |
| --- |
| Please notice that the risk assessment for the environment (section 2.2.8) is reported as provided by the applicant. The FR CA position is presented in **green evaluation boxes.** |

#### Effects assessment on the environment

***Background levels***

Iodine and iodine compounds are ubiquitously distributed and there is a natural cycle of iodine species in the environment. Accordingly, environmental background values as presented in the table below are likely to be encountered for soil, water and air.

|  |
| --- |
| **Infobox 1 - FR CA position:**  We agree with the following summary of background levels. These background levels cover also the iodine compounds. |

|  |  |
| --- | --- |
| **Summary table of background levels** | |
| Compartment | Background level (as iodine) |
| Soil | Typically 0.5 - 20 mg/kg dwt but with extremes up to 98 mg/kg  Global mean value of 5 mg/kg |
| Groundwater | Mean concentration: 1 µg/L  Range: < 1 - 70 µg/L with extremes up to 400 µg/L |
| Freshwater (river and lake) | 0.5 - 20 µg/L |
| Marine water | 45 - 60 µg/L |
| Rainwater | 0.1 - 15 µg/L |
| Freshwater sediment | Typically: 6 mg/kg |
| Marine sediment | Typically: 3 - 400 mg/kg |
| Air | Atmosphere: 10 - 20 ng/m3  Atmospheric concentration: over land 2 - 14 ng/m3; over ocean 17 - 52 ng/m3  Marine air contains: 100 µg/L (may refer to local inhalable air) |

**Route and rate of degradation in water:**

In water, iodide and iodate are the predominant species. In addition a natural background level of methyl iodide might also be found in water. Photolytic dissociation of these compounds can result in the formation of elemental iodine and inorganic iodine species.

Hydrolysis reaction of iodine occurs to a very small extent because iodine is sparingly soluble. Hydrolysis of I2 as the reactant is a pH-dependent dynamic equilibrium reaction with iodide (I-) and iodate (IO3) as products.

At pH values between 4 and 9, iodide is the predominant species. In alkaline and well oxidized waters iodate is the predominant specie.

In natural water/sediment system, iodide would be the predominant species under aerobic conditions. Iodine can enter sediments through accumulation of plant matter or fixation of iodide in water to humic substances. Weaker and reversible binding of iodide to inorganic components in sediments may also occur (Kd values ranging from -0.22 mL/g for chlorite minerals to 15.14 mL/g for iolite minerals).

**Route and rate of degradation in soil:**

Iodine is an element so no degradation will occur in soil.

**Adsorption/desorption:**

Lab-data:

Ka = 1.22 to 124 cm3/g (five soils); 5.8 cm3/g (geometrical mean)

Kao c = 51.3 to 3650 cm3/g (five soils)

No pH dependency

Data from open literature

Kpsusp = 220 cm3/g (geometrical mean)

Kpsoil = 0.01- 580 cm3/g; 6.9 cm3/g (geometrical mean)

Values used for the risk assessment:

Kpsusp = 220 cm3/g

Kpsoil = 5,8 cm3/g

**Fate and behaviour in air:**

Methyl iodide and molecular iodine are the predominant iodine species in air. Both iodine and methyl iodide undergo photochemical reactions to form iodine radicals, which can then go on to form a number of other iodine species through a complex series of reaction pathways.

Lifetime = 5-10 s for an overhead sun

In view of the high background values of iodine in air, emission to air resulting from application of iodine as disinfectant is not considered to be relevant.

**Distribution of iodine species in sewage treatment plants:**

When assessing the distribution of iodine species in sewage treatment plants (STP), it was established that the Simple Treat model normally used, and that resulted in a sludge retention factor of 1.93%, was not appropriate. Molecular iodine is a chemically unstable element with oxidizing properties and it is assumed that when iodine reaches the wastewater stream it will speciate into iodate and iodide. Therefore, sludge retention factors are based on literature data and laboratory and field experiments, which range between 20 and 80% retention. Considering that iodide is not highly adsorbed to sludge under typical conditions and iodate can form complexes with calcium which easily adsorb to negatively charged particle surfaces, the majority of the iodine that passes an STP will most probably not be retained in sludge and a sludge retention factor of 20% is chosen for the risk assessment (i.e. 80% of the iodine discharged to the STP remains in the effluent). Exposure to air is not considered as iodide and iodate are assumed not to be volatile.

Estimation of Kow and bioaccumulation potential for an inorganic substance such as iodine is not considered relevant.

***PNEC derivation:***

PNEC values (source: assessment report iodine PT 1,3,4,22 – 13 December 2013)

|  |  |  |
| --- | --- | --- |
| Environmental compartment | | PNEC |
| Aquatic freshwater | Surface water | 0,00059 mg/L (iodine) |
| 0,00083 mg/L (iodide) |
| 0,0585 mg/L (iodate) |
| Freshwater sediment | 0,028 mg/kg sediment |
| Aquatic marine | Seawater | 0,000059 mg/L (iodine) |
| 0,000083 mg/L (iodide) |
| 0,00585 mg/L (iodate) |
| Marine sediment | 0,0028 mg/kg sediment |
| Terrestrial | | 0,0043 mg/kg (iodide) |
| 0,0118 mg/kg (iodine) |
| 0,304 mg/kg (iodate) |
| STP | | 2.9 mg/L (iodine) |
| Groundwater | | 4,43E-03 mg/L (iodide) |
| 1,29E-02 mg/L (iodine) |
| 1,78E-02 mg/L (iodate) |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Infobox 2 -** **FR CA position:**  The following PNEC are applicable.   |  |  |  |  | | --- | --- | --- | --- | | **Summary table on PNEC** | | | | | Environmental compartment | | Iodine species | PNEC | | Aquatic, freshwater | Surface water | Iodine (I**2**) | 0.00059 mg/L | | Iodate (IO**3**-) | 0.0585 mg/L | | Iodide (I-) | 0.00083 mg/L | | Freshwater sediment | - | Not used in the risk assessment\* | | Aquatic, marine | Seawater |  | Not used in the risk assessment | | Marine sediment |  | Not used in the risk assessment | | Terrestrial | | Iodine (I**2**) | 0.0118 mg/kg wwt | | Iodate (IO**3**-) | 0.304 mg/kg | | Iodide (I-) | 0.0043 mg/kg | | STP | | Iodine (I**2**) | 2.9 mg/L | | Groundwater | |  | 0.1 µg/L\*\* |   \* According to the iodine CAR (December,2013), The PNECsediment values were calculated on the basis of the PNECaquatic values, using the equilibrium partitioning method.  PNEC(I2)sediment = 0.029 mg iodine/kg.  The natural background levels of iodine in freshwater sediments is typically 6 mg/kg. Thus, in analogy with the PNECaquatic the derived PNECsediment values are very conservative and may be regarded as unrealistic. Given that both PEC’s and PNEC’s are calculated using the partitioning equilibrium method, the derived PNEC will not be used in the risk assessment.  \*\*The PNECgroundwater proposed by the applicant are not presented in the iodine CAR (December,2013). The calculated PECgroundwater will be compared with the threshold value of 0.1 µg/L provided in the Drinking Water Directive 98/83/EC and with the natural background level of iodine. |

***Information relating to the ecotoxicity of the biocidal product which is sufficient to enable a decision to be made concerning the classification of the product is required***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Infobox 3 - FR CA position:**   |  |  | | --- | --- | | **Conclusion used in Risk Assessment – Environmental Hazards** | | | Value/conclusion |  | | Justification for the value/conclusion | - | | Classification of the product according to CLP and DSD | Based on calculation method (Guidance on the application of the CLP criteria, ECHA, version 4.1, June 2015), the following classification is proposed:   * **In accordance with the criteria in Regulation (EC) No 1272/2008:** the product is classified H412. | |

#### Exposure assessment

**General information**

IODIGUARD is applied to cows, ewes and goats teats after milking.

The route of exposure of iodine to the environment is either via application of manure/slurry to agricultural land or by release from the facility drain to an STP and subsequent compartments. Relevant receiving compartments are soil, groundwater and surface water. PEC values are reported as iodine, iodide and iodate. The reason is that it is assumed that iodine is transformed to iodide in the alkaline anaerobic conditions in the manure, whilst when it is spread and mixed into the top layer of agricultural soil it will predominantly be transformed into iodate. In the case of release via STP iodine will be transformed into iodide and iodate, depending on the redox conditions. PECsoil, PECgw and PECsw values were calculated for application to grassland and arable land, each based on phosphate and nitrogen standards. It should be noted that the nitrogen standard is the most relevant in Europe and the focus during the evaluation of iodine species is put on the nitrogen standard.

Sewage treatment plants (STP) are an important emission pathway. Release of STP effluents containing potential iodine residues leads to emissions to surface water and sediment, both freshwater and marine. Emissions to soil could arise indirectly, via the application of STP sludge and via aerial deposition. Furthermore, soil pore water concentrations as an indicator for potential groundwater levels will be assessed.

For spreading of sewage sludge on arable land it is assumed that 100% of iodine is transformed into iodate and 14% into iodide. For the calculation of PECsoil it is assumed that 100% of iodine is transformed into iodate and 14% into iodide.

Release to seawater may occur in the case of teat dip use and disinfection of milking equipment through runoff after sewage sludge application.

Accordingly, also the PEC’s calculated for freshwater and marine sediments are negligible compared to the natural background levels and not further summarised here.

The iodine concentrations in pore water of agricultural soil (after application of sewage sludge – case A) or in the pore water of cemetery soil (due to direct release from buried embalmed corpses – case B) are taken as indication of potential groundwater levels, assuming that the concentration in soil pore water is identical to the concentration in groundwater. PECgw values are thus calculated using this “pore water approach” based on PECsoil.

The biocidal product IODIGUARD is used as ready-to-use product. The IODIGUARD container is equiped with an outlet tap by screwing on the container. Teat dips are filled in with 500 mL of IODIGUARD, the top of the dip is screwed. The correct quantity of liquid to cover a teat is pushed in the top of the dip by pression on the flexible reserve flask containing IODIGUARD. After the milking, teats of cows, sheep or goats are treated with IODIGUARD by quickly dipping of the teats into the top of the dip. The top of the dip contains approximately 30 mL of IODIGUARD and it is designed in order not to allow a flow back in the reserve to avoid contaminations between cows. 8mL are enough to treat the four teats of a cow. The content of the flexible reserve flask will stay in it. IODIGUARD is moreover a viscous solution for two purposes: the first is to adhere to the teats and stay on it (the total drying time is approximately 50 minutes) and the second is to avoid any spill during manipulation by the operator. Nevertheless, for hygiene reasons mainly, operators wear simple gloves during the operation. Thus direct dermal contact is not foreseen even if the top of the dip is spilled. Each teat is quickly dipped into the solution; a cow is treated in 4 or 5 seconds. Once the teats are dipped IODIGUARD forms a droplet on the sphincter at the basis of the teat. This place is the crucial place to be protected since it is the entry point of the contaminants. The cows are then maintained walking during at least 30 minutes in order to let dry the product. Before the next milking, the potential remaining product is washed with a foaming soap and wipes in order to have disappeared for the next milking. Between two milking, the teats are thus protected from contamination by the film formed by IODIGUARD and no IODIGUARD remains during the milking.

IODIGUARD remains in contact with teat dips as a protective film (DVG, 2009). The fraction of the product remaining on teats depends on the viscosity of the solution. The worst case is used in this assessment according to ESD TP3: as a conservative approach, the fraction of disinfectant remaining on teats is considered to be 0,5.

In the various environmental compartments, the presence of different forms of iodine is largely dependant on the redox potential and pH.

* Iodide and iodate are the dominant iodine species in soil
* In water the prevalent forms of iodine are iodide and iodate
* When iodine reaches the waste water stream, it will speciate into iodate and iodide
* Kp susp and Kp soil values as stated in the List of Endpoints of the European assessment (2013)

Considering that iodide is not highly adsorbed to sludge under typical conditions and iodate can form complexes with calcium which easily adsorb to negatively charged particle surfaces, the majority of the iodide that passes an STP will most probably not be retained in sludge and a sludge retention factor of 20% is chosen for the risk assessment (ie 80% of the iodine discharges to the STP remains in the effluent).

Thus for the environmental risk assessment, the following quantities of iodine species in IODIGUARD will be considered (see also discussion “iodine compounds quantities in IODIGUARD” attached in section 13):

* In soil: 0,182% iodine, 0,182% iodide and 0,182% iodate in first intention and as a worst case
* In water: 0,182% iodine, 0,182% iodide and 0,182% iodate in first intention and as a worst case
* In waste water: 0,182% iodide and 0,182% iodate in first intention and as a worst case
* 80% of the iodine discharges to the STP remains in the effluent

According to the European assessment (2013), in view of the high background values for iodine in air, emission to air resulting from application of iodine as disinfectant is not considered to be relevant.

As the amount of iodine potentially released into the environment through biocidal uses are within the natural occurring background levels, there is no concern with respect to secondary poisoning. Thus, emissions to air and secondary poisoning will not be examined in this risk assessment.

According to ESD TP3, after dipping, two pathways are possible:

* Emission to waste water
* Emission to the slurry

According to the Iodine assessment report (2013), the route of exposure of iodine to the environment is either:

* via application of manure/slurry to agricultural land or
* by release from the facility drain to an STP and subsequent compartments.

Relevant receiving compartments are:

* soil,
* groundwater and
* surface water

To calculate the various predicted environmental concentrations, we have used:

* ESD TP3 use: disinfection for veterinary hygiene: non-medicinal teat dips:
  + Estimation of exposure of iodine to the environment via application of manure/slurry to agricultural land (based on nitrogen standard since nitrogen standard is the most relevant in Europe)
  + Calculation of the release from the facility drain to an STP
* R16 ECHA guidance document: environmental exposure estimation

The parameters used to make the calculations don’t make the difference between iodine, iodide or iodate. Actually, no additional parameter other than the AS content of the biocidal product is taken into account in the calculations. The repartition between the 3 iodine species in the environment is not clearly stated in the publicly available documents but the maximum iodine content (taking into account PVPI and KI) in IODIGUARD is 0,182% meaning 1,82 g/L. Thus, is we compare PEC values calculated for “iodine total content” and if we compare them to the lowest PNEC between the three forms of iodine, we will figure out the worst case. It will probably not be representative of the reality but it will demonstrate the absence of risk.

END CALCULATION – OUTPUT PARAMETERS / risk assessment

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|  |  | PEC | unit | PNEC used | RCR = PEC/PNEC |
| Concentration of the biocide AI in soil in the case of an immission standard for nitrogen and land application on grassland | PIECgrs-N | 0,00214813 | mg/kgwwt | 0,0043 | 0,5 |
| Concentration of the biocide AI in soil in the case of an immission standard for nitrogen and land application on arable land | PIECars-N | 0,00214813 | mg/kgwwt | 0,0043 | 0,5 |
| concentration of substance in the STP effluent | Clocal eff /PEC stp | 0,00095737 | mg/L | 2,9 | 0,0003 |
| local concentration in surface water during release episode from STP | Clocal water = PEC local water | 9,5422E-05 | mg/L | 0,00059 | 0,2 |
| predicted environmental concentration in sediment freshwater | PEClocalsed | 0,04571133 | mg/kg | 0,028 | 1,6 |
| local concentration in seewater during release episode | Clocal seawater = PEC local seawater | 9,5422E-06 | mg/L | 0,000059 | 0,2 |
| predicted environmental concentration in sediment marine water | PEClocal sed | 0,00457113 | mg/kg | 0,0028 | 1,6 |
| predicted environmental concentration in soil following spreading of sewage sludge | PEC soil | 0,00098748 | mg/kg | 0,0043 | 0,2 |
| PEC local groundwater following spreading of sewage sludge | PEC groundwater sewage sludge | 0,00018862 | mg/L | 4,43E-03 | 0,04 |
| PEC local groundwater following spreading of manure/slurry to grassland | PEC groundwater manure grassland | 0,00041032 | mg/L | 4,43E-03 | 0,09 |
| PEC local groundwater following spreading of manure/slurry to arable land | PEC groundwater manure arable land | 0,00041032 | mg/L | 4,43E-03 | 0,09 |

The only compartments found at risk in this risk assessment are the sediment compartments for marine water and freshwater. But the PEC values calculated are well below the natural background levels which are typically 6 mg/kg for freshwater and 10 times lower for marine water.

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| **Infobox 4 -** **FR CA position:**   |  |  | | --- | --- | | Assessed PT | *PT 3* | | Assessed scenarios | *Scenario 1: Teat disinfection; Liquid dipping after milking* | | ESD(s) used | *Emission Scenario Document for Product Type 3: Veterinary hygiene biocidal products, 2011* | | Approach | *Scenario 1: Average consumption* | | Distribution in the environment | *Calculated based on ECHA Guidance on the BPR Vol IV, Part B; April 2015* | | Groundwater simulation | *No models was performed* | | Confidential Annexes | *No* | | Life cycle steps assessed | *Application phase* |   The environmental risk assessment for the product is based on the emission scenario document for Product Type 3 (JRC Scientific and Technical Reports; 2011[[10]](#footnote-10)) as well as on the ECHA Guidance for Environmental Risk Assessment Vol IV, Part B (2015[[11]](#footnote-11)). |

***Fate and distribution in exposed environmental compartments***

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| **Infobox 5 -** **FR CA position:**   | **Identification of relevant receiving compartments based on the exposure pathway** | | | | | | | | | | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | |  | Fresh-water | Freshwater sediment | Sea-water | Seawater sediment | STP | Air | Soil | Ground-water | Other | | Scenario 1 | *yes* | *yes* | *no* | *no* | *yes* | *no* | *yes* | *yes* | *no* | |

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| **Infobox 6 - FR CA position:**  The table below presents the physico-chemical parameters needed for the PEC calculations.   |  |  | | --- | --- | | **Input parameters used in the environmental exposure assessments according to the CAR (December,2013)** | | | **Parameters for iodine** | Value | | Molecular mass (g.mol-1) | 253.81 | | Vapour pressure (Pa) | 40.7 | | Water solubility (mg.L-1) | 290 | | Henry’s law constant (Pa.m3.mole-1) | 34.43 | | Kpsusp: Partition coefficient solid-water in suspended matter (L/kg) | 220 | | Ksusp-water: Susp-water partition coefficient (m3/m3) | 55.9 | | Kpsoil: Partition coefficient organic carbon-water (L/kg) | 5.8 | | Ksoil-water: Soil-water partition coefficient (m3/m3) | 8.903 | | Fstp water: Fraction of emission directed to water by STP released (-) | 0.8 | | Fstp sludge: Fraction of emission directed to water by STP released (-) | 0.2 | | SLUDGERATE: Rate of sewage sludge production (kg/d) | 790 | | DT50 soil (days) | 1E06 | | **Parameters for iodide** |  | | Transformation rate in surface water iodine to iodide (%) | 100 | | Transformation rate in soil iodine to iodide via the STP (%) | 14 | | Transformation rate in soil iodine to iodide via manure (%) | 100 | | Molecular equivalent iodide/iodine | 1 | | **Parameters for iodate** |  | | Transformation rate in surface water iodine to iodide (%) | 100 | | Transformation rate in soil iodine to iodide via the STP (%) | 100 | | Transformation rate in soil iodine to iodide via manure (%) | 100 | | Molecular equivalent iodate/iodine | 1.382 | |

***Emission estimation***

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| **Infobox 7 - FR CA position:**  Regarding the environment, all forms of iodine will be examined separately since PNEC exist for each form.  In IODIGUARD formulation, two components contain either I2 or I-: PVP iodine (PVPI) present in the formulation at 1.5% w/w and potassium iodide (KI) present in the formulation at 0.05% w/w (including 0.038% of iodide).  The accelerated storage stability study shows a quantity of total iodine (I2 and I-) in IODIGUARD of 0.25% w/w. On the other hand, the potassium iodide (KI) most probably only brings iodine to the mixture under I- form. Nevertheless the quantity of iodine from KI is added to the measured quantity of iodine from PVPI in a worst case approach Thus, the quantity of the various forms of iodine in IODIGUARD is: 0.25 + 0.038 =0.29% for the environmental risk assessment.  Remark: According to the section 2.1.1 Identity, Physico-Chemical Properties & Methods of Analysis in the Assessment Report of Iodine (p.10), the identity details for PVP-iodine show the following specification compounds: 9.0-12.0% available iodine (dried substance), max 2.0% formic acid, max. 8.0% water, max. 6.0% iodide, loss on drying max 8.0%, sulphated ash max 0.1%. Thus, the PVP is used to bring iodine (I2) (9 to 12%) into the formulation in a soluble form and it released also iodide (I-) (6%). These elements demonstrate the previous approximation in the quantification of iodide (I-) in IODIGUARD product. Nevertheless, PNEC are based on ecotoxicological tests realized with PVP-iodine. So only the quantity of iodide from potassium iodide (KI) had been added to iodine measure to assess the environmental risk of IODIGUARD product uses. |

**Scenario**

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| **Infobox 8 -** **FR CA position:**  The table below presents the input parameters for the calculation of emissions to manure or STP in accordance with the characteristics of the product and the ESD for PT03[[12]](#footnote-12). It should be noted that the nitrogen immission standard is the most relevant in Europe notably in France. Therefore, regarding emission via manure application, PEC values were calculated for application to grassland and arable land on the nitrogen standard only.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Input parameters for emission calculations** | | | | | | Parameter | Nomenclature | Value | Unit | Origin | | Type of housing/manure storage (for application of the notification) | cat-subcat (i1) | 1 – Dairy cows | [-] | S (ESD Appendix 1: Table 7) | | Type of biocide | bioctype (i2) | 1 - Disinfectant | [-] | S (ESD Appendix 1: Table 7) | | Type of application | appway (i3) | 1-Dipping | [-] | S (ESD Appendix 1: Table 7) | | Relevant emission stream | stream(i4) | 1 and 3- Manure/waste water | [-] | P (Appendix 1: Table 7) | | Content of active ingredient in formulation (product) | Fbioc | 2.9 | g/L | S | | Amount of product prescribed to be used for one treatment (dipping of the four teats) of one animal | Vprod**i1,i2,i3** | 8.00E-3 | L | S | | Dilution factor (for preparation of the working solution from the formulation (product)) | F**dil** | 1 | [-] | S | | Fraction of active ingredient released | F **slurry/manure or STP** | 0.5 | [-] | D | | F **air** | 0 | [-] | D | | F**teat** | 0.5 | [-] | D | | Number of teat dipping events for one animal and one day (dipping of the four teats of one animal = one disinfectant application | Napp-teat | 2 (post milking) | [-] | D | | Number of days of lactation period | Nday-lact | 300 | [-] | D | | Number of disinfectant applications in one year | Napp-bioc | 600 | [-] | D | | Interval between two disinfectant applications | Tbioc-int | 0.5 | [-] | D | | Number of manure applications for grassland | Napp-grass | 1 | [-] | D | | Number of manure applications for arable land | Napp-arab | 1 | [-] | D | | Manure application time interval for grassland | Tgr-int | 53 | [-] | D/S (ESD-PT3, 2011; Appendix1: Table 12) | | Manure application time interval for arable land | Tar-int | 212 | [-] | D/S (ESD-PT3, 2011; Appendix1: Table 12) | | Number of animal in housing for category/subcategory i1=1 | Nanimali1 | 100 | [-] | D/S (ESD-PT3, 2011; Appendix1: Table 8) | | Amount of nitrogen per animal for category/subcategory i1=1 | Qnitrogi1 | 0.3389 | [kg.d-1] | D (ESD-PT3, 2011; Appendix1: Table 11) | | *If nitrogen immission standards are applied:* | | | | | | Nitrogen immission standard for one year on grassland | QN,grassland | 170 | [kg.ha-1] | D (ESD-PT3, 2011; Appendix1: Table 13) | | Nitrogen immission standard for one year on arable land | QN,arable\_land | 170 | [kg.ha-1] | D (ESD-PT3, 2011; Appendix1: Table 13) | | Mixing depth with soil, grassland | DEPTHgrassland | 0.05 | [m] | D | | Mixing depth with soil, arable land | DEPTHarable \_land | 0.2 | [m] | D | | Density of wet bulk soil | RHOsoilwet | 1700 | [kg.m-3] | D |   \*D: default from ESD, S: set based on product. |

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| **Infobox 9 -** **FR CA position:**  The table below presents input parameters, intermediate calculations and output needed for the PEC calculations for emission via slurry and manure.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Additional Input parameters and intermediate calculations**  **"Input parameters for emission calculations to soil via manure application"** | | | | | | Parameter | Nomenclature | Value | Unit | Origin | | Number of biocide applications during storage period for application on grassland | Napp-manuregr | 106 | [-] | O | | Number of biocide applications during storage period for application on arable land | Napp-manurear | 424 | [-] | O | | Amount of active ingredient to be used for one application | Qai-prescri1,i2,i3 | 2.32E-05 | [kg] | O | | Amount of active ingredient in relevant stream i4 after one application for all animals | Qai i1,i2,i3,i4 | 1.16E-03 | [kg] | O | | Amount of active ingredient in manure or slurry after the relevant number of biocide applications for the manure application to grassland | Qai-grassi1,i2,i3,i4 | 1.23E-01 | [kg] | O | | Amount of active ingredient in manure or slurry after the relevant number of biocide applications for the manure application to arable land | Qai-arabi1,i2,i3,i4 | 4.92E-01 | [kg] | O | | Amount of nitrogen produced during the relevant period for every relevant (sub)category of animal/housing i1 and application to grassland | Qnitrog-grassi1,i4 | 1.80E+03 | [kg] | O | | Amount of nitrogen produced during the relevant period for every relevant (sub)category of animal/housing i1 and application to arable land | Qnitrog-arabi1,i4 | 7.18E+03 | [kg] | O | | ***OUTPUT*** | | | | | | Concentration of the biocide (active ingredient) in soil in the case of immission standard for nitrogen and land application on grassland | PIECgrs-Ni1,i2,i3,i4 | 1.37E-02 | [mg.kg-1wwt] | O | | Concentration of the biocide (active ingredient) in soil in the case of immission standard for nitrogen and land application on arable land | PIECars-Ni1,i2,i3,i4 | 3.42E-03 | [mg.kg-1wwt] | O | | Local emission to a standard STP or on-site waste water treatment plant | Qai-stpi1,i2,i3,i4 = Elocalwaste water | 1.91E-03 | [kg.d-1] | O |   For the emission via the application of manure/slurry to land, according to recommendations of the BPC Ad hoc Working Group on Environmental Exposure, the revised equation to calculate PIECsoil grassland via manure application is provided below:  100 x Qai-grass i1,i2,i3,i4 x QN, grassland  PIECgrs- N i1,i2,i3,i4 =  Qnitrog-grass i1,i4 x DEPTH grassland x RHOsoil wet  In a first time, manure and slurry applications were considered only on 1 year as proposed in the ESD for PT03. However, following the European discussions, applications on 10 years have been added. It worth noting that no dissipation processes were considered over the ten years of exposure.  Consequently, in the following assessment, we will consider concentrations of the active substance after one year of manure application and also after 10 years.  Finally, according to the CAR, all considered compartment with PEC/PNEC ratio above 1 will be assessed by a comparison between PEC values and background level determined for each compartment. |

***Calculated PEC values***

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| **Infobox 10 -** **FR CA position:**  Exposure characterization  It should be noted that the nitrogen standard is the most relevant in Europe notably in France. Therefore, regarding emission via manure application, PEC values were calculated for application to grassland and arable land on the nitrogen standard only.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Summary table on calculated PEC and background levels (as iodine)** | | | | | |  | **Values for Iodine** | | **Values for Iodide** | **Values for Iodate** | | **Background** | **PEC** | **PEC** | **PEC** | | Via manure application (one year applications) | | | | | | Surface water grassland (µg.L-1)  via run-off from soil | 0.5-20 | 2.61E-01 | 2.61E-01 | 3.61E-01 | | Surface water arable (µg.L-1)  via run-off from soil | 6.54E-02 | 6.54E-02 | 9.03E-02 | | Soil grassland (mg.kgwwt ) | 0.565-22.6  extremes up to 110.74 | 1.37E-02 | 1.37E-02 | 1.89E-02 | | Soil arable (mg.kgwwt ) | 3.42E-03 | 3.42E-03 | 4.73E-03 | | Groundwater grassland (µg.L-1) | 1-70  extremes up to 400 | 2.61E+00 | 2.61E+00 | 3.61E+00 | | Groundwater arable (µg.L-1) | 6.54E-01 | 6.54E-01 | 9.03E-01 | | Via manure application (10 years applications) | | | | | | Surface water grassland (µg.L-1)  via run-off from soil | 0.5-20 | 2.61 | 2.61 | 3.61 | | Surface water arable (µg.L-1)  via run-off from soil | 6.54E-01 | 6.54E-01 | 9.03E-01 | | Soil grassland (mg.kgwwt ) | 0.565-22.6  extremes up to 110.74 | 1.37E-01 | 1.37E-01 | 1.89E-01 | | Soil arable (mg.kgwwt ) | 3.42E-02 | 3.42E-02 | 4.73E-02 | | Groundwater grassland (µg.L-1) | 1-70  extremes up to 400 | 26.1 | 26.1 | 36.1 | | Groundwater arable (µg.L-1) | 6.54 | 6.54 | 9.03 | | Via STP | | | | | | Elocal (kg/d) | 1.91E-3 | | | | | STP (mg/L) | - | 7.63E-04 | 7.63E-04 | 1.05E-03 | | Surface water (µg/L) | 0.5-20 | 7.60E-02 | 7.60E-02 | 1.05E-01 | | Soil (mg/kgwwt) | 0.565-22.6  extremes up to 110.74 | 4.72E-03 | 6.61E-04 | 6.52E-03 | | Groundwater(µg/L) | 1-70  extremes up to 400 | 8.83E-01 | 1.24E-01 | 1.22 | |

***Primary and secondary poisoning***

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| **Infobox 11 -** **FR CA position:**  As iodine is an essential element for many organisms and its absorption is regulated in animals of several taxonomic groups, estimation of bioaccumulation potential for iodine is not considered relevant. In addition, as the amounts of iodine potentially released into the environment through biocidal uses are within the natural occurring background levels, there is no concern with respect to secondary poisoning. Primary poisoning is not expected for the intended use, which is taking place indoors.  Hence the risk to birds and mammals is acceptable. |

#### Risk characterisation

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| **Infobox 12 - FR CA position:**  In addition to the classical risk assessment approach (PEC/PNEC ratios), the PEC values for iodine were compared to natural background levels to assess the environmental risk. |

***Atmosphere***

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| **Infobox 13 -** **FR CA position:**  In view of the high background values of iodine in air, emission to air resulting from application of iodine as disinfectant is not considered to be relevant. This approach is in line with the one taken in the Assessment Report. A risk assessment for the atmosphere is therefore not considered necessary. |

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| **Infobox 14 - FR CA position:**  **Risk characterization**  The risk assessments via manure and STP are summarized in the table below. It should be noted that the nitrogen standard is the most relevant in Europe notably in France. So, for emission via manure, the PEC values were calculated for application to grassland and arable land on the nitrogen standard.   |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | **Summary table on calculated PEC/PNEC and background levels (as iodine)** | | | | | | | | |  | **Values for Iodine** | | | **Values for Iodide** | | **Values for Iodate** | | |  | **Background**  (µg.L-1 or mg.kgwwt ) | **PEC**  (µg.L-1 or mg.kgwwt ) | **PEC/PNEC** | **PEC**  (µg.L-1 or mg.kgwwt ) | **PEC/PNEC** | **PEC**  (µg.L-1 or mg.kgwwt ) | **PEC/PNEC** | | **Via manure application (one year applications)** | | | | | | | | | Surface water grassland via run-off from soil | 0.5-20 | 2.61E-01 | 4.43E-01 | 2.61E-01 | 3.15E-01 | 3.61E-01 | 6.18E-03 | | Surface water arable via run-off from soil | 6.54E-02 | 1.11E-01 | 6.54E-02 | 7.87E-02 | 9.03E-02 | 1.54E-03 | | Soil grassland | 0.565-22.6  extremes up to 110.74 | 1.37E-02 | 1.16  Lower to the background level | 1.37E-02 | 3.18E+00  Lower to the background level | 1.89E-02 | 6.22E-02 | | Soil arable | 3.42E-03 | 2.90E-01 | 3.42E-03 | 7.96E-01 | 4.73E-03 | 1.56E-02 | | Groundwater grassland | 1-70  extremes up to 400 | 2.61E+00 | > 0.1 µg/L  In the background level | 2.61E+00 | > 0.1 µg/L  In the background level | 3.61E+00 | > 0.1 µg/L  In the background level | | Groundwater arable | 6.54E-01 | > 0.1 µg/L  Lower to the background level | 6.54E-01 | > 0.1 µg/L  Lower to the background level | 9.03E-01 | > 0.1 µg/L  Lower to the background level | | **Via manure application (10 years applications)** | | | | | | | | | Surface water grassland via run-off from soil | 0.5-20 | 2.61 | 4.43  In the background level | 2.61 | 3.15  In the background level | 3.61 | 6.18E-02 | | Surface water arable via run-off from soil | 6.54E-01 | 1.11  In the background level | 6.54E-01 | 7.87E-01 | 9.03E-01 | 1.54E-02 | | Soil grassland | 0.565-22.6  extremes up to 110.74 | 1.37E-01 | 1.16E+01  Lower to the background level | 1.37E-01 | 3.18E+01  Lower to the background level | 1.89E-01 | 6.22E-01 | | Soil arable | 3.42E-02 | 2.90  Lower to the background level | 3.42E-02 | 7.96  Lower to the background level | 4.73E-02 | 1.56E-01 | | Groundwater grassland | 1-70  extremes up to 400 | 26.1 | > 0.1 µg/L  In the background level | 26.1 | > 0.1 µg/L  In the background level | 36.1 | > 0.1 µg/L  In the background level | | Groundwater arable | 6.54 | > 0.1 µg/L  In the background level | 6.54 | > 0.1 µg/L  In the background level | 9.03 | > 0.1 µg/L  In the background level | | **Via STP** | | | | | | | | | STP | **-** | 7.63E-04 | 2.63E-04 | 7.63E-04 | **Not relevant** | 1.05E-03 | **Not relevant** | | Surface water | 0.5-20 | 7.60E-02 | 1.29E-01 | 7.60E-02 | 9.16E-02 | 1.05E-01 | 1.80E-03 | | Soil | 0.565-22.6  extremes up to 110.74 | 4.72E-03 | 4.00E-01 | 6.61E-04 | 1.54E-01 | 6.52E-03 | 2.15E-02 | | Groundwater | 1-70  extremes up to 400 | 8.83E-01 | > 0.1 µg/L  Lower to the background level | 1.24E-01 | > 0.1 µg/L  Lower to the background level | 1.22 | > 0.1 µg/L  In the background level |   **Conclusion:**  Concerning the risk assessment via manure application after 10 years applications:  ***In surface water***  - For iodine, iodide and iodate, PEC values in surface water are below or in the background level which indicates acceptable risks.  ***In soil***  - For iodine and iodide, PEC/PNEC values above 1 have been identified for spreading of manure. However, in the worst case the PECsoil values are below the typically background concentrations ranging from 0.565 to 22.6 mg/kg wwt.  - For iodate, PEC values in soil are all below the background level which indicates acceptable risks.  ***In groundwater***  In the risk assessment for groundwater, the PECgw values are compared with the limit value of 0.1 µg/L provided for pesticides in the Drinking Water Directive 98/83/EC. However, as iodine and iodine compounds are not xenobiotics, this threshold value can be considered as over conservative. Maximum calculated PECgw values are 26.1 µg/L for iodine /iodide and 36.1 µg/L for iodate. Although these concentrations are above the mean natural background concentration of 1 µg/L in groundwater, they are still below the maximum natural background concentration of 70 µg/L.  Concerning the risk assessment via STP:  ***In STP***  - For iodine PEC/PNEC value is below 1 which indicates acceptable risks. Iodide and iodate are not relevant for the STP.  ***In surface water***  - For iodine, iodide and iodate, PEC/PNEC values for surface water are all below 1 which indicates acceptable risks.  ***In soil***  - For iodine, iodide and iodate, PEC/PNEC values for soil are all below 1 which indicates acceptable risks.  ***In groundwater***  - For iodine, iodide and iodate, the concentrations in groundwater are all far below the maximum natural background concentration of 70 µg/L, which indicates acceptable risks. |

***Primary and secondary poisoning***

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| **Infobox 15 - FR CA position:**  As iodine is an essential element for many organisms and its absorption is regulated in animals of several taxonomic groups, estimation of bioaccumulation potential for iodine is not considered relevant. In addition, as the amounts of iodine potentially released into the environment through biocidal uses are within the natural occurring background levels, there is no concern with respect to secondary poisoning. Primary poisoning is not expected for the intended use, which is taking place indoors.  Hence the risk to birds and mammals is acceptable. |

***Mixture toxicity***

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| **Infobox 16 -** **FR CA position:**  The benzene sulfonic acid is classified H412 at a level higher than 0.1%.  According to the appendix 1 of the Transitional Guidance on mixture toxicity assessment for biocidal products for the environment, the calculation of the relative toxic units of compounds shows that the toxicity of product is principally linked (more than 95%) to the toxicity of iodine compounds. So, the benzene sulfonic acid is not considered as substance of concern in this formulation. |

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| --- | --- | --- |
| **Infobox 17- FR CA position:**   |  | | --- | | **Overall conclusion on the risk assessment for the environment of the product** | | The levels of exposure for the non-target organisms of the aquatic (STP and surface water) and terrestrial compartments following the use of the product IODIGUARD on teats are lower than the threshold values or still in the range of the background level for each compartment under the use conditions provided in the SPC.  Considering the profile of the active substance and the uses of the products on teats, the predicted concentrations in groundwater are higher than the threshold values of 0.1 µg/L provided in the Drinking Water Directive 98/83/EC, but still in the range of the background level considered acceptable under the use conditions provided in the SPC. | |

### Measures to protect man, animals and the environment

*Please see SPC.*

### Assessment of a combination of biocidal products

*Not relevant.*

### Comparative assessment

*Not relevant.*

# Annexes

## List of studies for the biocidal product

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Author(s) | Year | Title Source Company Report No. GLP or GEP Status (where relevant) Published or not | Member State Data Protection Claimed (Y/N) | **Owner** |
| A.J. Wooley  Report N°41500716 | 2015 | IODIGUARD : Determination of accelerated storage stability for PVP iodine in the biocidal product IODIGUARD | Y | Harlan |
| A.J. Wooley  Report N°41500717 | 2015 | PVP iodine : determination of long term stability | Y | Harlan |
| Morel A. | 2015 | Dosage de l’iode actif | Y | LABORATOIRE SOLUTIO |
| Thierry MERGNAT | 2011 | essai quantitatif de suspension pour l'évaluation de l'activité bactéricide des antiseptiques et désinfectants chimiques utilisés dans le domaine vétérinaire. Selon la norme NF EN 1656 de mars 2010 | Y | CTH |
| A. Morel | 2010 | Rapport d'essai NF 1656, activité bactéricide, Mars 2010 | Y | CTH |
| CTH |  | Test d’efficacité bactéricide terrain Antiseptiques et désinfectants chimiques dans le domaine vétérinaire / produit post traite | Y | CTH |
| Laboratoire Solutio | 2014 | Essai screening selon la norme NF EN 1657 (avril 2006) Dilution - Neutralisation | Y | CTH |
| N. Warren | 2015 | Iodiguard : The Bovine Corneal Opacity and Permeability (BCOP) Assay | Y | CTH |

## Output tables from exposure assessment tools

ConsExpo web data sheet: 

## Residue behaviour

Following the same approach as for the other iodine UA, which has been discussed at WG and BPC, the followings have been taken into consideration for the proposed decision on the authorisation of iodine teat disinfection products:

- The reference values for iodine of 600 µg/d for adults and 200 µg/d for children are not toxicological reference values but upper intake levels. These values have been derived with the aim of setting recommendations for intake and do not represent toxicological cut-off values for risk assessment. For trace elements like iodine, generally no toxicologically cut-off values are set. Therefore, it was agreed at Human Health Working Group II-2017 to use the upper intake levels as reference values. It is further noted that WHO derived a value of 1000 µg/d for adults but no value for children was set. The limit values used in this assessment as insecure, as opposed to conservative. The UL for children is set by extrapolation from adults, which is not optimal considering the different hormonal status between adults and children. At the moment, it is not possible to obtain a better setting of the UL due to data gaps.

- The estimated intakes are based on theoretical worst case levels of iodine in milk and were calculated based on a chronic exposure, which was considered to be the most appropriate based on how the UL was derived. Furthermore, it is noted that the SCF (from which the UL for adult and toddler are included in the CAR for iodine) also reports adapted UL values for older children. The estimated residue levels of iodine in milk are based on a worst case assessment and the data are based on short term consumption studies.

- Within Europe iodine deficiency is considered a major public health problem and iodine supplementation programs are ongoing nationally and internationally to improve the iodine intake and thereby to prevent consequences for public health, e.g. by the addition of iodine in food or salt (e.g. The Netherlands) or the advice to use iodine containing dietary supplements. Other EU countries (e.g. United Kingdom, Czech Republic) regulate adequate iodine intake through addition of iodine to cattle feed. It is recognised that both insufficient and excessive iodine intakes can cause diseases.

- The actual amount of iodine intake in the EU is highly variable and difficult to estimate, as levels of iodine intake depend on the geographical location, the soil, people’s diet, the season, farming practices, iodine fortification of feed for dairy animals, iodine supplementation programs and other factors. From iodine supplementation programs, monitoring data on iodine nutrition will become available and a clearer picture of the iodine status across Europe will emerge. It has been discussed in the CA-meeting whether the generation of additional data on residue levels from teat disinfection in milk should be requested from applicants for post-authorisation. However, in the September 2017 CA meeting it was agreed that such a requirement cannot be imposed to the applicants for product authorisation.

It can be concluded that all available data have been provided to verify the outcome and conclusions, and permit authorisation of the biocidal product family. When using the products belonging to this biocidal product family according to the conditions as stated in the SPC, the products will be efficacious and will not present an unacceptable risk to human and animal health nor the environment. So it is important to obtain more reliable information on iodine background levels in food items in the EU, and consequently to update the data supporting the current UL. Iodine exposure pathways that are not a consequence of biocidal use are outside the remit of the BPC. Where unacceptable risks are identified as a result of consideration of total dietary intake of iodine in addition to exposure arising from biocidal use, a risk management decision cannot be taken in isolation with respect to the biocides use only. It would be advisable that this issue is addressed at European level in order to ensure that all relevant regulatory bodies can be involved in agreeing a way forward. So for the background levels all sources of iodine, and not just those arising from teat treatments, would need to be taken into consideration. Therefore a wider approach for the consumer risk assessments encompassing different regulatory areas would need to be considered.

**References:**

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* Etude Individuelle Nationale des Consommations Alimentaires - 2006-2007 : http://www.anses.fr/fr/glossaire/1205.
* ECHA Note, december 2016: Union authorisation applications for iodine/PVP iodine (PT3): follow-up of the proposal for assessing animal health and consumer exposure to iodine through milk.
* Committee for Veterinary Medicinal Products – Iodine – Summary Report (1996).
* EFSA (European Food Safety Authority), 2013. Scientific Opinion on the safety and efficacy of iodine compounds (E2) as feed additives for all species: calcium iodate anhydrous and potassium iodide, based on a dossier submitted by HELM AG, EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP). The EFSA Journal, 11(2), 3101.
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* European Commission, HEEG opinion, Default human factor values for use in exposure assessments for biocidal products, 2013.
* EFSA (European Food Safety Authority), use of the EFSA comprehensive European food consumption database in exposure assessment, March 2011. EFSA Journal 2011;9(3):2097.
* EFSA ((European Food Safety Authority), Reasoned opinion on the potential chronic and acute risk to consumers health arising from proposed temporary EU MRLs, March 2007.
* EFSA (European Food Safety Authority), 2014. Scientific Opinion on Dietary Reference Values for iodine. Panel on Dietetic Products, Nutrition and Allergies (NDA). The EFSA Journal 2014;12(5):3660.
* Flachowsky G. 2007 iodine in animal nutrition and iodine transfer from feed into food of animal orifin. Lohmann information Vol 42(2), Oct 2007, page 47.
* Hemling TC. 2002, Teat condition prevention and cure through teat dips. Proceedings of the British Mastitis Conference (2002) Brockworth, p 1-14 Institute for Animal Health/Milk Development Council. Iodine CAR, available on S-CIRCABC at <https://webgate.ec.europa.eu/echa-scircabc/w/browse/4c8d9091-caf3-493d-9f81-0464337f8d4f>.
* Opinion on the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine (2002), SCF/CS/NUT/UPPLEV/26 Final.
* WHO/UNICEF (World Health Organization/United Nations Children's Fund), 2007. Iodine deficiency in Europe. A continuing public health problem.
* WHO/UNICEF (World Health Organization/United Nations Children's Fund), 2009. Iodine and inorganic iodides: Human health aspects, Concise international chemical assessment document 72.
* US Department of Health and Human Services (US HHS), 2014: Toxicological profile for Iodine, US Department of Health and Human Services (2004)

**Regulation and Guidance documents:**

* Council Regulation (EEC) No. 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. Official Journal of the European Communities, No L 224/1.
* Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. Official Journal of the European Union, L 15/1.
* EFSA (European Food Safety Authority), 2012. Guidance on Dermal Absorption. EFSA Panel on Plant Protection Products and their Residues (PPR).
* ARTFood/DRAWG (2016), draft Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products – Teat dip scenario (ongoing guidance).
* EMEA/CVMP/187/00-FINAL, note for guidance on the risk analysis approach for residues of veterinary medicinal products in food of animal origin, 2001.

## Summaries of the efficacy studies

See IUCLID files

1. Please fill in here the identifying product name from R4BP. [↑](#footnote-ref-1)
2. Pankey, J.W., Eberhardt, R.J., et al. Our Industry Today. Uptake on Post-milking Teat Antisepsis. Journal of Dairy Science, Vol. 67, No. 6, 1984. pp. 1336-1353. See Table 2. <http://cytalabs.com/wp-content/uploads/2015/01/our-industry-today-deeping-products.pdf>. [↑](#footnote-ref-2)
3. National Mastitis Council (NMC). Summary of Peer-Reviewed Publications on Efficacy of Pre-milking and Post-milking Teat Disinfectants. Published Since 1980 (revised 2014). 14 pages. <http://www.cfsph.iastate.edu/Infection_Control/Species/Teatbibliography.pdf>. [↑](#footnote-ref-3)
4. The value of 17% of total iodine is not given in the CAR because it is not part of specifications of PVPI. However, FR CA considers it is a worst case compared to using the 12% of free iodine value for risk assessment and takes into account the presence of non available iodine in PVPi. [↑](#footnote-ref-4)
5. Recommendation no. 13 of the BPC Ad hoc Working Group on Human Exposure, Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3) (Agreed at the Human Health Working Group I on 19 January 2017) [↑](#footnote-ref-5)
6. EFSA Journal 2013 ; 11(2) :3099 : Scientific opinion on the safety and efficacy of iodine compounds (E2) as feed additives for all animal species : calcium iodate anhydrous and potassium iodide, based on a dossier submitted by Ajay Europe SARL [↑](#footnote-ref-6)
7. Council Regulation (EEC) No. 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. Official Journal of the European Communities, No L 224/1. [↑](#footnote-ref-7)
8. Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. Official Journal of the European Union, L 15/1. [↑](#footnote-ref-8)
9. SCF (Scientific Committee on Food), 2002. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine. 15 pp. [↑](#footnote-ref-9)
10. JRC Scientific and Technical Reports (2011) : Emission Scenario Document for Product Type 3 - Veterinary hygiene biocidal products. EUR 25116 EN - 2011 [↑](#footnote-ref-10)
11. ECHA (2015): Guidance on the biocidal Products Regulation - Volume IV Environment - Part B Risk Assessment (active substances) Version 1.0; April 2015 [↑](#footnote-ref-11)
12. JRC Scientific and Technical Reports (2011) : Emission Scenario Document for Product Type 3 - Veterinary hygiene biocidal products. EUR 25116 EN - 2011 [↑](#footnote-ref-12)