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)



**ALGOFILM**

Product type 3

Polyvinylpyrrolidone iodine (PVPI) and L(+) lactic acid as included in the Union list of approved active substances

Case Number in R4BP: BC-MF051349-39

Evaluating Competent Authority: FR CA

Date: [28 November 2023]

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# CONCLUSION

**Introduction of the application**

France, as e-CA, received an application from Centre Technique d’Hygiène (CTH) for national authorisation for the biocidal product ALGOFILM.

The biocidal product ALGOFILM, containing 0.9 % of polyvinylpyrrolidone iodine (PVPI) and 0.08 % of L-(+)-lactic acid, is a product type (PT 3) against bacteria and yeasts for teats disinfection after milking. The biocide product is a RTU used by professional users.

**Summary and overall conclusion of the assessment**

**Conclusion****on physico-chemical and physical hazards properties**

The physico-chemical properties of the product ALGOFILM have been described and considered acceptable in the conditions of use detailed in the SPC.

The content of active substance decrease more than 10% after long-term storage stability but efficacy is demonstrated on a 12 months aged product.

Therefore, a 12 months shelf life can be granted at this step.

A new ongoing long-term storage study should be provided in post-authorization.

Analytical methods for the determination of the active substances, iodine and L-(+)-lactic acid, and the two degradation products of iodine, iodide and iodate, have been developed and validated for their determination in the biocidal product ALGOFILM.

**Conclusion on efficacy**

The product ALGOFILM has demonstrated a sufficient efficacy for the teat disinfection after milking by manual or automated dipping, as ready-to use, with a contact time of 5 minutes, against bacteria and yeasts, in the conditions of use detailed in the SPC.

**Substances of concern (SoCs)**

No substance of concern (SoC) has been identified

**Conclusion on risk for human health**

The product ALGOFILM is not classified.

The risk is considered acceptable for professional users during:

* + application by manual dipping and cleaning of the equipment
  + application by automatic dipping and cleaning of the equipment

Exposure of the general public is not relevant. The general public does not have access to the milking parlour.

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

Considering the intended use of ALGOFILM 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 exceeds Upper Limits (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 regimes would need to be considered.

**Conclusion on risk assessment for the environment**

No substance of concern has been identified for the environment. Following the application of the ALGOFILM product in post-milking only, acceptable risks are reached for Iodine and iodine compounds and for L(+)Lactic acid for all the environmental compartments and for all the uses presented in SPC.

**Overall conclusion**

The conformity to the uniform principles, as defined in the Regulation (EU) n°528/2012, for the product ALGOFILM is reported in the table below, for each use.

|  |  |  |  |
| --- | --- | --- | --- |
| **Uses** | **Doses** | **Conditions of use** | **Conclusions** |
| Bacteria  Yeasts | 2 mL product/teat (4 teats/animals equal to 8 mL product by animal  or 2 teats/animal equal to 4 ml of product by animal)  Twice a day after each milking | The ready to use product is applied after milking on dairy animals (cows, ewes or goats)  Manual or automatic application by dipping the teats  Professional users  Contact time: 5 minutes  Ambient temperature | **Acceptable** |

# ASSESSMENT REPORT

## Summary of the product assessment

### Administrative information

#### Identifier of the product

| **Identifier[[1]](#footnote-2)** | **Country (if relevant)** |
| --- | --- |
| ALGOFILM  Trade names:  TEAT FILM by CTH  IODIFILM by CTH  EPRO |  |

#### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | Centre Technique d’Hygiène (CTH) |
| **Address** | 128 avenue chateau fleury  26104 Romans sur isere  France |
| **Authorisation number** |  | |
| **Date of the authorisation** |  | |
| **Expiry date of the authorisation** |  | |

#### Manufacturer(s) of the products

|  |  |
| --- | --- |
| **Name of manufacturer** | Laboratoire Solutio |
| **Address of manufacturer** | Parc d'activités des Chasses BP147  26100 Romans sur isere  FRANCE |
| **Location of manufacturing sites** | Parc d'activités des Chasses BP147  26100 Romans sur isere  FRANCE |

#### Manufacturer(s) of the active substance(s)

|  |  |
| --- | --- |
| **Active substance** | Polyvinylpyrrolidone iodine (PVPI) |
| **Name of manufacturer** | Alcoholes Montplet, S.A |
| **Address of manufacturer** | American Iodine Company Inc.  3120 Golden Springs Drive  Plano TX 75025  United States of America |
| **Location of manufacturing sites** | Cosayach S.A. Compania de Salitre y Yodo  Amunategui 178  Santiago  Chile |

|  |  |
| --- | --- |
| **Active substance** | Polyvinylpyrrolidone iodine (PVPI) |
| **Name of manufacturer** | Alcoholes Montplet, S.A |
| **Address of manufacturer** | Norkern Limited  Bexton Lane, Knutsford  Cheshire, WA 16 9FB  United-Kingdom |
| **Location of manufacturing sites** | Cosayach S.A. Compania de Salitre y Yodo  Amunategui 178  Santiago  Chile |

|  |  |
| --- | --- |
| **Active substance** | Polyvinylpyrrolidone iodine (PVPI) |
| **Name of manufacturer** | Alcoholes Montplet, S.A |
| **Address of manufacturer** | Pantheon European Office  Norkern Limited  Julianalaan 11  3708 BA Zeist  Netherlands |
| **Location of manufacturing sites** | Cosayach S.A. Compania de Salitre y Yodo  Amunategui 178  Santiago  Chile |

|  |  |
| --- | --- |
| **Active substance** | Polyvinylpyrrolidone iodine (PVPI) |
| **Name of manufacturer** | Alcoholes Montplet, S.A |
| **Address of 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 |

|  |  |
| --- | --- |
| **Active substance** | L-(+)-lactic acid |
| **Name of manufacturer** | Jungbunzlauer S.A. |
| **Address of manufacturer** | Z.I et Portuaire, B.P. 32  67390 Marckolsheim  France |
| **Location of manufacturing sites** | Z.I et Portuaire, B.P. 32  67390 Marckolsheim  France |

|  |  |
| --- | --- |
| **Active substance** | L-(+)-lactic acid |
| **Name of manufacturer 1** | Purac Bioquimica sa |
| **Address of manufacturer 1** | Gran Vial 19-25, E-08160 Montmeló, Spain |
| **Location of manufacturing sites 1** | PURAC bioquímica  Gran Vial 19-25  E-08160 MONTMELÓ  Spain |
| **Name of manufacturer 2** | PURAC Biochem |
| **Address of manufacturer 2** | Arkelsedijk 46  NL-4206 GORINCHEM  Netherlands |
| **Location of manufacturing sites 2** | PURAC Biochem  Arkelsedijk 46  NL-4206 GORINCHEM  Netherlands |

\* Please note that company logo has been changed to *CORBION*, but pharma registrations stay under the existing legal entity names (PURAC Biochem bv and PURAC bioquimica SA). The logo change will have no impact on our pharma registrations.

### 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

|  |  |
| --- | --- |
| **Active substance 1** | |
| **ISO name** | - |
| **IUPAC or EC name** | Polyvinylpyrrolidone iodine (PVPI) |
| **EC number** | n/a |
| **CAS number** | 25655-41-8 |
| **Index number in Annex VI of CLP** | 053-001-00-3  CLP00 |
| **Minimum purity / content** | Minimum content iodine in PVPi: 9%  Purity of iodine: 995 g/kg |
| **Structural formula** |  |

|  |  |
| --- | --- |
| **Active substance 2** | |
| **ISO name** | L-(+) Lactic acid |
| **IUPAC or EC name** | (2S)-2-hydroxypropanoic acid |
| **EC number** | 201-196-2 |
| **CAS number** | 79-33-4 |
| **Index number in Annex VI of CLP** | No current Annex VI entry |
| **Minimum purity / content** | L-(+)-Lactic acid in solution of 50% w/w (SDS)  Min. purity of L-(+)-lactic acid: 95.5% w/w |
| **Structural formula** | [L-(+)-Lactic acid ≥98%](https://www.sigmaaldrich.com/catalog/product/sigma/l1750?lang=fr&region=FR) |

#### Candidate(s) for substitution

Polyvinylpyrrolidone iodine (PVPI) and L-(+) Lactic acid contained in the biocidal product are not candidates for substitution in accordance with Article 10 of BPR.

#### Qualitative and quantitative information on the composition of the biocidal product[[2]](#footnote-3)

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| --- | --- | --- | --- | --- | --- |
| PVPI | Polyvinylpyrrolidone iodine | Active substance | 25655-41-8 | N/A | 0.9 |
| Min. Iodine\* | Iodine |  | 7553-56-2 | 231-442-4 | 0.081 |
| L-(+)-lactic acid\* | (2S)-2-hydroxypropanoic acid | Active substance | 79-33-4 | 201-196-2 | 0.08 |

*\*Min. content iodine in PVPi: 9%; min. purity of lactic acid: 95.5%*

#### Information on technical equivalence

The active substance PVPI is supplied by ALCOHOLES MONPLET who is a RP participant. Technical equivalence has thus been assessed and confirmed at the active substance evaluation level.

The active substance L-(+)-lactic acid is supplied by two sources:

* Jungbunzlauer S.A. Technical equivalence has been granted by ECHA on the 9 September 2019 under the related case number BC-HL044251-48.
* Corbion Puras Bioquimica sa, which is the RP participant (as indicated in the list of Article 95) and he is the reference source of active substance for this PT.

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

No substance of concern (SoC) has been identified (refer to confidential annex for details).

#### Assessment of endocrine disruption (ED) properties of the biocidal product

The biocidal product contains the active substances Polyvinylpyrrolidone iodine and L-(+)-lactic acid, which have not yet been evaluated according to the scientific criteria set out in the Regulation (EU) 2017/2100. It will be performed at the renewal stage.

None of the co-formulants contained in the products ALGOFILM are regulatory identified as endocrine disruptors or have significant ED properties.

However, there is indication that one co-formulant has ED properties and it should be further assessed in the frame of REACH Regulation.

Hence, it is not possible to conclude whether this co-formulant should be considered to have ED properties or not before the end of the assessment. In case it is finally identified as ED, the biocidal product will be considered as ED and authorisation will have to be revised accordingly.

#### Type of formulation

|  |
| --- |
| AL- Any other liquid |

### Hazard and precautionary statements

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

| **Classification** | |
| --- | --- |
| Hazard category | - |
| Hazard statement | - |
|  | |
| **Labelling** | |
| Signal words | - |
| Hazard statements | - |
| Precautionary statements | - |
|  | |
| Note | **-** |

### Authorised use(s)

#### Use description

Table 1. Use # 1 – Teat disinfection after milking – Professional

|  |  |
| --- | --- |
| **Product Type** | PT3 - Veterinary hygiene |
| **Where relevant, an exact description of the authorised use** | Non-medical teat disinfection post-milking |
| **Target organism (including development stage)** | Bacteria  Yeasts |
| **Field of use** | The ready to use product is applied after milking on dairy animals (cows, ewes or goats) |
| **Application method(s)** | Manual or automatic application by dipping the teats |
| **Application rate(s) and frequency** | Ready-to-use  2 mL product/teat (4 teats/animals equal to 8 mL product by animal or 2 teats/animal equal to 4 ml of product by animal)  Twice a day after each milking  Contact time: 5 minutes  Ambient temperature |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Can – 20 L, opaque HDPE, hermetically closed.  Barrels – 60, 220 L, opaque HDPE, hermetically closed. |

#### Use-specific instructions for use

|  |
| --- |
| - |

#### 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

|  |
| --- |
| * Comply with the instructions for use. * Respect the conditions of use of the product (concentration, contact time, temperature, pH, etc.). * Inform the registration holder if the treatment is ineffective. * 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). |

#### Risk mitigation measures

|  |
| --- |
| * In case a combination of pre- and post-milking disinfection is necessary, using another product not containing iodine has to be considered for pre-milking disinfection. |

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

|  |
| --- |
| * IF SWALLOWED: If symptoms occur call a POISON CENTRE or a doctor. * IF ON SKIN: If symptoms occur call a POISON CENTRE or a doctor. * IF IN EYES: If symptoms occur rinse with water. Remove contact lenses, if present and easy to do. Call a POISON CENTRE or a doctor. |

#### 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. * 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. * Do not store at a temperature above 25°C. * Shelf life: 12 months * Protect from direct sunlight. |

### Other information

|  |
| --- |
| The product contains pyrrolidones derivatives. Do not use in case of known hypersensitivity. |

### 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

New data have been submitted in the purpose of product authorisation. All documents are available in section 13 of IUCLID and are listed in annex.

#### 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 (including PVP-iodine).

*Centre Technique d’Hygiène* has access to analytical methods on the active substance L-(+)-lactic acid with a Letter of Access of *Jungbunzlauer.*

## Assessment of the biocidal product

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

Table 2. Intended use # 1 – Teat disinfection after milking / Professional

|  |  |
| --- | --- |
| Product Type(s) | 3 |
| Where relevant, an exact description of the authorised use | Teat disinfection in post milking |
| Target organism (including development stage) | *Streptococcus uberis*  *Staphyloccocus aureus*  *Escherichia coli*  *Candida albicans* |
| Field of use | Indoor |
| Application method(s) | Manual application  Automatic application |
| Application rate(s) and frequency | 2 mL product/teat (4 teats/animal equal to 8 mL product by animal).  Twice a day after each milking |
| Category(ies) of user(s) | Professional |
| Pack sizes and packaging material | Can – 20L, opaque HDPE, hermetically closed.  Barrels – 60, 220L, opaque HDPE, hermetically closed. |

### Physical, chemical and technical properties

The biocidal product is an Another Liquid (AL) formulation, ready-to-use.

The product does not contain hydrocarbons or H304 co-formulant content above 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 | ALGOFILM  Batch 13001002 | Viscous brown liquid  Characteristic odour: missing data | N | A. Morel, 2015 Report N° D041-39 | Acceptable |
| Colour at 20 °C and 101.3 kPa |
| pH | CIPAC MT 75.3 | ALGOFILM  Batch 13001002 | pH of neat formulation at 25°C : 3.84 | N | A. Morel, 2015 Report N° D041-39 | Acceptable |
| Acidity / alkalinity | CIPAC MT 191 | ALGOFILM  Batch 20001421 | 0.004% w/w (as H2SO4) | - | P. Padilla, 2020  Report N°20-912017-004 | Acceptable |
| Relative density / bulk density | OECD 109 | ALGOFILM  Batch 13001002 | Density: 1.013 g/mL | N | A. Morel, 2015 Report N° D041-39 | Acceptable |
| Storage stability test – **accelerated storage** | Method validated in section 2.2.4 | ALGOFILM  Batch 20001421 | Accelerated storage procedure at 40°C for 8 weeks.   |  |  |  | | --- | --- | --- | |  | Before storage | After storage | | Appearance | Homogeneous dark brown opaque liquid with a characteristic odour | Homogeneous red brown opaque liquid with a characteristic odour | | Packaging | Black opaque HDPE can | Black opaque HDPE can\* | | L-(+)-lactic acid (% w/w) | 0.0689 | 0.0736 | | Iodine (% w/w) | 0.0911 | 0.0125 (-86%) | | Iodide (% w/w) | 0.144 | 0.215 | | Iodate (% w/w) | < 0.00079 (LOQ) | < 0.00079 (LOQ) | | Acidity (% w/w as H2SO4) | 0.004 | 0.088 |   \*: no sign of degradation or leak was observed.  A slight change of colouration of the product was noted. This is due to the degradation of iodine, responsible for the dark brown colour.  An increase in the product’s acidity was observed. This is also due to the degradation of iodine, as iodine transformation into iodide implies the formation of H+.  L-(+)-lactic acid was found to be stable after the accelerated storage procedure, indicating that its will be stable for an ambient storage of two years as well.  Unsurprisingly, the iodine content decreased significantly, because iodine is sensitive to high temperatures. Its decrease (86.3%) was greater than in the available ambient storage results (55%).  The iodide content increased, since it is the degradation product of iodine. There is a good correspondence between the lost iodine content and the increase in iodide.  The iodate content remained very low throughout the storage, below its validated LOQ of 0.00079% w/w.  Those results allow to show that the active substance L-(+)-lactic acid is expected to be stable for a period of two years of storage at ambient temperature and that the acidity (only relevant parameter not assessed in the currently available long term study) increases in accordance with the degradation pattern or iodine to reach values that remain low.  Also, iodine degrades in the most part (> 90%) into iodide. Since, in the risk assessments, both iodine and iodide have been taken into account and the total content of the two cannot increase during storage, the increasing presence of iodide in the product during storage does not cause additional unacceptable risks for human health or the environment.  Therefore, the defining factor for the shelf-life of the product will be the losses of iodine during storage, and their impact on the efficacy of the product (see long term storage below). | - | P. Padilla, 2020  Report N°20-912017-004 | Content of iodine decrease of 86% after accelerated storage.  The product should be stored at a temperature below 25°C. |
| Storage stability test – **long term storage at ambient temperature** | OECD 109 CIPAC MT 75.3  OECD 114  Titrimetric quantification of total iodine: « dosage de l’iode actif” | ALGOFILM  Batch 13001002 | The storage stability study was conducted during 24 months at ambient temperature (within the range 15 - 25 °C) in 20kg black, opaque, HDPE can   |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | **Initial** | **After 6 months** | **After 1 year in opaque HDPE** | **After 2 years in opaque HDPE** | | **Active ingredient content** (total active iodine) | 0.1030% w/w | 0.0915% w/w  (-11%) | 0.0723% w/w  (-30%) | 0.0463% w/w  (-55%) | | **Active ingredient content**  (L(+)-lactic acid) | On going | On going | On going | On going | | **Appearance** | Formulation: Viscous brown liquid.  Packaging: no signs of corrosion, degradation or seepage, no weight change. | | | | | **Density (g/mL)** | 1.013 | 1.016 | 1.016 | 1.016 | | **pH at 25°C**  Neat | 3.84 | 3.77 | 3.67 | 3.65 | | **Viscosity at 20°C**  **(mPa.s)** | 590 | 546 | 486 | 420 |   A decrease of iodine over 10% has been observed in the study. The physicochemical parameters remained acceptable throughout the storage period. Therefore, the shelf-life should be set by considering further elements attesting of the sufficient stability of the product:   * The absence of risk from the degradation products of the active substance. * The remaining of the efficacy of the product despite the loss of active substance.   As explained by the accelerated storage results summarised above, iodine degrades into iodide. Since the risk assessments already consider the sum of the iodide and iodine contents, the transformation of iodine into iodide is covered and no additional risk for human health of the environment occurs during the storage of the product.  As regards the efficacy, a test on an aged sample of 12 months was performed. This test is summarised in section 2.2.5 of this PAR. From this, it can be considered that the product is still efficacious after one year of storage. | N | A. Morel, 2015 Report N° D041-39 | A shelf life study of 12 months is proposed by the applicant.  There is no significant change in the physical and chemical properties of the formulation ALGOFILM after 2-year storage at ambient temperature.  The total iodine content decreased significantly after 2 years (-55%). Monitoring method of L-(+)-lactic acid content during storage is on going, the final report will be provided when it is available. Based on accelerated storage (see above), the content of L-(+)-lactic acid is not expected to decrease higher than acceptable limits.  A new long term storage study is on-going and should be provided in post-authorization.  Efficacy isdemonstrated on the product after 6 months storage with a dilution of 80%, which correspond to 0.073% of active substance (equivalent to as the degradation of 12 months storage product). The fate of iodine over time in the biocidal product could be explain in the following way:  The biocidal products is formulated with Iodine (I2) and Iodide (I-). Iodate (IO3-) is not present. Iodine reduces over time to Iodide. In conclusion, Iodine, Iodide and Triiodide are expected to be the predominant species in the formulation ALGOFILM after 1 and 2-year storage at ambient temperature. A study is currently ongoing to quantify these three iodine forms in the formulation after storage, the report will be provided when it is available.  Efficacy is demonstrated on a product after 12months storage (see efficacy section 2.2.5).  Therefore, a 12 months shelf life can be granted at this step  Viewing the results of accelerated storage, the content of iodine decrease while content of iodide increase, as the acidity (see justification above). |
|  | Gifap monograph no.17 | ALGOFILM | A second study, which is ongoing, aims at assessing the stability of the missing parameters from the first study. The following elements will be determined before and after storage:   * L-(+)-lactic acid content. * Iodine content. * Iodide content. * Iodate content. * Acidity.   An accelerated storage study which assesses the stability of these parameters is already available, as is a long term study measuring the iodine content over time. Hence, this new long term study’s main purpose is to confirm the results of the aforementioned studies. |  |  | On going |
| Storage stability test – **low temperature stability test for liquids** |  |  |  |  |  | This study is not provided.  Therefore, the product should be protected from frost. |
| 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. |  |  | Acceptable  Protect from direct sunlight. |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** |  |  | See “Storage stability test – **accelerated storage**”  The effect of humidity is not relevant because the product is a water-based formulation stored in an impermeable plastic packaging.  Temperature has an adverse effect on the iodine content. The product should not be stored at temperatures exceeding 30°C. |  |  | Acceptable |
| 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”**  The accelerated/long-term storage was performed in commercial packaging (HDPE) no signs of corrosion, degradation or seepage and no weight change were recorded. Therefore, the packaging is suitable. |  |  | Acceptable |
| Wettability |  |  | Not relevant for a liquid formulation. |  |  |  |
| Suspensibility, spontaneity and dispersion stability |  |  | Not relevant for a ready-to-use formulation. |  |  |  |
| Wet sieve analysis and dry sieve test |  |  | Not relevant for a liquid formulation. |  |  |  |
| Emulsifiability, re-emulsifiability and emulsion stability |  |  | Not relevant. |  |  |  |
| Disintegration time |  |  | Not relevant for a liquid formulation. |  |  |  |
| Particle size distribution, content of dust/fines, attrition, friability |  |  | Not relevant for a liquid formulation. |  |  |  |
| Persistent foaming |  |  | Not relevant for a ready-to-use formulation. |  |  |  |
| Flowability/Pourability/Dustability |  |  | Not relevant for a liquid formulation. |  |  |  |
| 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 (the formulation is not intended to be co-applied with other substances, mixtures or biocidal or non-biocidal products). |  |  |  |
| Chemical compatibility |  |  | Not relevant (the formulation is not intended to be co-applied with other substances, mixtures or biocidal or non-biocidal products). |  |  |  |
| Degree of dissolution and dilution stability |  |  | Not relevant for a ready-to-use formulation. |  |  |  |
| Surface tension | OECD 115 | ALGOFILM  Batch 17001724 | 65.6 mN/m for a 1g/L solution at 20°C (mean of 6 measurements) | Y | Servajean, E., 2018  Report N°17-26-126-ES | Acceptable  The formulation has no surface-active properties. |
| Viscosity | OECD 114 | ALGOFILM  Batch 17001724 | |  |  | | --- | --- | | **Kinematic viscosity at 20°C**  (mean of 3 measurements) | 3296.4 mm2/s | | **Kinematic viscosity at 40°C**  (mean of 3 measurements) | 1574.6 mm2/s | | Y | Servajean, E., 2018  Report N°17-26-126-ES | Acceptable |

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| --- |
| **Conclusion on the physical, chemical and technical properties of the product** |
| The formulation ALGOFILM is an Another Liquid (AL) formulation, ready-to-use. All studies have been performed in accordance with the current requirements of the Biocidal Products Regulation. The appearance of the product is that of a viscous brown liquid. The product is not classified regarding any physical hazards.  A shelf-life of one year could be proposed after the consideration of all available information:   * The physicochemical parameters of the product were observed to be stable or to vary in proportions that will not prevent the proper use of the product. * L-(+)-lactic acid was found to be stable in an accelerated storage study. * The iodine content decreases by more than 10% during storage. * Its degradation product, iodide, has already been considered in the risk assessments. * The aged product is still efficacious at a dilution corresponding to the iodine concentration in the product after one year of storage.   Efficacy is demonstrated on a product after 12 months storage (see efficacy section 2.2.5).  Therefore, a 12 months shelf life can be granted at this step.  The ongoing long-term storage study should be provided in post-authorization.  **Implication concerning labelling for the product:**  Protect from frost.  Protect from direct sunlight.  Store at a temperature below 25°C.  Shelf life: 12 months. |

### Physical hazards and respective characteristics

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **GLP** | **Reference** | **Comments** |
| --- | --- | --- | --- | --- | --- | --- |
| Explosives | Statement |  | Waived on the basis of the functional groups present in the constituents of the product.  (The product does not contain any component classified regarding this physical hazard, it is thus not classified for this physical hazard).  Moreover, as the product is a water-based formulation (see details in confidential annex), it is not expected to have explosive properties |  |  | Acceptable  According to CLP regulation, product is not expected to have explosive properties. |
| Flammable gases |  |  | Not relevant |  |  |  |
| Flammable aerosols |  |  | Not relevant |  |  |  |
| Oxidising gases |  |  | Not relevant |  |  |  |
| Gases under pressure |  |  | Not relevant |  |  |  |
| Flammable liquids | Statement |  | Waived on the basis of the classification of each co-formulant, the product does not contain any component classified regarding this physical hazard, it is thus not classified for this physical hazard).  As no co-formulant has a flash point under 150°C, the product is not expected to have flammable properties.  Moreover, as the product is a water-based formulation (see details in confidential annex), it is not expected to have flammable properties |  |  | Acceptable  According to CLP regulation, product is not expecting to have flammable properties. |
| Flammable solids |  |  | Not relevant |  |  |  |
| Self-reactive substances and mixtures | Statement |  | Waived on the basis of the functional groups present in the constituents of the product.  (see details in confidential annex) |  |  | Acceptable |
| Pyrophoric liquids | Statement |  | Waived on the basis of the classification of each co-formulant  The product does not contain any component classified regarding this physical hazard, it is thus not classified for this physical hazard. (see details in confidential annex) |  |  | Acceptable.  Based on the fact that the product is water based, no pyrophoric properties is expected. |
| Pyrophoric solids |  |  | Not relevant |  |  |  |
| Self-heating substances and mixtures |  |  | Not relevant, the product is liquid. |  |  | Acceptable |
| Substances and mixtures which in contact with water emit flammable gases | Statement |  | Waived on the basis of the classification of each co-formulant  The product does not contain any component classified regarding this physical hazard and is already a water based product, it is thus not classified for this physical hazard. (see details in confidential annex)  Moreover, as the product is already a water-based formulation (see confidential annex), it is not expected to react with water. |  |  | Acceptable.  Based on the fact that the product is water based, no classification for this hazard is expected. |
| Oxidising liquids | Statement |  | Waived on the basis of the classification of each co-formulant  The product does not contain any component classified regarding this physical hazard, it is thus not classified for this physical hazard. (see details in confidential annex) |  |  | Acceptable  According to CLP regulation, product is not expecting to have oxidising properties. |
| Oxidising solids |  |  | Not relevant |  |  |  |
| Organic peroxides |  |  | Not relevant |  |  | Acceptable, the product does not contain any organic peroxide. |
| Corrosive to metals | UN Test C.1 Section 37.4 of UN-MTC according to CLP regulation | IODIGUARD - LOT 16001693 | ALGOFILM is used for teat disinfection and does not contain any substance classified for such hazard.  A test was performed with a similar formulation, IODIGUARD (property of CTH company),  Mass loss of aluminum specimen after 7-day exposure: 0,4%  Mass loss of steel specimen after 7-day exposure: 1,1%  For Aluminium and Steel specimen no corrosion phenomena occurred (mass loss in all cases less than 13.5% for an exposure time of 7 days).  Only a small uniform corrosion was detected (no pitting corrosion)  According to the UN Test C.1 classification criteria, the test is considered negative. The formulation IODIGUARD is not classified as corrosive to metals. | N | Conte E., 2016 | The product IODIGUARD was tested.  The content of iodine is a little higher in IODIGUARD (min. 1,13% vs. 0,089% in ALGOFILM) and the pH is almost the same (4,0 for IODIGUARD, 3,84 for ALGOFILM).  Therefore, ALGOFILM is not expected to be classified corrosive to metals according to CLP regulation.  Please refer to the Confidential annex for further comments. |
| Auto-ignition temperatures of products (liquids and gases) | Statement |  | Waived on the basis of the composition of the product.  (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 |  |  |  |

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| **Conclusion on the physical hazards and respective characteristics of the product** |
| The product is not classified regarding any physical hazards. |

### Methods for detection and identification

**Iodine**

**Analytical method for determination of iodine in the biocidal product**

Stability studies have been performed at two different laboratories: Laboratoire Solutio and Défitraces. Both laboratories have validated the method used for determination of the iodine content in the Algofilm product.

Method from Laboratoire Solutio

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.

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| **Report:** | Morel A., 2015 |
| Title: | Rapport sur les essais de stabilité : ALGOFILM |
| Document No | - |
| Test facility | Laboratoire Solutio  BP 147 – Les Chasses – 26100 ROMANS SUR ISERE - 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:**

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| --- | --- | --- |
| 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 = 1.1% < 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% |

Method from Défitraces

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| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of diode in IODIGUARD |
| Document No | 20-912017-002 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

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| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of diode in ALGOFILM |
| Document No | 20-912017-006 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

The validation of the method for the determination of iodine in the Algofilm was performed in two steps. First, a full validation was performed on the product Iodiguard, whose composition is close to that of the Algofilm (H. Ricau, 2020, Report No. 20-912017-002). This validation included the determination of the linearity, specificity, accuracy and precision of the method. Then, an additional validation was carried out on the Algofilm by assessment of the specificity and accuracy of the method on this test item (H. Ricau, 2020, Report No. 20-912017-006).

*Principle of the method*

Iodine is analysed and quantified by titration with sodium thiosulfate:

I2 + 2 Na2S2O3 🡪 2 NaI + Na2S4O6.

A quantity of about 4.0 g of the test item was weighed into a 250-mL beaker. Volumes of 10 mL of a potassium iodide solution at 10% and 100 mL of buffer solution at pH 5 were added. The solution was magnetically stirred until homogenisation. The solution was titrated with a sodium thiosulphate solution at 0.005N and the values of the potential were taken at each addition. The point of equivalence was indicated by a potential jump.

*Validation of the analytical method*

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| **Test item = Iodiguard** | |
| Linearity | 5 concentrations were analysed. Linearity was shown between 2.01 and 6.12 mg of iodine.  Calibration curve: Veq = 1.5776 x Q + 0.0473  r = 0.9998 |
| Precision | The precision was determined by analysing five test item solutions. The content of diiode for each analysis was calculated. Then, the average value of the content, the standard deviation and the Relative Standard Deviation (R.S.D.) were calculated.  Mean = 0.105% w/w  RSD = 0.66% < Horwitz value = 3.76% |
| **Test item = Algofilm** | |
| Specificity | To define the specificity of the analytical method, the following solutions were analysed:  - Solvent blank  - Formulation blank  - Formulation blank with L-(+)-lactic acid  - Reference item  - Test item  For the reference item and the test item, nearly the same volume of the sodium thiosulfate solution at 0.005N was necessary to reach the end point of the titration. For the solvent blank and the formulation blanks, a volume of reagent was found during the titration with the sodium thiosulfate solution at 0.005N. As these volumes were less than 3% of the volume found during the titration of the test item this volume was not taken into account in the calculation  Solvent blank: 0.1mL  Test item: 4.8mL  Reference item: 7mL |
| Accuracy | To define the accuracy of the method, two reconstituted samples of the test item were analysed.  The mean recovery was found to be 101.9%. |

**Analytical method for determination of iodide in the biocidal product**

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| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of iodide in IODIGUARD |
| Document No | 20-912017-001 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

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| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of iodide in ALGOFILM |
| Document No | 20-912017-007 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

Iodide is an impurity of PVPI. It is also a degradation product of iodine, which naturally transforms into iodide. The determination of iodide in the biocidal product is therefore relevant.

The validation of the method for the determination of iodide in the Algofilm was performed in two steps. First, a full validation was performed on the product Iodiguard, whose composition is close to that of the Algofilm (H. Ricau, 2020, Report No. 20-912017-001). This validation included the determination of the linearity, specificity, accuracy, precision and LOQ of the method. Then, an additional validation was carried out on the Algofilm by assessment of the specificity and accuracy of the method on this test item (H. Ricau, 2020, Report No. 20-912017-007).

*Principle of the method*

The total content of iodide is analysed after extraction from the formulation and quantified by liquid chromatography using a reverse phase column and a UV detector after conversion of iodine into iodide using sodium thiosulfate in excess.

Iodide content in the test item is calculated by subtracting iodine content (determined by using the method described above) from the total iodide determined.

A quantity of about 0.25 g of the test item was weighed (to the nearest 0.01 mg) into a 20-mL volumetric flask. A volume of 0.4 mL of the sodium thiosulfate 0.1N solution was added and the volume was made up with water. The solution was manually stirred.

*Instrumental analysis*

|  |  |  |
| --- | --- | --- |
| Liquid chromatographic conditions | | |
| Column | Type | Phenomenex |
| Phase | Luna Omega 3 µm Polar C18 |
| Length (cm) | 25 |
| Internal diameter (mm) | 4.6 |
| Granulometry (µm) | 3.0 |
| Detector | Type | Ultraviolet absorption |
| Wavelength (nm) | 220 |
| Mobile phase | Eluent A: Buffer solution at pH 6  Eluent B: Acetonitrile |
| Flow (mL/min) | |  |  |  |  | | --- | --- | --- | --- | | Time  (*min*) | Eluent A  *(%)* | Eluent B  *(%)* | Flow (*mL/min*) | | 0 | 80 | 20 | 0.4 | | 10 | 80 | 20 | 0.4 | |
| Volume injected *(µL)* | 5 |
| Oven | Temperature *(°C)* | 25 |
| Retention time (min) | | About 7.2 |

*Validation of the analytical method*

|  |  |
| --- | --- |
| **Test item = Iodiguard** | |
| Linearity | 5 concentrations were analysed. Linearity was shown between 6.76 and 69.85 mg/L of iodide.  Calibration curve: A = 2.43E+05 x C - 1.38E+04  r = 0.9999 |
| Precision | The precision was determined by analysing five test item solutions. The content of iodide for each analysis was calculated with the calibration curve. Then, the average value of the content, the standard deviation and the Relative Standard Deviation (R.S.D.) were calculated.  Mean = 0.158% w/w  RSD = 0.92% < Horwitz value = 3.54% |
| LOQ | 0.09 mg/L |
| **Test item = Algofilm** | |
| Specificity | To define the specificity of the analytical method, the following solutions were analysed:  - Solvent blank  - Formulation blank  - Formulation blank with L-(+)-lactic acid  - Reference item  - Test item  No peak was observed in the solvent blank and in the formulation blank near the retention time of iodide peak.  No additional peak appears in the reference item and in the test item near the retention time of iodide peak.  The specificity is therefore demonstrated.  Chromatograms were provided. |
| Accuracy | The accuracy was determined by analysing two spiking solutions The content of iodide for each analysis was calculated with the calibration curve.  The mean recovery was found to be 100.8%. |

**Analytical method for determination of iodate in the biocidal product**

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| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of iodate in IODIGUARD |
| Document No | 20-912017-003 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

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| --- | --- |
| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of iodate in ALGOFILM |
| Document No | 20-912017-008 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

Iodate can be a degradation product of iodine. Since it was chosen to follow its content in stability studies (accelerated and ambient studies), the analytical method used for its determination in the product was validated.

The validation of the method for the determination of iodate in the Algofilm was performed in two steps. First, a full validation was performed on the product Iodiguard, whose composition is close to that of the Algofilm (H. Ricau, 2020, Report No. 20-912017-003). This validation included the determination of the linearity, specificity, accuracy, precision and LOQ of the method. Then, an additional validation was carried out on the Algofilm by assessment of the specificity and accuracy of the method on this test item (H. Ricau, 2020, Report No. 20-912017-008).

*Principle of the method*

Iodate is analysed and quantified by ionic chromatography using conductimetric detection.

A quantity of about 0.8 g of the test item was weighed (to the nearest 0.01 mg) into a 25-mL volumetric flask and the volume was made up with water for HPLC. The solution was manually stirred.

*Instrumental analysis*

|  |  |  |
| --- | --- | --- |
| Ionic chromatographic conditions | | |
| Gard column | Type | Thermoscientific |
| Phase | Ion Pac AG20 |
| Length (cm) | 5.0 |
| Internal diameter (mm) | 2.0 |
| Granulometry (µm) | 7.5 |
| Column | Type | Thermoscientific |
| Phase | Ion Pac AG20 |
| Length (cm) | 25 |
| Internal diameter (mm) | 2.0 |
| Granulometry (µm) | 7.5 |
| Detector | Type | Conductimetric |
| Mode | Anionic |
| Mobile phase | |  |  | | --- | --- | | Time  (*min*) | Concentration  KOH  *(mM)* | | 0 | 25.0 | | 10 | 25.0 | | 11 | 10.0 | | 22 | 10.0 | | 23 | 2.5 | | 45 | 2.5 | |
| Flow (mL/min) | 0.35 |
| Volume injected *(µL)* | 50 |
| Oven | Temperature *(°C)* | 35 |
| Retention time (min) | | About 8.0 |

*Validation of the analytical method*

|  |  |
| --- | --- |
| **Test item = Iodiguard** | |
| Linearity | 5 concentrations were analysed. Linearity was shown between 0.27 and 3.71 mg/L of iodate.  Calibration curve: A = 1.85E-01 x C - 7.36E-03  r = 0.9997 |
| Precision | The precision was determined by analysing five test item solutions. The content of the iodate for each analysis was calculated with the calibration curve.  Then, the average value of the content, the standard deviation and the Relative Standard Deviation (R.S.D.) were calculated.  Mean = 0.00097% w/w  RSD = 4.01% < Horwitz value = 7.62 % |
| LOQ | 0.25 mg/L |
| **Test item = Algofilm** | |
| Specificity | To define the specificity of the analytical method, the following solutions were analysed:  - Solvent blank  - Formulation blank  - Reference item  - Test item  Retention times for iodate between reference item and test item confirm the identity of the analyte.  A trace of iodate was detected in the formulation blank. As this trace of iodate was less than the LOQ value (0.00079% w/w), this trace was not considered to be interfering peak for the analysis.  An unknown peak appears in the reference item, the formulation blank and the test item near the peak of iodate. As the calculation of the resolution between the unknown peak and the iodate peak was more than 1.5, the unknown peak were not considered to be interfering peaks for the analysis.  No other interference was observed in the solvent blank, the reference item, the formulation blank and the test item at the retention time of iodate. Chromatograms were provided.  Therefore, the analytical method showed a good specificity for analysis of iodate in ALGOFILM. |
| Accuracy | Accuracy was checked by analysis of two spiked solutions at LOQ and 10LOQ level with iodate reference item.  The recoveries were equal to 90.8% and 107.6% (mean 99.2%). |

**Analytical method for determination of L-(+)-lactic acid in the biocidal product**

|  |  |
| --- | --- |
| **Report:** | Ricau H., 2020 |
| Title: | Validation of the analytical method for the determination of L-(+)-lactic acid (CAS [79-33-4]) in ALGOFILM |
| Document No | 20-912017-005 |
| Test facility | DEFITRACES  Z.A. des Andrés  150, rue Pré-Magne  69126 BRINDAS  FRANCE |
| Guidelines: | - |
| GLP | Yes |

A method for the determination of L-(+)-lactic acid in the Algofilm has been validated by assessment of the linearity, specificity, accuracy and precision of the method (H. Ricau, 2020, Report No. 20-912017-005).

*Principle of the method*

L-(+)-lactic acid is analysed after extraction from the formulation and quantified by liquid chromatography using a reverse phase column and a UV detector.

A quantity of about 1.0 g of the test item was weighed (to the nearest 0.01 mg) into a 10-mL volumetric flask and the volume was made up with a sulfuric acid 1N solution. The solution was manually homogenised. The flask was put in a water-bath between 85 °C and 90 °C for 1 hour then the solution was left to stand at room temperature. An aliquot was filtered on a 0.45-μm nylon filter before analysis.

*Instrumental analysis*

|  |  |  |
| --- | --- | --- |
| Liquid chromatographic conditions | | |
| Column | Type | Phenomenex |
| Phase | Synergi 4µm Hydro-RP 80A |
| Length (cm) | 25 |
| Internal diameter (mm) | 4.6 |
| Granulometry (µm) | 4.0 |
| Detector | Type | Ultraviolet absorption |
| Wavelength (nm) | 210 |
| Mobile phase | buffer phosphate pH 2.8 solution |
| Flow (mL/min) | 0.8 |
| Volume injected *(µL)* | 20 |
| Oven | Temperature *(°C)* | 15 |
| Retention time (min) | | About 6.1 |

*Validation of the analytical method*

|  |  |
| --- | --- |
| Linearity | 5 concentrations were analysed. Linearity was shown between 39.85 and 121.15 mg/L of L-(+)-lactic acid.  Calibration curve: 4.40E+03 x C - 1.71E+03  r = 0.9998 |
| Precision | The precision was determined by analysing twice five test item solutions. The content of L-(+)-lactic acid for each analysis was calculated with the average value of the response factor of the two calibration solutions bracketing the test item. Then, the average value of the content, the standard deviation and the Relative Standard Deviation (R.S.D.) were calculated.  Mean = 0.072% w/w  RSD = 1.08% < Horwitz value = 3.98% |
| Specificity | To define the specificity of the analytical method, the following solutions were analysed:  - Solvent blank  - Formulation blank  - Reference item  - Test item  No peak appears in the solvent blank and in the formulation blank near the peak of L-(+)-lactic acid.  In the reference item and in the test item, the peak at the retention time at about 6.128 min represents L-(+)-lactic acid.  No additional peak appears in the reference item and in the test item near the peak of L-(+)-lactic acid.  Chromatograms were provided. The specificity is therefore defined. |
| Accuracy | The accuracy was determined by analysis of two reconstituted test items.  Mean recovery = 98.0%. |

**Analytical methods for determining relevant components and/or residues of iodine 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 supporting 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). | 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

**Analytical methods for determining relevant components and/or residues of L-(+)-lactic acid in different matrices**

According to the Assessment Report on L-(+)-lactic acid (Germany, June 2017), relevant residues in food of plant and animal origin and in the environmental compartments arising from the application of L-(+)-lactic acid are not expected. Therefore, residue analytical methods for L-(+)-lactic acid in food of plant and animal origin, in soil, air, drinking and surface water are not required. Since L-(+)-lactic acid is not classified as toxic or very toxic, analytical methods in body fluids and tissues are not required.

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| **Conclusion on the methods for detection and identification of the product** |
| Analytical methods for the determination of the active substances, iodine and L-(+)-lactic acid, and the two degradation products of iodine iodide and iodate have been developed and validated for their determination in the biocidal product ALGOFILM. |

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| **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.  Analytical methods for the determination of L-(+)-lactic acid residue in soil, air, drinking and surface water, as well as in food and feeding stuffs and in animal are not required since no residues is expected in those matrices.  Iodine and L-(+)-lactic acid are not toxic (T) or very toxic (T+) active substances. 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 ALGOFILM is intended to be used as ready-to-use bactericide and yeasticide product for teats disinfection after milking, for professional users.

The frequency of application is twice a day.

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

The product ALGOFILM 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.

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

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

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).

#### 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.

Concerning L(+) lactic acid Assessment Report June 2017), this acid exists in solution in a pH-dependent equilibrium between the non-dissociated and dissociated form. Only in its non-dissociated state, the acid is able to go through the cell membrane. At a relatively low pH, the uncharged acid enters the cell. Inside the cell, the L(+) lactic acid dissociates due to the higher pH. The molecules remain inside the cell, because the resulting ions cannot go through the membrane. The pH inside the cell is lowered and metabolic reactions are inhibited.

Further effects are also reported, such as decrease of the membrane permeability for amino acids, organic acids, phosphates resulting in uncoupling of both substrate transport and oxidative phosphorylation from the electron transport system. Furthermore, an inhibition of the glycolysis by the lactate ion is observed.

ALGOFILM is effective after a contact time of 5 minutes at the application rate used against target organisms.

#### Efficacy data

Laboratory studies were conducted with the product ALGOFILM in accordance with the guidance on the Biocidal Products Regulation, Volume II Efficacy – Assessment and Evaluation (Parts B+C).

The results are summarized in Section 6.7 of the IUCLID file and the main points 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 | PT3  Teat disinfection | ALGOFILM  (0.9% of PVPI, 0.08% lactic acid) | *Streptococcus uberis*  *Staphylococcus aureus*  *Escherichia coli* | EN 1656 (March 2010) | Phase 2 step 1 test (suspension test)  Concentration tested: 10%, 40%, 60% and 80%  Temperature: 30°C  Contact time: 5 min  Interfering substance: 10 g/L skimmed milk  Criteria: at least a 5 log reduction | Bactericidal activity demonstrated at 40% v/v | Rapport d'essai NF EN 1656\_ Activité bactéricide  RI : 1 |
| Yeasticide | PT3  Teat disinfection | *ALGOFILM*  *(0.9% of PVPI, 0.08% lactic acid)* | *Candida albicans* | EN 1657 (May 2016) | Phase 2 step 1 test (suspension test)  Concentration tested: 50% and 80%  Temperature: 30°C  Contact time: 5 min  Interfering substance: 10 g/L skimmed milk  Criteria: at least a 5 log reduction | Yeasticidal activity is demonstrated at 50% v/v | Rapport d'essai NF EN 1657\_ Activité fongicide  RI : 1 |
| Bactericid*e* | PT3  Teat disinfection | *ALGOFILM (0.9% of PVPI, 0.08% lactic acid)*  *fresh sample* | *Streptococcus uberis Staphylococcus aureus Escherichia coli* | prEN17422 (June 2020) | Phase 2 step 2 test (surface test)  Concentration tested: 10% – 80% – 100%  Temperature: 30°C  Contact time: 5 min  Interfering substance: 1% skimmed milk powder  Criteria: at least a 4 log reduction | Bactericidal activity demonstrated at 80% v/v | LMH Efficacy test for bactericidal activity according to prNF EN17422 (june 2020) – No6166-1 – AF Gabillet  RI : 1 |
| Bactericide | PT3  Teat disinfection | *ALGOFILM (0.9% of PVPI, 0.08% lactic acid)*  *6 months aged sample* | *Streptococcus uberis Staphylococcus aureus Escherichia coli* | prEN17422 (June 2020) | Phase 2 step 2 test (surface test)  Concentration tested : 10% – 80% – 100%  Temperature: 30°C  Contact time: 5 min  Interfering substance: 1% skimmed milk powder  Criteria: at least a 4 log reduction | Bactericidal activity demonstrated at 80% v/v | *LMH Efficacy test for bactericidal activity according to prNF EN17422 (June 2020) – No6165-1 – AF Gabillet*  RI : 1 |
| Bactericide | PT3  Teat disinfection | *ALGOFILM (0.9% of PVPI, 0.08% lactic acid)*  *12 months aged sample* | *Streptococcus uberis Staphylococcus aureus Escherichia coli* | prEN17422 (June 2020) | Phase 2 step 2 test (surface test)  Concentration tested: 10% – 80% – 100%  Temperature: 30°C  Contact time: 5 min  Interfering substance: 1% skimmed milk powder  Criteria: at least a 4 log reduction | Bactericidal activity demonstrated at 80% v/v | *LMH Efficacy test for bactericidal activity according to prNF EN17422 (June 2021) – No6452-1– AF Gabillet*  RI : 1 |

* 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 min and skimmed milk (1%), showing the efficacy of the product at 40% v/v against bacteria and 50 % v/v against yeasts.
* Phase 2, step 2 tests have been performed for bactericidal activity, according to the requirements of the norm prEN 17422, on artificial skin by the method “drop/dip”. Efficacy of the product ALGOFILM is demonstrated at 30°C with a contact time of 5 min and skimmed milk, at 80% v/v.

In absence of phase 2 step 2 test available for yeasticidal activity, results from phase 2 step 1 test (EN 1657) are acceptable for the time being.

Since the active substance concentration Iodine decreases with more than 10% during shelf-life of the biocidal product ALGOFILM, at ambient temperature, additional efficacy tests have been performed with aged products. Additional phase 2 step 2 tests prEN 17422 performed with 6 and 12 months aged product, have been submitted. Indeed, according to EFF TAB v2.1 (WGV2018): “*If the active substance concentration decreases with more than 10% during shelf life of the biocidal product, efficacy tests should be performed demonstrating efficacy of stored product*”. Bactericidal activity is demonstrated at 30°C with a contact time of 5 min and skimmed milk, at 80% v/v with 6 and 12 months aged product.

As applicant submitted a P2S2 test (pre EN17422) with a 12 month aged product which demonstrated a bactericidal activity at 80% v/v, it was considered as a worst case (most difficult conditions) thus there is no need to demonstrate the yeasticidal activity of the aged product.

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| **Conclusion on the efficacy of the product** |
| The product ALGOFILM, has shown a sufficient efficacy in accordance with the requirements of the guidance on the Biocidal Products Regulation, Volume II Efficacy – Assessment and Evaluation (Parts B+C) for the following use:   * Teat disinfection after milking by manual or automated dipping: ready-to-use with a contact time of 5 minutes, against bacteria and yeasts. |

#### Occurrence of resistance and resistance management

According to the Assessment Report of L(+) lactic acid (June 2017), no reduction in efficacy was reported in the literature for such applications indicating that no development of resistant microorganisms has occurred.

According to the Assessment Report of L(+) lactic acid (2013), resistance is unlikely to develop.

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

#### Known limitations

None.

#### Evaluation of the label claims

The product ALGOFILM, has demonstrated a sufficient efficacy for the following use:

* Teat disinfection after milking by manual or automated dipping: ready-to-use with a contact time of 5 minutes, against bacteria and yeasts.

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

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

The product is not inteded to be used with other biocidal product.

### Risk assessment for human health

#### Assessment of effects on Human Health

***Skin corrosion and irritation***

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No *in vitro/in vivo* study is considered necessary. |
| Justification | pH of the product (3.84) is superior to 2 and inferior to 11.5. None of AS/formulants are above the threshold of 1% (to be used for additive approach) for this endpoint. Therefore, no classification is warranted under CLP. |

***Eye irritation***

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No *in vitro/in vivo* study is considered necessary. |
| Justification | pH of the product (3.84) is superior to 2 and inferior to 11.5. None of AS/formulants are above the threshold of 1% (to be used for additive approach) for this endpoint. Therefore, no classification is warranted under CLP. |

***Respiratory tract irritation***

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No *in vivo* study is considered necessary. |
| Justification | None of AS/formulants are above the threshold of 20% so no classification is warranted under CLP. |

***Skin sensitization***

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No *in vitro/vivo* study is considered necessary. |
| Justification | None of AS/formulants are classified for this endpoint.  No classification is warranted under CLP.  However, a sensitivity to pyrrolidone is known in the medical sector. Therefore, the following sentence is added in the section 6 of the SPC: “The product contains pyrrolidones derivatives. Do not use in case of known hypersensitivity.” |

***Respiratory sensitization (ADS)***

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No in vitro/vivo study is considered necessary. |
| Justification | None of AS/formulants are classified for this endpoint.  No classification is warranted under CLP. |

***Acute toxicity***

*Acute toxicity by oral route*

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No in vivo study is considered necessary. |
| Justification | None of AS/formulants are classified for this endpoint.  No classification is warranted under CLP. |

*Acute toxicity by inhalation*

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No in vivo study is considered necessary. |
| Justification | Only Iodine is classified H332 and is below the threshold of 1% so, no classification is warranted under CLP. |

*Acute toxicity by dermal route*

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No in vivo study is considered necessary. |
| Justification | Only Iodine is classified H312 and is below the threshold of 1% so, no classification is warranted under CLP. |

***Information on dermal absorption***

*[*

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | No dermal absorption study was provided on the product ALGOFILM. |
| Justification | According to the Guidance on dermal absorption, EFSA, 2017, the default dermal absorption value of 50% for dilutions water-based with a concentration in substance inferior to 5% is used. |

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

No substance of concern has been identified in the product ALGOFILM (see confidential annex).

***Available toxicological data relating to a mixture***

None

***Other***

The components classified for the other endpoints are not at a content sufficient to classify the product.

To conclude, the product ALGOFILM is not classified.

#### Exposure assessment and risk characterisation on Human Health

ALGOFILM is a biocidal product containing ready-to-use product packaged in can of 20 L and barrels of 60 and 220 L.

It is intended to be used by professionals to disinfect teats. It is applied by manual or automatic dipping on the teats after milking and two milkings per day are performed.

The assessment follows the recommendation n°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 january 2017.

The exposure calculations presented below are conducted with the values of  
0.222% of total iodine (PVP iodine + co-formulants containining iodine), since the reference values is expressed as iodine (and not as PVPi).

For L-(+)-lactic acid, no reference value was derived at the active substance level. According to the discussion which took place on March 2021 during the Human Health WG I 2021, it has been agreed not to perform the comparison of the systemic exposure linked to biocidal uses to the endogenous L-(+)-lactic acid at the product authorization level. Consequently, any calculation regarding the estimation of level of exposure of L-(+)-lactic acid is performed. Moreover, L-(+)-lactic acid is not at a sufficient concentration to trigger local effect.

**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** | **Via food** |
| Inhalation\* | nr | No | nr | nr | nr | nr | nr |
| Dermal | nr | Yes | nr | nr | nr | nr | nr |
| Oral | nr | nr | nr | nr | nr | nr | Yes |

\*Inhalation exposure of vapour of iodine from this type of product (teat disinfectant) was a point of discussion at the WGIV-2017, and it was concluded that inhalation exposure to vapours could be considered as negligible for this type of formulation since iodine is captured within a polymeric matrix (PVP) and/or micelles. Therefore, inhalation exposure to vapours does not need to be assessed.

nr: not relevant

***List of scenarios***

**Table Summary table: exposure scenarios**

|  |  |  |
| --- | --- | --- |
| **Summary table: exposure scenarios** | | |
| **Scenario and task number** | **Description of scenario and tasks** | **Exposed group**  (e.g. professionals, non-professionals, professional bystanders, nonprofessional bystanders/general public) |
| **Primary exposure** | | |
| **[Scenario 1]** | ***Application on teats by manual dipping*** | |
| Task 1 | *Mixing and loading of RTU* | professionals |
| Task 2 | *Application by dipping* | professionals |
| Task 3 | *Wipping of potential remaining product before the next milking* | professionals |
| **[Scenario 2]** | ***Application on teats by automatic dipping*** | |
| **[Scenario 3]** | ***Cleaning of equipment*** | |
| Task 1 | *Cleaning of equipment* | professionals |
| **Combined primary exposure** | | |
| **[1+3]** | ***Application by manual dipping AND cleaning of equipment*** | |
| **[2+3]** | ***Application by automatic dipping AND cleaning of equipment*** | |

**Reference values to be used in risk characterisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF1** | **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. | - | - | - | - |

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)[[3]](#footnote-4). 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 for iodine union authorisations at the European level.

Both risk assessment have been performed in this report.

##### Industrial exposure

No industrial exposure is foreseen. Therefore the assessment of industrial exposure is not relevant.

##### Professional exposure

|  |
| --- |
| **Description of Scenario [1] *Application on teats by manual dipping*** |
| ALGOFILM is used as ready-to-use product. Several tasks are necessary to applied the products on teats. They are described below.     * **Task 1.1: Mixing and loading of RTU**   82 milk producing cows are milked per day. Each cow has 4 teats and are milked 2 times a day. 2 mL product/teat are applied (4 teats/animal equal to 8 mL of product).  Therefore, 16 ml of product/day is needed for a cow. Considering 82 cows, 1312 ml of product/day is needed. This scenario covers the scenario for ewes and goats which have two teats.  The mixing and loading model 4 as proposed in HeadHoc recommendation 13 was chosen as a reasonable worst-case scenario.   * **Task 1.2: Application by dipping**   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 ALGOFILM. The top of the dip contains approximately 8 mL of ALGOFILM and it is designed in order not to allow a flow back in the reserve to avoid contaminations between animals. The 8 mL of product 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.  Direct dermal contact is not foreseen even if the top of the dip is spilled. Exposure during the use of dipping cups is considered covered by the dermal exposure as calculated by the scenario of mixing and loading according to the HeadHoc recommendation 13.  Then the cows are maintained walking during 30 minutes in order to let dry the product.   * **Task 1.3: Before, the next milking the teats are wiped.**   According to the HeadHoc recommendation 13, the exposure is considered limited and no exposure calculation is required. |

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for Scenario [1]** | | | |
| *Task 1.1, dermal exposure* | | | |
|  | Parameters1 | Value | Reference and  justification3 |

|  |  |  |  |
| --- | --- | --- | --- |
| Tier 1 (no PPE) | Dermal expsoure | 0.2 ml /day | Mixing and loading model 4  1.312 l are handled per day. Therefore the value considering the handling of 5 L is used. The model covers all relevant mixing and loading tasks performed by a worker on an 8-h working day. |
| Weight fraction compound (%) | 0.222% | Applicant data |
| Density of algofilm product | 1.013 g/ml | Applicant data |
| Body weight (kg) | 60 | Ad hoc recommendation 14 |
| Dermal absorption (%) | 50% | Default value |
| Penetration factor PPE | 100% | No PPE |

|  |
| --- |
| *Task 1.2, no direct dermal contact and inhalation are foreseen. Exposure of task 1 covers task 2* |
| *Task 1.3, exposure is considered limited* |

**Outcome of systemic exposure and risk characterisation**

**Summary table: estimated systemic exposure and risk characterisation for professional users**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table: estimated systemic exposure and risk characterisation for professional users** | | | | | | | |
| **Exposure scenario** | **Tier/PPE** | **Estimated oral uptake [mg/kg bw/day]** | **Estimated dermal uptake [mg/kg bw/day]** | **Estimated inhalation uptake [mg/kg bw/day]** | **Estimated total uptake [mg/kg bw/day]** | **Estimated uptake/ AEL**  **(%)**    UL = 0.01  mg/kg bw/d | **Exposure < UL (Yes/No)** |
| Scenario [1] | 1/no PPE | nr | 3,75E-03 | nr | 3,75E-03 | 37% | Yes |

|  |
| --- |
| **Description of Scenario [2] *Application on teats by automatic dipping*** |
| Farms can be equiped of automatic system. Loading can be manual or automatic and application is carried out with automatic dipcups which reduce significantly exposure of user.  No exposure calculation is provided here as manual use exposure is considered as worst case. |

|  |
| --- |
| **Description of Scenario [3] *Cleaning of equipment*** |
| According to HeadHoc recommendation 13, exposure during cleaning of equipment is modelised with the RISKOFDERM “Loading liquid, automated or semi-automated” model. |

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for Scenario [3]** | | | |
| *Task 3.1, dermal exposure* | | | |
|  | Parameters1 | Value | Reference and  justification3 |

|  |  |  |  |
| --- | --- | --- | --- |
| Tier 1 (no PPE) | Expsoure | 0.92 mg/min | RISKOFDERM “Loading liquid, automated or semi-automated” model |
| Duration | 5 min | Ad hoc recommendation 13 |
| Weight fraction compound (%) | 0.222% | Applicant data |
| Body weight (kg) | 60 | Ad hoc recommendation 14 |
| Dermal absorption (%) | 50% | Default value |
| Penetration factor PPE | 100% | No PPE |

**Outcome of systemic exposure and risk characterisation**

**Summary table: estimated systemic exposure and risk characterisation for professional users**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table: estimated systemic exposure and risk characterisation for professional users** | | | | | | | |
| **Exposure scenario** | **Tier/PPE** | **Estimated oral uptake [mg/kg bw/day]** | **Estimated dermal uptake [mg/kg bw/day]** | **Estimated inhalation uptake [mg/kg bw/day]** | **Estimated total uptake [mg/kg bw/day]** | **Estimated uptake/ AEL**  **(%)**    UL = 0.01  mg/kg bw/d | **Exposure < UL (Yes/No)** |
| Scenario [3] | 1/no PPE | nr | 8.51E-05 | nr | 8.51E-05 | 1% | Yes |

**Combined scenarios**

**Outcome of combined systemic exposure and risk characterisation**

**Summary table: combined local exposure and risk characterisation for professional users**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table: combined systemic exposure and risk characterisation for professional users** | | | | | | | |
| **Scenarios combined** | **Tier/PPE** | **Estimated oral uptake**  **[mg/kg bw/day]** | **Estimated dermal uptake [mg/kg bw/day]** | **Estimated inhalation uptake [mg/kg bw/day]** | **Estimated total uptake [mg/kg bw/day]** | **Estimated uptake/ AEL**  **(%)**    AEL = 0.01  mg/kg bw/d | **Acceptable (Yes/No)** |
| Scenario [1]  + Scenario  [3] | 1/no PPE | nr | 3.83E-03 | nr | 3.83E-03 | 38% | Yes |
| Scenario [2]  + Scenario  [3] | Covers by Scenario [1] + Scenario [3] | | | | | | |

**Conclusion**

The combined exposures linked to the following biocidal uses are inferior to the UL of iodine:

* + application by manual dipping + cleaning of the equipment
  + application by automatic dipping + cleaning of the equipment

As mentioned above, the exposure of iodine linked to the biocidal uses is added to the dietary intake:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Tier/PPE** | **Estimated biocidal uptake/ AEL**  **(%)**    **AEL = 0.01**  **mg/kg bw/d** | **Estimated uptake/ AEL due to biocidal use**  **+ dietary intake 46% UL (%)** | **Estimated uptake/ AEL due to biocidal use**  **+ dietary intake 25% UL (%)** |
| Scenario [1]  + Scenario  [3] | 1/no PPE | 38% | 84% | 63% |

The risk for human health is acceptable for:

* + application by manual dipping + cleaning of the equipment
  + application by automatic dipping + cleaning of the equipment

##### Non-professional exposure

Non-professional exposure is not foreseen.

##### Exposure of the general public

Exposure of the general public is not relevant. The general public does not have access to the milking parlour.

***Monitoring data***

Not necessary

##### Dietary exposure

Considering the intended uses of the product ALGOFILM, livestock can be exposed to both active substances iodine and lactic acid. Residues can be found in food and food products of animal origin. As a consequence, the human dietary assessment needs to be performed in the framework of this application.

**Residue definitions**

Iodine

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 species. 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-).

| **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  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 conditions,
* 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 sanitizers 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[[4]](#footnote-5) 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[[5]](#footnote-6) and later, in Annex of Commission Regulation (EU) No.37/2010[[6]](#footnote-7) . |

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 meetings 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.

Estimating Livestock Exposure to Active Substances used in Biocidal Products

In place of trials data to determine residues of iodine in milk following use of ALGOFILM, 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 using ARTFood approach (see Annex Residue). Nevertheless, considering the 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 have been calculated:

* Iodine intakes resulting only from the proposed teat treatment.
* Iodine intakes resulting 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)).

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 performed. 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 and O’Brien 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 | | |
| *O’Brien 2013\** | 0.5 | 2x post milking  2x pre- and post-milking | 475  690 | 224 | | 251 (+112.1%)  467 (+208.5%) |

*\** *These data were reported in µg/kg and have been converted to µg/L based on the density of whole milk being 1030 g/L*

The data from O’Brien 2013 in the table above have 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. The study with the highest additional iodine residues in milk has been selected representing this way a worst case scenario.

ALGOFILM contains a maximum in-use concentration of iodine of 0.222% (a max of 0.108% iodine with a min of 0.045% iodide and iodates from PVPi and 0.069% of iodide from co-formulants. 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 *O’Brien 2013)* the maximum the available iodine content has been considered in the dietary risk assessment (0.222 %). For information, the total application rate for ALFOFILM is considered 16 mL of product per animal in one day for animals with 4 teats and 8 ml of product per animal in one day for animals with 2 teats.

**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; O’Brien, 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) |
| *O’Brien 2013* | 0.500 | 2x post-milking | 251 | 451 |
| *ALGOFILM* | 0.222 | 2x post-milking | 111.4 | 311.4 |

*Calculation for 2x post-milking:*

*For 2 milkings at 0.222 % iodine intended treatment = 251 µg/L x (0.222/0.5) = 111.4 µg/L*

*For 2 milkings at 0.222 % iodine total = 111.4 µg/L + 200 µg/L = 311.4 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. Chronic intake values from the EFSA PRIMo rev 3.1 have not been considered in the framework of this application as they do not greatly differ from the ones agreed at WG TOX IV 2017 (**0.54 L adult and 0.58 L toddler**). The estimated dietary exposure results are presented in Table 3.

**Intake values (from diet 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.

**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 (0.222% available iodine)** | | |
| Intake from milk due to teat treatment1 | 50 | 51 |
| Total milk intake2 | 140 | 143 |
| Total dietary intake3 | 325 | 239 |

1 Iodine intake from milk due to teat treatment is derived from BP specific residue values (based on O’Brien 2013). [Additional iodine residues in milk (µg/L)/ iodine (%), O’Brien 2013] x iodine (%) in ALGOFILM x milk consumption (L)

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.

**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

**L(+) lactic acid residues**

Because of the very low systemic toxicity of L(+) lactic acid, derivation of any systemic toxicological reference dose was regarded unnecessary. Considering the intended uses, exposure is estimated to be clearly below endogenous production (>100 g/person/day) and dietary exposure (>1 g/person/day). Therefore, neither an ADI nor an ARfD have been set. Likewise, L-(+)-lactic acid has been approved in the EU as a food additive without an ADI or upper limit (quantum satis; Dir. 95/2/EC), as a cosmetics ingredient, and as veterinary medicinal product without the requirement for MRL setting (EMEA 2008).

Furthermore, according to the assessment report of L(+) lactic acid, residues in food and feed from the intended use PT3 in biocidal products are not expected. Therefore, dietary exposure of humans from the use of lactic acid as a biocide of PT3 can be excluded.

*Estimating transfer of biocidal active substances into foods as a result of professional and/or industrial application(s)*

Regarding the intended uses, no direct exposure of food is expected.

*Estimating transfer of biocidal active substances into foods as a result of non-professional use*

Non-professional use is not intended.

#### Risk characterisation for consumers

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

**Iodine residues**

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 ALGOFILM biocide product (0.222% 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 (0.222% available iodine)** | | |
| Intake from milk due to teat treatment1 | 50 [8 % UL] | 51 [26 % UL] |
| Total milk intake2 | 140 [23 % UL] | 143 [72 % UL] |
| Total dietary intake3 | 325 [54 % UL] | 239 [120 % UL] |

1 Iodine intake from milk due to teat treatment is derived from BP specific residue values (based O’Brien 2013). [Additional iodine residues in milk (µg/L)/ iodine (%), O’Brien 2013] x iodine (%) in ALGOFILM x milk consumption (L)

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= (50/600) = 8 % or (140/600) = 23 % or (325/600) = 54 %*

*Percentage UL for children= (51/200) = 26 % or (143/200) = 72 % or (239/200) = 120 %*

As stated before, if chronic milk intake values are calculated using milk consumption values from the EFSA PRIMo rev 3.1, there will be no significant differences to the above estimations.

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 realized 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 ALGOFILM. 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 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.

To minimize the iodine contamination in milk the following risk mitigation measure should be added:

* In case a combination of pre- and post-milking disinfection is necessary, using another product not containing iodine has to be considered for pre-milking disinfection

**L(+) lactic acid residues**

See exposure evaluation for lactic acid (section 2.2.6.2.5, lactic acid).

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

Considering the intended use of ALGOFILM and based on overall available information with a very worst case scenario, a risk via food cannot be formally excluded for children, for which total daily intake exceeds the 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 regimes would need to be considered.

To minimize the iodine contamination in milk the following risk mitigation measure should be added:

* In case a combination of pre- and post-milking disinfection is necessary, using another product not containing iodine has to be considered for pre-milking disinfection

### Risk assessment for animal health

As no guidance is currently available to assess animal health, no assessment for animal health has been performed.

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

ALGOFILM product is a PT3 disinfectant (disinfection for veterinary hygiene) containing 2 active substances: free iodine released from PVPI (Polyvinylpyrrolidone iodine), and L(+) Lactic acid. ALGOFILM product is applied by professionals for teat disinfection after milking. The data on active substances are provided by the assessment report of Iodine (including PVP-iodine) for PT1, 3, 4, 22 (Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products, Assessment Report Iodine (including PVP-iodine) for PT1, 3, 4, 22, December 2013) and assessment report of L(+) Lactic acid for PT2, 3, 4 (Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products, Assessment Report L(+) Lactic acid Product-type 2, 3 and 4, June 2017). The available ecotoxicological information and e-fate data are used for risk assessment for the environment.

Details about the non-classification of co-formulants as substance of concern (SoC) can be found in the confidential PAR.

#### Effects assessment on the environment

***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***

No new environmental studies have been carried out with the ALGOFILM product. No substance of concern is defined for the environment. All data pertaining to the active substances are therefore derived from the Iodine (including PVP-iodine) assessment report (PT1, 3, 4, 22, December 2013) and the L(+) Lactic acid assessment report (PT2, 3, 4, June 2017).

Lactic acid is not classified for the environment. Concerning iodine, classification was based on the total iodine contents in the product. Iodine is currently classified as H400 (harmonised classification). Chronic classification is not harmonised and in absence of chronic endpoints; it was agreed at WGII2018 that iodine is classified as Aquatic Chronic 1 H410 (M =1). Considering an iodine concentration between 0.081 and 0.108% in the product, this does not lead to any classification.

The product is not classified for the environment.

***Further Ecotoxicological studies***

No new data is available

***Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk (ADS)***

No new data is available

***Supervised trials to assess risks to non-target organisms under field conditions***

No new data is available

***Studies on acceptance by ingestion of the biocidal product by any non-target organisms thought to be at risk***

No new data is available

***Secondary ecological effect e.g. when a large proportion of a specific habitat type is treated (ADS)***

No new data is available

***Foreseeable routes of entry into the environment on the basis of the use envisaged***

Please refer to the exposure assessment below.

***Further studies on fate and behaviour in the environment (ADS)***

At WGII2020, it was stated that Lactic acid is a naturally occurring simple organic acid found in plants, animals and humans. It is an endogenous metabolite in many organisms, a common naturally occurring food constituent and also a growth regulator intended to increase nut and fruit set. Furthermore, the environment is exposed to Lactic acid via the excretion of faeces and urine by humans (and their subsequent release from the STPs), as well as the direct disposal of excreta by other mammals. In soils, L(+) Lactic acid naturally occurs as a fermentation by-product of anaerobic degradation of organic matter. This substance may covalent bind with organic material in sewage sludge, manure, and soils. In microorganisms, lactate formation is one of the usual pathways for NAD+ regeneration and when formed, lactate can be further metabolized through the pathway of pyruvate metabolism. As lactate is metabolized by microorganisms, its degradation in the environment is rapid. It should also be noted that biodegradation during storage of sludge as well as transformation and dilution in deeper soil layers is not taken into account in soil concentration calculations – and thus in subsequent groundwater concentrations (Tier 1). Modelling of groundwater exposure in case of Lactic acid largely overestimates concentrations and is considered unrealistic.

For all these reasons, it can be stated that (L+) Lactic acid does not cause unacceptable risk for groundwater, without need for further calculations.

For soil calculations, a DT50 of 30 days was stated without the need of further studies.

The two following studies on L(+) lactic acid biodegradation were also included in the report by the applicant:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table on further studies on fate and behaviour in the environment** | | | | | | | | |
| Method, Guideline, GLP status, Reliability | Test Item | Test Species | Test period | pH | Temp [°C] | Initial TS concentration, C0[mol/l] | Results | Reference |
| − Commission Regulation 440/2008/EC, Method C.4-E  of May 30, 2008: Closed Bottle Test (EEC Publication  No. L 142/497-502, May 2008)  − OECD Guideline for Testing of Chemicals No. 301 D:  "Ready Biodegradability: Closed Bottle Test", adopted  July 17, 1992.  *GLP*  *Reliability: 1* | Lactic acid | Activated sludge | 28 days | *7.2* | 22+1°C | 5.06 mg/L corresponding to an oxygen demand of 4.32 mg O2/L based on ThOD of 0.853 mg oxygen per mg test  item. | Biodegradation of Lactic acid:  Under the test conditions the percentage biodegradation  of Lactic acid 80% food grade reached in the mean 50 %  after 3 days of incubation and continuously increased to  71 % after 14 days and 80% after 28 days. The percentage  biodegradation did exceed 60 % within the 10-day window. The test item can therefore be considered as ready biodegradable.  Biodegradation of the Toxicity Control:  In the toxicity control containing both, the test item and the reference item sodium benzoate, a mean of 74 %  biodegradation was noted within 14 days and 76 % biodegradation after 28 days of incubation. Thus, the test  item can be assumed to be not inhibitory on the activated  sludge microorganisms. | *Title: Ready Biodegradability of*  *Lactic acid 80% food grade in a Closed Bottle Test*  *Author: Dr. Ute Hammesfahr*  *Sponsor:*  *Jungbunzlauer International AG*  *Test Facility:*  *Institut für Biologische Analytik und Consulting IBACON GmbH* |
| QSAR models:   * EPISuite (BIOWIN v4.10 module) * VEGA 1.1.4   *Reliability: 2* | Lactic acid | N/A | N/A | N/A | N/A | N/A | Based on multiple QSAR models applied, L-(+)-lactic acid was predicted as readily biodegradable.  The half life for L-(+)-lactic acid for bulk soil based on results from standardised biodegradation test results was calculated as 30 days. | *Title: In silico prediction of Ready Biodegradability for*  *L-(+)-lactic acid*  *Sponsor: Jungbunzlauer S.A.*  *Study organisation: Kreatis* |

***Leaching behaviour (ADS)***

No new data is available

***Testing for distribution and dissipation in soil (ADS)***

No new data is available

***Testing for distribution and dissipation in water and sediment (ADS)***

No new data is available

***Testing for distribution and dissipation in air (ADS)***

No new data is available

***If the biocidal product is to be sprayed near to surface waters then an overspray study may be required to assess risks to aquatic organisms or plants under field conditions (ADS)***

Not relevant

***If the biocidal product is to be sprayed outside or if potential for large scale formation of dust is given then data on overspray behaviour may be required to assess risks to bees and non-target arthropods under field conditions (ADS)***

Not relevant

***Hazard endpoints for the risk assessment***

Iodine and iodine compounds are ubiquitously distributed and there is a natural cycle of iodine species in the environment. Consequently, natural background levels have to be taken into account in the environmental risk assessment. Literature data were compiled in the CAR of Iodine. Environmental background values are presented in the table below:

|  |  |
| --- | --- |
| **Summary table of background levels** | |
| **Compartment** | **Background level (Iodine and cover the iodine compounds)** |
| Freshwater (river and lake) | 0.5 - 20 µg/L |
| Freshwater sediment | 6 mg/kg wwt |
| Soil | 0.565-22.6 mg/kg wwt with extremes up to 110.74 mg/kg wwt |
| Groundwater | mean concentration: 1 µg/L  < 1 - 70 µg/L with extremes up to 400 µg/L |

Different forms of iodine can be found in the environment and iodine, iodate and iodide will be examined in the environmental risk assessment.

Based on the Iodine assessment report, the relevant PNECs for the environmental risk characterisation are reported below:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Summary table on PNEC values Iodine and iodine compounds** | | | | |
| **Active substance** | **PNECSTP** | **PNECwater** | **PNECsed** | **PNECsoil** |
| [mg/L] | [mg/L] | [mg/kgwwt] | [mg/kgwwt] |
| **Iodine (I2)** | 2.90 | 5.90E-04 | Not used in the risk assessment\* | 1.18E-02 |
| **Iodide (I-)** | - | 8.30E-04 | 4.30E-03 |
| **Iodate (IO3-)** | - | 5.85E-02 | 3.04E-01 |

\* According to the iodine CAR (December, 2013), the PNECsediment values were calculated on the basis of the PNECaquatic values, using the equilibrium partitioning method.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Summary table on PNEC values L (+) lactic acid** | | | | |
| **Active substance** | **PNECSTP** | **PNECwater** | **PNECsed** | **PNECsoil** |
| [mg/L] | [mg/L] | [mg/kgwwt] | [mg/kgwwt] |
| **L(+) Lactic acid** | 10 | 3.9 | Not used in the risk assessment\* | 1.9\* |

\* The PNECsoil and the PNECsediment are derived using the equilibrium partitioning method (ECHA Guidance on BPR Vol IV, Part B, v2.0, 2017, equations 89 and 91).

#### Exposure assessment

**General information**

|  |  |
| --- | --- |
| Assessed PT | PT 3 |
| Assessed scenarios | Teat disinfection; Liquid dipping after milking (Manual and automatic application):  - Emission to the STP via wastewater  - Emission to soil via manure/slurry |
| ESD(s) used | Emission Scenario Document for Product Type 3: Veterinary hygiene biocidal products, 2011  OECD SERIES ON EMISSION SCENARIO DOCUMENTS, Number 14: Emission Scenario Document for Insecticides for Stables and Manure Storage systems ENV/JM/MONO(2006)4  Technical Agreements for Biocides v2.1, December 2019 |
| Approach | Average consumption |
| Distribution in the environment | Calculated based on ECHA Guidance on the BPR Vol IV, Part B; April 2015  Assessment report: L(+) Lactic acid Product-type 02, 03 and 04, June 2017 and Iodine Product-type 1, 3, 4, 22, December 2013  Technical Agreements for Biocides v2.1, December 2019 |
| Groundwater simulation | No |
| Confidential Annexes | No |
| Life cycle steps assessed | Production: No  Formulation:No  Use: Yes  Service life: No |
| Remarks | */* |

***Emission estimation***

The quantity of iodine (I2) in PVPI is at a minimum concentration of 0.081% and maximum concentration of 0.108 % w/w. The quantity of iodide/iodate (I- form) in PVPI is at concentration of 0.045% w/w. Therefore, the total of iodine forms contained in PVPI is 0.153% w/w.

On the other hand, some co-formulants can also bring iodine to the mixture under I- form, at a rate of maximum 0.069% w/w. Thus, to integrate the total of the various form of iodine in the product, the quantity of iodine from co-formulants is added to the quantity of iodine from PVPI in a worst case approach. The quantity of the various forms of iodine in ALGOFILM is therefore: 0.153 + 0.069 =0.222% for the environmental risk assessment.

Only the predicted environmental concentrations (PECs) based on the nitrogen emission standards are presented in the current PAR as a worst case situation.

Although iodine being an element that does not degrade, it disappears from soils between two subsequent manure events due to leaching. The leaching rate constants and resulting PECs were calculated according to the guidance by applying an experimentally-derived solid-water partitioning coefficient for soils of 5.8 L/kg. The corresponding half-lives for leaching from the topsoil layer are 2571 d in arable land (20 cm) and 643 d in grassland (5 cm). These two values have been validated in WG for Union Authorisations containing iodine.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | | |
| **Input** | **Nomenclature** | **Value** | | **Unit** | **Remarks** |
|  |  | **Iodine** | **L(+) Lactic acid** |  |  |
| 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) | 2 / 3 - Waste water / Slurry | | [-] | P (Appendix 1: Table 7) |
| Content of technical active ingredient in formulation (product) | Fbioc | 2.22 | 0.8 | g/L | S |
| Amount of product prescribed to be used for one treatment (dipping of the four teats) of one animal | Vprodi1,i2,i3 | 8.00E-03 | | L | S |
| Dilution factor (for preparation of the working solution from the formulation (product)) | Fdil | 1 | | [-] | S |
| Fraction of active ingredient released | F slurry/manure or STP | 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 | 3 (post milking only) | | [-] | D - Automatic Application |
| Number of days of lactation period | Nday-lact | 300 | | [-] | D |
| Number of disinfectant applications in one year | Napp-bioc | 900 | | [-] | D |
| Interval between two disinfectant applications | Tbioc-int | 0.33 | | [-] | D |
| Number of manure applications for grassland | Napp-grass | 4 | | [-] | 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) |
| Number of milk producing animals per day | Nmp\_animal | 82 | | [-] | TAB ENV 63 |
| 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 | DEPTHarableland | 0.2 | | [m] | D |
| Density of wet bulk soil | RHOsoilwet | 1700 | | [kg.m-3] | D |
| Intermediate calculations | | | | | |
| Number of biocide applications during storage period for application on grassland | Napp-manuregr | 159 | | [-] | O |
| Number of biocide applications during storage period for application on arable land | Napp-manurear | 636 | | [-] | O |
| Amount of active ingredient to be used for one application on one animal | Qai-prescri1,i2,i3 | 1.78E-05 | 6.40E-06 | [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 | 1.16E-01 | 4.17E-02 | [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 | 4.63E-01 | 1.67E-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 |

| **Resulting local emission to relevant environmental compartments** | | | | |
| --- | --- | --- | --- | --- |
| **Compartment** | | **Local emission (Elocalcompartment)** | | **Remarks** |
| **Iodine** | **L(+) Lactic acid** |  |
| STP | | 2.19E-03 | 7.89E-04 | [kg.d-1] |
| Intermediate PECsoil calculations | | | | |
| Soil | Grassland | 3.22E-03 | 1.16E-03 | [mg.kg-1wwt] (after one manure application) |
| 1.19E-02 | 1.37E-03 | [mg.kg-1wwt] (after four manure applications) |
| Arable land | 3.22E-03 | 1.16E-03 | [mg.kg-1wwt] (after one manure application) |

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

| **Identification of relevant receiving compartments based on the exposure pathway** | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Fresh-water | Freshwater sediment | Sea-water | Seawater sediment | STP | Air | Soil | Ground-water | Other |
| via STP | Yes | Yes | No | No | Yes | No | Yes | Yes | No |
| via Slurry/Manure | Yes | Yes | No | No | No | No | Yes | Yes | No |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Input parameters (only set values) for calculating the fate and distribution in the environment of Iodine** | | | | | |
| Input | | Value | Unit | | Remarks |
| Molecular weight | | 253.81 | g.mol-1 | | Assessment Report for Iodine (including PVP-iodine) product types 1, 3, 4, and 22, December 2013 |
| Vapour pressure (at 20°C) | | 40.7 | Pa | |
| Water solubility (at 20°C) | | 290 | mg/L | |
| Log Octanol/water partition coefficient | | - | - | | Inorganic substance |
| Organic carbon/water partition coefficient (Koc) | | Not relevant | L/kg | | Inorganic substance |
| Henry’s Law Constant (at 20°C) | | 34.43 | Pa/m3/mol | |  |
| DT50 for degradation in soil | | 1.0E+06 | D | | Inorganic substance |
| Solids-water partition coefficient in soil (Kp, soil) | | 5.8 | L/kg | | OECD 106 screening study and supported by the IAEA report |
| Solids-water partition coefficient in suspended matter (Kp, susp)\_ | | 220 | L/kg | | IAEA Technical report No 472 |
| Solids-water partition coefficient in soil (Ksoil-water) | | 8.90 | m3.m-3 | | Calculated |
| kleach (0.2 m relevant for STP and slurry/manure arable land) | | 2.70E-04 | d-1 | | Agreed at the WG level |
| kleach (0.05 m relevant for slurry/manure grass land) | | 1.08E-03 | d-1 | | Agreed at the WG level |
| **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 iodate | | 100 | [%] | |  |
| Transformation rate in soil iodine to iodate via the STP | | 100 | [%] | |  |
| Transformation rate in soil iodine to iodate via manure | | 100 | [%] | |  |
| Molecular equivalent iodate/iodine | | 1.382 |  | |  |
| **Calculated fate and distribution in the STP of Iodine** | | | | | |
| Compartment | Percentage [%] | | | Remarks | |
| Air | 0 | | | Assessment Report for Iodine (including PVP-iodine) product types 1, 3, 4, and 22. 13 December 2013\* | |
| Water | 80 | | |
| Sludge | 20 | | |
| Degraded in STP | 0 | | |

\* The distribution in the STP was directly taken from the CAR and not recalculated with SimpleTreat as iodine is a very specific inorganic element.

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters (only set values) for calculating the fate and distribution in the environment of L(+) Lactic acid** | | | |
| Input | Value | Unit | Remarks |
| Molecular weight | 90.08 | g.mol-1 | Assessment Report L(+) lactic acid Product-type 02, 03 and 04, June 2017 |
| Vapour pressure (at 20°C) | 0.4 | Pa |
| Water solubility (at 12°C) | 1.00E+06 | mg/L | Completely miscible with water |
| Log Octanol/water partition coefficient | -0.74 | Log 10 | Assessment Report L(+) lactic acid Product-type 02, 03 and 04, June 2017 |
| Organic carbon/water partition coefficient (Koc) | 20 | L/kg |
| Biodegradability | Readily biodegradable failing the 10-days window criterion | - |
| DT50 for degradation in soil (at 12ºC) | 30 | d | 30d as refinement for 90d value in AR (WGII2020) |
| ktotal (0.2 m relevant for STP and slurry/manure arable land) | 2.61E-02 | d-1 | Calculated |
| ktotal (0.05 m relevant for slurry/manure grass land) | 3.51E-02 | d-1 | Calculated |

|  |  |  |
| --- | --- | --- |
| **Calculated fate and distribution in the STP of L(+) Lactic acid** | | |
| Compartment | Percentage [%] | Remarks |
| Air | 2.50E-05 | Simple treat v4.0 |
| Water | 22.5 |
| Sludge | 0.20 |
| Degraded in STP | 77.3 |

***Calculated PEC values***

PECs for sediments were not calculated neither for iodine and iodine compounds nor for L(+) Lactic acid. PNECs sediment being calculated using equilibrium partitioning, they are covered by PNECs water.

| **Summary table on calculated PEC values for iodine** | | | | |
| --- | --- | --- | --- | --- |
|  | **PECSTP** | **PECwater** | **PECsoil** | **PECGW** |
| [mg/l] | [mg/l] | [mg/kgwwt] | [μg/l] |
| ***via STP*** | 8.76E-04 | 8.73E-05 | 5.42E-03 | **1.04** |
| ***via slurry/manure – concentrations after ten years*** | | | | |
| grassland | - | 6.82E-04 | 3.57E-02 | **6.81** |
| arable land | - | 4.11E-04 | 2.15E-02 | **4.11** |

| **Summary table on calculated PEC values for iodide** | | | | |
| --- | --- | --- | --- | --- |
|  | **PECSTP** | **PECwater** | **PECsoil** | **PECGW** |
| [mg/l] | [mg/l] | [mg/kgwwt] | [μg/l] |
| ***via STP*** | 8.76E-04 | 8.73E-05 | 7.59E-04 | **0.142** |
| ***via slurry/manure – concentrations after ten years*** | | | | |
| grassland | - | 6.82E-04 | 3.57E-02 | **6.81** |
| arable land | - | 4.11E-04 | 2.15E-02 | **4.11** |

| **Summary table on calculated PEC values for iodate\*** | | | | |
| --- | --- | --- | --- | --- |
|  | **PECSTP** | **PECwater** | **PECsoil** | **PECGW** |
| [mg/l] | [mg/l] | [mg/kgwwt] | [μg/l] |
| ***via STP*** | 1.21E-03 | 1.21E-04 | 7.50E-03 | **1.40** |
| ***via slurry/manure – concentrations after ten years*** | | | | |
| grassland | - | 9.43E-04 | 4.93E-02 | **9.42** |
| arable land | - | 5.68E-04 | 2.97E-02 | **5.68** |

\*PECs for iodate were derived by multiplying those for iodine with 1.382 (differences in molar weight).

| **Summary table on calculated PEC values for L(+)lactic acid** | | | | |
| --- | --- | --- | --- | --- |
|  | **PECSTP** | **PECwater** | **PECsoil** | **PECGW** |
| [mg/l] | [mg/l] | [mg/kgwwt] | [μg/l] |
| ***via STP*** | 8.88E-05 | 8.88E-06 | 2.04E-06 | 1.32E-03 |
| ***via slurry/manure – concentrations after ten years*** | | | | |
| grassland | - | 2.92E-04 | 1.37E-03 | **2.92** |
| arable land | - | 2.47E-04 | 1.16E-03 | **2.47** |

***Primary and secondary poisoning***

Primary poisoning

Primary poisoning via the direct consumption of the products by wild birds and mammals is unlikely. Therefore, primary poisoning is not considered relevant for this evaluation.

Secondary poisoning

The secondary poisoning assessment is not relevant for the active substances iodine and L(+) lactic acid. Iodine is an essential element and internal concentrations are expected to be regulated within small boundaries. These substances are unlikely to bioaccumulate in aquatic or terrestrial environment according to the ECHA Guidance Vol IV Part B+C. They have a low Log Kow (2.49 for Iodine and -0.74 for L(+)Lactic acid) and these values indicate a negligible potential for bioconcentration in biota and no accumulation of this substance in the food chain is expected.

|  |  |  |  |
| --- | --- | --- | --- |
| **Summary table on Log Kow and BCF values** | | | |
|  | **Log Kow** | **BCF fish** | **BCF earthworm** |
| Iodine | 2.49 | - | - |
| L(+) Lactic acid | -0.74 | 4.80E-02 | 6.78 |

#### Risk characterisation

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.

|  |  |
| --- | --- |
| **Summary table of background levels** | |
| **Compartment** | **Background level (Iodine and cover the iodine compounds)** |
| Freshwater (river and lake) | 0.5 - 20 µg/L |
| Freshwater sediment | 6 mg/kg wwt |
| Soil | 0.565-22.6 mg/kg wwt with extremes up to 110.74 mg/kg wwt |
| Groundwater | mean concentration: 1 µg/L  < 1 - 70 µg/L with extremes up to 400 µg/L |

***Atmosphere***

Emissions and PECs in air are considered as negligible. It can be concluded that the use of the ALGOFILM product will not pose a significant risk to the atmospheric compartment.

***Sewage treatment plant (STP), Aquatic compartment, Terrestrial compartment and Groundwater***

A summary of the calculated PEC/PNEC values for each scenario and all the relevant environmental compartments are indicated in the following table:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Summary table on calculated PEC/PNEC values** | | | | |
|  | **PEC/PNECSTP** | **PEC/PNECwater** | **PEC/PNECsoil** | **GW (µg/L)** |
| **Via STP** | | | | |
| Iodine | 3.02E-04 | 1.48E-01 | 4.60E-01 | **1.04**  but < to natural background |
| Iodide | n.r. | 1.05E-01 | 1.77E-01 | **0.142**  but < to natural background |
| Iodate | n.r. | 2.06E-03 | 2.47E-02 | **1.40**  but in the natural background |
| L(+) Lactic acid | 8.88E-06 | 2.28E-06 | 1.07E-06 | 1.32E-03 |
| **Via slurry/manure – concentrations after ten years** | | | | |
| Iodine | | | | |
| Grassland | n.r. | **1.16E+00**  but in the natural background | **3.02E+00**  but < to natural background | **6.81**  but in the natural background |
| Arable land | n.r. | 6.97E-01 | **1.82E+00**  but < to natural background | **4.11**  but in the natural background |
| Iodide | | | | |
| Grassland | n.r. | 8.18E-01 | **8.30E+00**  but < to natural background | **6.81**  but in the natural background |
| Arable land | n.r. | 4.94E-01 | **5.01E+00**  but < to natural background | **4.11**  but in the natural background |
| Iodate | | | | |
| Grassland | n.r. | 1.60E-02 | 1.62E-01 | **9.42**  but in the natural background |
| Arable land | n.r. | 9.68E-03 | 9.78E-02 | **5.68**  but in the natural background |
| L(+) Lactic acid | | | | |
| Grassland | n.r. | 7.49E-05 | 7.21E-04 | **2.92** |
| Arable land | n.r. | 6.33E-05 | 6.11E-04 | **2.47** |

n.r.: not relevant

After a comparison with the background concentrations in iodine in the different compartments, risks are deemed acceptable whatever the emission pathway.

In fact Iodine is a natural occurring compound for which aquatic background levels are reported between 0.5 and 20 µg/L. The PEC value obtained for iodine via slurry manure application on grassland of 0.679 µg/L is in the range of the environmental background.

Iodine and iodide species occur naturally in the terrestrial environment for which the natural global mean background concentration is 5 mg/kg dwt and varies with geographical locations and local geology. The background concentrations vary between 0.565 to 22.6 mg/kg wwt, with extremes up to 110.74 mg/kg wwt. The expected PECs via STP (0.0236 mg iodine/kg wwt) and via slurry/manure after ten years (0.0357 mg iodine/kg wwt in grassland and 0.0215 mg iodine/kg wwt in arable land) are lower to the background concentrations.

The highest concentration in the soil’s pore water for iodine compounds is expected to be 9.42 µg iodate/L after repeated manure applications for ten successive years. However, it should be noted that the 0.1 µg/L limit is set for organic chemicals and therefore not feasible for iodine. Therefore, the predicted concentrations were also compared to natural background concentrations. Iodine is a natural occurring compound occurring in groundwater for which the concentration ranges from 1 to 70 µg/L (the latter are found in coastal and arid areas). Anthropogenic emission may therefore increase the natural background concentrations multiple times in case groundwater is low in iodine, but the expected concentrations are still within the natural background concentrations. The calculated exceeding of the 0.1 µg/L limit is therefore considered acceptable.

Risks are acceptable regarding all the relevant environmental compartments for the active substance L(+) Lactic acid when releases are directed to the STP.

Risks are acceptable for the aquatic and terrestrial compartment for the active substance L(+) Lactic acid via slurry/manure application on both grassland and arable land. The concentration of the active substance L(+) Lactic acid in groundwater exceeds the quality standard for pesticides and biocidal products according to Directive 2006/118/EC for drinking water (0.1 μg/L). However, as explained in section “2.2.2.1 - Effects assessment on the environment”, there is no need for further calculation in groundwater risk assessment for active substance L(+) Lactic acid. Therefore, a Tier 2 assessment using Focus Pearl model is not required and all the risk for the active substance L(+) Lactic acid are considered acceptable.

***Primary and secondary poisoning***

Primary poisoning is not expected for the intended use, which is taking place indoors.

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.

The secondary poisoning assessment is not relevant for the active substance L(+) Lactic acid. This substance is unlikely to bioaccumulate in aquatic or terrestrial environment according to the low Log Kow (<3) and a BCF <100 indicating a negligible potential for bioconcentration in biota and no accumulation of this substance in the food chain is expected.

Hence the ALGOFILM product does not pose an unacceptable risk to birds and mammals.

***Mixture toxicity***

ALGOFILM product contains two active substances and a mixture assessment should be performed. However, iodine and iodine compounds are compared to the environmental background levels, and it is not relevant to sum the PEC/PNEC values to determine the mixture toxicity. Moreover worst case assumptions are considered in degradation of iodine to iodide and iodate. Summing up the RCR would lead to two worst case conclusions.

Therefore the only compartment for which a mixture assessment of the two active substances Iodine and L(+) Lactic acid was performed is the STP.

No synergistic interaction is foreseen between L(+) Lactic acid and iodine.

|  |  |
| --- | --- |
| **Summary table on calculated ∑PEC/PNEC values** | |
|  | **∑PEC/PNECSTP** |
| Via STP | 3.11E-04 |

Conclusion:

It can be concluded that the mixture toxicity assessment shows acceptable risks for the relevant compartments for the use of the ALGOFILM product.

***Aggregated exposure (combined for relevant emmission sources)***

Although iodine is released from multiple sources, aggregated exposure assessment is not deemed necessary as there is no overlap in space and time. Iodine as a teat disinfectant is predominantly released to agricultural soils and therefore not mixed with iodine from other anthropogenic sources.

Since the amount of L(+) Lactic acid that is used annually in biocidal products accounts for less than 10% compared to the annual production and import volume of L(+) Lactic acid in the EU, no aggregated risk assessment was performed.



|  |
| --- |
| **Overall conclusion on the risk assessment for the environment of the product** |
| Following the application of the ALGOFILM product, acceptable risks are reached for Iodine and iodine compounds and for L(+)Lactic acid for all the environmental compartments and for all the uses presented in SPC. |

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

Please refer to the summary of the product assessment and to the relevant sections of the assessment report.

### Assessment of a combination of biocidal products

Not relevant.

### Comparative assessment

Not relevant.

# Annexes[[7]](#footnote-8)

## List of studies for the biocidal product

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author(s)** | **Year** | **Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published** | **Data Protection Claimed (Yes/No)** | **Owner (PUB / ORG)** |
| Alcoholes monptlet S.A. | Not specified | Admin\_LoA\_PVPI | Yes | CTH |
| Junbunzlauer S.A. | 2019 | Admin\_LoA\_L-(+)-lactic acid\_JBLM  Title of document: Reliance on Article 95 Letter of Access for product authorisation | Yes | CTH |
| Purac Biochem bv | 2019 | Admin\_LoA\_L-(+)-lactic acid\_Purac  Title of document: Letter of Access for company CTH | Yes | CTH |
| Morel A. | 2015 | Title of file : Phys-chem\_Long term stability on ALGOFILM  Title of document: Rapport sur les essais de stabilitié - ALGOLFILM | Yes | CTH |
| Elisabeth servajean | 2018 | Title of file: Phys-chem\_Viscosity and surface tension on ALGOFILM  Title of document: Surface tension and kinematic viscosity of ALGOFILM before and after accelerated storage | Yes | CTH |
| Merieux Nutrisciences | 2016 | Title of file: Phys-chem\_Corrosion to metals\_IODIGUARD  Title of document: Metal corrosion test for the product IODIGUARD – Lot 16001693 | Yes | CTH |
| Morel A. | 2015 | Title of file : Phys-chem\_Analytical method Iodine in ALGOLFILM  Title of document : Méthode de dosage de l’iode actif | Yes | CTH |
| Pauline Padilla | 2020 | Physico-chemical tests and analyses before and after an accelerated storage procedure for 8 weeks at 40 °C ± 2 °C on ALGOFILM  Défitraces  20-912017-004  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of iodide in IODIGUARD In compliance with SANCO/3030/99 rev.5 from 22/03/2019  Défitraces  20-912017-001  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of diiode in IODIGUARD In compliance with SANCO/3030/99 rev.5 from 22/03/2019  Défitraces  20-912017-002  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of iodate in IODIGUARD In compliance with SANCO/3030/99 rev.5 from 22/03/2019  Défitraces  20-912017-003  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of L-(+)-lactic acid (CAS [79-33-4]) in ALGOFILM  Défitraces  20-912017-005  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of diiode in ALGOFILM In compliance with SANCO/3030/99 rev.5 from 22/03/2019  Défitraces  20-912017-006  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of iodide in ALGOFILM In compliance with SANCO/3030/99 rev.5 from 22/03/2019  Défitraces  20-912017-007  GLP; Unpublished | Yes | CTH |
| Hélène Ricau | 2020 | Validation of the analytical method for the determination of iodate in ALGOFILM In compliance with SANCO/3030/99 rev.5 from 22/03/2019  Défitraces  20-912017-008  GLP; Unpublished | Yes | CTH |
| Dr. Ute Hammesfahr | 2018 | Ready Biodegradability of  Lactic acid 80% food grade in a Closed Bottle Test | Yes | Jungbunzlauer International AG |
| |  | | --- | | Paul THOMAS, | | Faizan SAHIGARA | | 2018 | In silico prediction of Ready biodegrability for L-(+)-lactic acid | Yes | Jungbunzlauer S.A. |
| Amandine MOREL | 2017 | Essai quantitative de suspension pour l’évaluation de l’activité bactericide des antiseptiques et des désinfectants chimiques utilisés dans le domaine vétérinaire | Yes | CTH |
| Amandine MOREL | 2017 | Essai quantitative de suspension pour l’évaluation de l’activité levuricide des antiseptiques et des désinfectants chimiques utilisés dans le domaine vétérinaire | Yes | CTH |
| Mélanie SORRE | 2020 | Test d’efficacité bactericide selon le projet de norme prEN 17422 (juin 2020) | Yes | CTH |
| Mélanie SORRE | 2020 | Efficacy test for bactericidal activity according to the project of the standard prNF EN 17422 (June 2020) | Yes | CTH |
| Anne Françoise GABILLET | 2021 | Efficacy test for bactericidal activity according to the project of the standard prNF EN 17422 (June 2020) | Yes | CTH |

## Output tables from exposure assessment tools



## Residue behaviour

***Iodine assessment context***

Following the same approach as for the other iodine UA, which has been discussed at WG and BPC, the following has 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 UL for children is set by a normal 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 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 to the consumer risk assessments encompassing different regulatory areas would need to be considered.

***Iodine : applicant assessment fo scenario 1: TP03 – teat dip disinfection***

The applicant proposed to estimate the dietary exposure using ARTFood approach, the calculations are presented below:

There is currently no guidance document to perform dietary exposure assessment following teat dip application. However, a draft guidance is under discussion (ARTFood, 2016). A dietary risk assessment on the basis of this draft document has been performed and is detailed hereafter.

| **Description of Scenario [1] PT03: teat dip disinfection** | | |
| --- | --- | --- |
|  | Parameters | Value |
| Tier 1 | Daily milking (ndaily milking) | 2 |
| Volume applied (Vapplied)(ml/teat) | 2 |
| Vmilk yield (L/jour)1 | 20 |
| Iodine density | 1.013 |
| Iodine content (% w/w) | 0.222 |
| Tier 2 | Surface of teat end (%)2 | 10 |
| Dermal absorption (%)3 | 50 |

1 ARTFood draft Guidance on teat dip scenario, 2016

2 Teat surface calculation: teat is assumed to be a cylinder of 6 cm length (lteat) and 1.2 cm radius (rteat) teat surface (single teat) covered with teat dip: Steat = 2π rteat \* lteat + π \*rteat2 = 45.23 cm2 + 4.52 cm2 = 49.75 cm2 only substance covering the bottom of the teat will be directly transferred into the milk (estimated surface of teat end: Steat end = π \*rteat2 = 4.52 cm2)

3 Default dermal absorption value of 50% for dilutions water-based coming from Guidance on dermal absorption, EFSA, 2017.

*Calculations for estimating livestock exposure (concentration of iodine in milk) for Scenario 1:*

*For Tier 1* (screening), concentration of iodine in milk was estimated with the following calculation:

Concentration a.s. in milk = ndaily milking x (c a.s. in biocidal product x Vapplied) ÷ Vmilk yield

In tier 1, it is considered that the entire amount of the product applied on the teats is directly transferred into milk (assuming 0% dermal absorption and 0% degradation of the active substance).

concentration a.s. in milk = 2 x (0.222/100x8)/20

= 0.00178 g/ L = 1.78 mg of iodine/ L of milk

*For Tier 2,* it is assumed that only the product covering the bottom of the teat will be transferred directly into the milk. Considering the surface of teat end, it has been estimated that 10%[[8]](#footnote-9) of the volume of the applied product is transferred directly into the milk whereas the other 90 % are considered to be transferred indirectly into milk via dermal absorption. It is assumed that the amount absorbed is excreted entirely in milk (as a worst case). Concentration in milk was estimated with the following calculation:

Concentration a.s. in milk = {[10% (ndaily milking x (c a.s. in biocidal prod x Vapplied)] + [90% (ndaily milking x (c a.s. in biocidal prod x Vapplied)xdermal absorption] } ÷Vmilk yield

Concentration a.s. in milk = {[10% x 2 x (0.222/100x8)] +[90% x 2 x (0.222/100x8) x 50%]} / 20 L

= 0.000977 g of iodine/pL of milk = 0.977 mg of iodine/L of milk

*Conclusion:*

The calculations are performed considering a worst case situation of 10% of the applied iodine dose transferred directly in milk and 90% of the applied iodine dose transferred indirectly into milk via dermal absorption. Furthermore, in the absence of data, no wiping factor was taken into account. Regarding monitoring and available knowledge on iodine uses, an increase of iodine in milk due to the teat dip biocidal uses is expected to range from 0.05 to 0.174 mg/L (ref iodine CAR). So the calculation presented in framework of this dossier is expected to overestimate the iodine exposure, and the level of contamination in milk.

It can be noted that it is a conservative approach that might overestimate the human dietary exposure.

First, consumer exposure for adult was estimated using EU consumption values for food of animal origin (Consumer standard food basket)[[9]](#footnote-10). It is assumed that the average person consumes 1.5 L of milk per day for an adult of 60 kg bw.

No value of milk consumption is available in EMA food basket for children, infants and toddlers, thus, values from the EFSA comprehensive European Food Consumption Database[[10]](#footnote-11) were used to assess dietary exposure for these classes of population. Average daily food consumption values are used in predicting pesticide intake for long-term hazard (EFSA, 2007)[[11]](#footnote-12). Then, mean consumption of milk from the EFSA Database were taken into account to assess chronic exposure. For each population class, the critical European consumer of milk was identified. These values are presented in the table below.

Mean consumption of milk and dairy products in grams/kg body weight per day

|  |  |  |
| --- | --- | --- |
| Population class | Country | Mean consumption g/ kg bw /d |
| Adult | Finland | 6.0 |
| Child | Finland | 32.9 |
| toddler | Finland | 40.5 |
| Infant | Italy | 80.35 |

Body weights (Recommendation n°14 of the BPC Ad hoc Working Group on Human Exposure : Default human factor values for use in exposure assessments for biocidal products (revision of HEEG opinion 17 agreed at the HH WG III on 12 June 2017))[[12]](#footnote-13) used for risk consumer calculations are reported in table below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | infant (6 weeks to <12 months) | toddler (1 to < 2 years) | child (2-6 years) | Adult |
| body weight (kg) | 8 | 10 | 15.6 | 60 |

WCCE[[13]](#footnote-14) = concentration a.s. in milk \* Imilk ÷ bwhuman

Tier 1 calculation with EMA food basket data consumption:

WCCE adult= (1.78 x 1.5 L of milk)/60 kg bw

WCCE adult = 0.044mg/kg bw/d >0.01 mg/kg bw/d

Tier 2 calculation with EMA food basket data consumption:

WCCE adult = (0.975 x 1.5 L of milk)/60 kg bw

WCCE adult = 0.024 mg/kg bw/d >0.01 mg/kg bw/d

These results show an exceedance of the Upper Intake Level (UL) for adult in tier 1 and in tier 2.

These results show an exceedance of the Upper Intake Level (UL) for adult in tier 1. However, no exceedance is shown in Tier 2.

Tier 1 calculation with EFSA Concise Database:

WCCE adult= 1.78 mg/kg of milk x (6.05 g/kg bw d/ 1000)

WCCE adult = 0.011 mg/kg bw/d ⬄ 646.14 µg/d >600 µg/d

WCCE children = 1.78 mg/kg of milk x (32.86 g/kg bw d /1000)

WCCE children = 0.058 mg/kg bw/d ⬄ 912.46 µg/d >250 µg/d

WCCE toddlers =1.78 mg/kg of milk x (40.51 g/kg bw d/1000)

WCCE toddlers = 0.072 mg/kg bw/d ⬄ 721.08 µg/d >250 µg/d

WCCE infants = 1.78 mg/kg of milk x (80.35 g/kg bw d/ 1000)

WCCE infants = 0.143 mg/kg bw/d ⬄ 1144.18 µg/d >200 µg/d

These results show an exceedance of the Upper Intake Level (UL) in tier 1.

Tier 2 calculation with EFSA Concise Database:

WCCE adult= 0.977 mg/kg of milk x (6.05 g/kg bw d/ 1000)

WCCE adult = 0.006 mg/kg bw/d ⬄ 354.65 µg/d <600 µg/d

WCCE children = 0.977 mg/kg of milk x (32.86 g/kg bw d /1000)

WCCE children = 0.032 mg/kg bw/d ⬄ 500.83 µg/d >250 µg/d

WCCE toddlers =0.977 mg/kg of milk x (40.51 g/kg bw d/1000)

WCCE toddlers = 0.040 mg/kg bw/d ⬄ 395.78 µg/d >250 µg/d

WCCE infants =0.977 mg/kg of milk x (80.35 g/kg bw d /1000)

WCCE infants =0.079 mg/kg bw/d ⬄ 628.02 µg/d >200 µg/d

An exceedance of the Upper Intake Level (UL) for children, toddlers and infants cannot be excluded based on the available data.

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

**Conclusion**

No exceedance of the Upper Intake Level (UL) is observed for adults with EFSA Concise Database. However, an exceedance is observed for children, toddlers and infants. Nevertheless, as the estimation of iodine contamination in milk is performed considering the worst-case situation, the dietary exposure calculation is probably overestimated and an exceedance of UL might be unlikely.

Furthermore, it has to be noted that several iodine based products have been authorised under BPR (via union authorisation process) with a total concentration iodine greater than 0.222% and despite an exceedance of the UL (Deosan Activate BPF, IODIGUARD, TEAT DISINFECTANTS BIOCIDAL PRODUCT FAMILY OF CVAS, etc). In conclusion, ALGOFILM does not bring a greater risk than the other iodine based biocidal products already authorized on the European market.

## Summaries of the efficacy studies

See IUCLID files

## Confidential annex

See separated confidential PAR.

1. Please fill in here the identifying product name from R4BP. [↑](#footnote-ref-2)
2. Please delete as appropriate. [↑](#footnote-ref-3)
3. 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-4)
4. 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-5)
5. 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-6)
6. 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-7)
7. When an annex in not relevant, please do not delete the title, but indicate the reason why the annex should not be included. [↑](#footnote-ref-8)
8. ARTFood draft Guidance on teat dip scenario, 2016. [↑](#footnote-ref-9)
9. Volume 8: Notice to applicants and Guideline – Veterinary medicinal products : Establishment of maximum residue limits (MRLs) for residues of veterinary medicinal products in foodstuffs of animal origin [↑](#footnote-ref-10)
10. http://www.efsa.europa.eu/en/food-consumption/comprehensive-database [↑](#footnote-ref-11)
11. Reasoned opinion on the potential chronic and acute risk to consumers’ health arising from proposed temporary EU MRLs - 15/03/2007 [↑](#footnote-ref-12)
12. https://echa.europa.eu/documents/10162/19680902/heeg\_opinion\_17\_default\_human\_factor\_values\_en.pdf [↑](#footnote-ref-13)
13. Worst Case Consumer Exposure [↑](#footnote-ref-14)