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

**PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT (FAMILY) FOR NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



DeLaval iodine-based teat disinfectant family

Product type PT03

Iodine as included in the Union list of approved active substances

Case Number in R4BP: BC-HG016382-55

Evaluating Competent Authority: Ctgb The Netherlands

Date: 29/04/2019

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# CONCLUSION

**Overall**

It is concluded by the eCA that sufficient data have been provided to verify the outcome and conclusions, and permit authorisation of the biocidal product family. When using the products 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 to the environment.

**Phys-chem**

The identity, physico-chemical properties and analytical methods were adequately addressed. The products within the family have a pH between 3.5 and 6. For meta SPCs 1 to 4, 6 and 7, a shelf-life of 1 year in HDPE is supported. For meta SPC 5, the shelf-life is 2 years. As no information was generated on the stability of the product at low and elevated temperatures, the products are to be stored below 30°C and protected from frost. With regard to physical and chemical hazards, for the products within the family no classification is proposed, with the exception of meta SPCs 6 and 7, which should be classified as metal corrosive cat 1 (H290).

**Efficacy**

For the 5 *meta* SPCs in this family efficacy test data have been submitted (phase 2 step 1 and phase 2 step 2 tests), under conditions for post-milking teat disinfection (skimmed milk 1% as soiling, 5 min contact time).

The tests demonstrated the following:

* All post-milking products in the family have bactericidal, yeasticidal, and virucidal effect at minimal contact time of 5 minutes, when used according to the use instructions.
* Concentrated products (Meta SPC 5) should be diluted to a use concentration of 0.15 % w/w iodine. The ready-to-use products (Meta SPC 1, 2, 3, 4) should not be diluted.

**Human Health**

The risk assessment for human health takes into account HEAdhoc recommendation 13, and agreements from working group and WebEx meetings on iodine based union authorisation applications.

Professional user risk assessment

When only exposures arising from the biocidal use are considered, acceptable risks are identified for manual dipping and spraying without PPE.

When exposure arising from biocidal use and total dietary intake are considered, acceptable risks are identified for post-milking disinfection by manual dipping with products included in the BPF; meta SPC 1-7 without the need for PPE (max 66 % of the iodine upper limit (UL). For post-milking disinfection by manual spraying using a trigger sprayer or electronic sprayer, acceptable risks are identified assuming appropriate PPE is worn with products included in the BPF; meta SPC 1-7 (chemical resistant gloves max 85% of the UL).

Consumer risk assessment

Based on the risk assessment of consumers, taking into account only the effect from the use of products included in the BPF, safe use is identified (adult 2% UL and infant/toddler 7% of UL). However, when taken into account all iodine sources (i.e. including background values from milk and other dietary sources), the UL for toddlers is slightly exceeded (i.e. 101% UL). However, as the background in milk and other sources together leads to 94% UL and considering that the basis of the calculations are conservative, this slight exceedance is considered acceptable.

**Environment**

No unacceptable risks are identified for the environment when the products are used according to the instructions for use and when the risk mitigation measures as indicated in the SPC are taken into account.

# ASSESSMENT REPORT

## Summary of the product assessment

### Administrative information

#### Identifier of the product family

| **Identifier** | **Country (if relevant)** |
| --- | --- |
| DeLaval iodine-based teat disinfectant family | Not applicable (not a trade name) |

***Identifier of the products within the product family[[1]](#footnote-1)***

Trade names to be used

| **Formula nr** | **Trade name** | **Where\*** |
| --- | --- | --- |
| GMP 44 | Blockade | All Member States |
| GMP 54 | IodoFence | All Member States |
| GMP 43 | Proactive | All Member States, except Belgium |
| Iobac RTU | Belgium |
| GMP 42 | Proactive Plus | All Member States |
| GMP 56 | Fortex | All Member States |
| GMP 51 | Tri-Fender | All Member States |
| F-2506 | TriActive | All Member States |
| GMP 34 | Dipal RTU | All Member States |
| GMP 36 | Dipal Plus | All Member States |
| GMP 48 | Dipal Conc | All Member States, except Belgium |
| Iobac Conc | Belgium |

\* please note that not all products are marketed in all countries

#### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | DeLaval NV |
| **Address** | Industriepark-Drongen 10  B-9031 Gent, Belgium |
| **Authorisation number** |  | |
| **Date of the authorisation** |  | |
| **Expiry date of the authorisation** |  | |

#### Manufacturer of the products of the family

|  |  |
| --- | --- |
| **Name of manufacturer** | DeLaval NV |
| **Address of manufacturer** | Industriepark-Drongen 10  B-9031 Gent, Belgium |
| **Location of manufacturing sites** | Industriepark-Drongen 10  B-9031 Gent, Belgium |

#### Manufacturer of the active substance

DeLaval NV is part of the Iodine Registration Group and listed as active substance supplier on the Article 95 list. Iodine used for the production of biocidal products of DeLaval NV is manufactured outside the EU. The current source for Iodine is listed in the table. This source is one of the reference sources in the dossier of the active substance.

|  |  |
| --- | --- |
| **Active substance** | Iodine |
| **Name of manufacturer** | Sociedad Quimica y Minera (SQM) S.A. |
| **Address of manufacturer** | Supplier EU: SQM Europe NV, Sint-Pietersvliet  7 bus 8, 2000 Antwerpen, Belgium |
| **Location of manufacturing sites** | Los Militares 4290 Piso 4, 8320000 Las Condes (Santiago), Chile |

### Product family composition and formulation

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

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

Yes

No

#### Identity of the active substance

|  |  |
| --- | --- |
| **Main constituent(s)** | |
| **ISO name** | Iodine |
| **IUPAC or EC name** | Iodine |
| **EC number** | 231-442-4 |
| **CAS number** | 7553-56-2 |
| **Index number in Annex VI of CLP** | 053-001-00-3 |
| **Minimum purity / content** | 99.5 % |
| **Structural formula** | I-I |

The products within this product family are based on iodophor 1 (surfactant complexed iodine).

#### Candidate(s) for substitution

Not applicable.

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

#### Not applicable, application is for a product family.

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

The product family consists of ten members, nine ready-to-use products and one concentrate. All products are iodine-based liquid solutions, intended for post-milking teat disinfection (PT03). The products are applied directly after milking on the teats. The iodine concentration in the ready-to-use solutions is: 0.15 – 0.25 %.

The products are divided in 7 Meta SPCs. The first Meta SPC consists of 2 products, all ready-to-use products containing iodate that are classified as Aquatic Chronic 3 (H412). The second Meta SPC consists of 3 products, again all ready-to-use that are labelled with hazard statement EUH 208, due to asodium iodate concentration equal or higher than 0.1%, and H412.

Meta SPC 4-5, comprised of products without iodate, were split up according to their classification or formulation type. Meta SPC 3 consists of one ready-to-use product without iodate that is not classified. The fourth Meta SPC consists of one ready-to-use formulation, classified as Eye Irrit Cat 2 (H319). Meta SPC 5 consists of the concentrate that is classified as H319 and H412. Meta SPCs 6 and 7 consist of a single product, classified as Metal corrosive 1 (H290) and H412, additionally Meta SPC 7 is classified with EUH 208 due to asodium iodate concentration equal or higher than 0.1%.

NB: the full composition of the product family is provided in the confidential annex.

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** | |
| --- | --- | --- | --- | --- | --- | --- |
| **Min** | **Max** |
| Iodine | iodine | Active substance | 7553-56-2 | 231-442-4 | 0.15 | 0.75 (conc) |
| Alcohol ethoxylate | Alcohols, C9-11, ethoxylated | Non-active substance | 68439-46-3 | Not available | 0 | 6.34 |
| Sodium iodide | Sodium iodide | Non-active substance | 7681-82-5 | 231-679 | 0.06 | 0.33 |

#### Information on technical equivalence

The source of the substance is the same as was evaluated for inclusion in the Union list of approved active substances.

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

The DeLaval iodine family contains two substances of concern, see 2.1.2.4 for its identity and concentration ranges and the confidential annex for more information on classification and labelling and trade name(s). Alcohol ethoxyclate is classified H318 (Eye Damage Cat 1) and H302 (Acute Tox Cat 4) and sodium iodide is classified with H372 (STOT RE 1). More information on the SoCs is included in section 2.6.2.1, Available toxicological data relating to non active substance(s) (i.e. substance(s) of concern).

#### Type of formulation

|  |
| --- |
| AL: Any other liquid (ready to use water-based liquids)  SL: Soluble concentrate |

### Hazard and precautionary statements

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

**Meta SPC 1**

The following classification applies to all products within Meta SPC 1:

(GMP 51 – Tri-Fender, F-2506 – TriActive)

| **Classification** | |
| --- | --- |
| Hazard category | Aquatic Chronic 3 |
| Hazard statement | H412 - Harmful to aquatic life with long lasting effects |
|  | |
| **Labelling** | |
| Signal words | - |
| Hazard statements | H412 - Harmful to aquatic life with long lasting effects |
| Precautionary statements | P102 - Keep out of reach of children  P273 -Avoid release to the environment |

**Meta SPC 2**

The following classification applies to all products within Meta SPC 2:

(GMP 44 – Blockade, GMP 54 – IodoFence, GMP 56 – Fortex)

| **Classification** | |
| --- | --- |
| Hazard category | Aquatic Chronic 3 |
| Hazard statement | H412 - Harmful to aquatic life with long lasting effects |
|  | |
| **Labelling** | |
| Signal words | - |
| Hazard statements | EUH208 - Contains sodium iodate. May produce an allergic reaction. |
| Precautionary statements | P102 - Keep out of reach of children  P273 -Avoid release to the environment |

**Meta SPC 3**

The following classification applies to all products within Meta SPC 3:

(GMP 34 – Dipal RTU)

| **Classification** | |
| --- | --- |
| Hazard category | Not classified |
| Hazard statement | Not classified |
|  | |
| **Labelling** | |
| Signal words | - |
| Hazard statements | - |
| Precautionary statements | P102 - Keep out of reach of children |

**Meta SPC 4**

The following classification applies to all products within Meta SPC 4:

(GMP 36 – Dipal Plus)

| **Classification** | |
| --- | --- |
| Hazard category | Eye Irrit 2 |
| Hazard statement | H319 - Causes serious eye irritation |
|  | |
| **Labelling** | |
| Signal words | Warning |
| Hazard statements | H319 - Causes serious eye irritation |
| Precautionary statements | P102 - Keep out of reach of children  P264 – Wash hands thoroughly after handling  P280 - Wear eye protection/face protection  P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing  P337 + P313 - If eye irritation persists: Get medical advice/attention |

**Meta SPC 5**

The following classification applies to all products within Meta SPC 5:

(GMP 48 – Dipal Conc / Iobac Conc)

| **Classification** | |
| --- | --- |
| Hazard category | Eye Irrit 2  STOT RE 2  Aquatic Chronic 3 |
| Hazard statement | H319 - Causes serious eye irritation  H373- May cause damage to thyroid through prolonged or repeated exposure, oral route.  H412 - Harmful to aquatic life with long-lasting effects |
|  | |
| **Labelling** | |
| Signal words | Warning |
| Hazard statements | H319 - Causes serious eye irritationH373- May cause damage to thyroid through prolonged or repeated exposure, oral route.  H412 - Harmful to aquatic life with long-lasting effects |
| Precautionary statements | P102 - Keep out of reach of children  P264 – Wash hands thoroughly after handling  P273 - Avoid release to the environment.  P280 - Wear eye protection/face protection  P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing  P337 + P313 - If eye irritation persists: Get medical advice/attention |

**Meta SPC 6**

The following classification applies to all products within Meta SPC 6:

(GMP 42 – Proactive Plus)

| **Classification** | |
| --- | --- |
| Hazard category | Metal corrosive 1  Aquatic Chronic 3 |
| Hazard statement | H290 – May be corrosive to metals  H412 - Harmful to aquatic life with long lasting effects |
|  | |
| **Labelling** | |
| Signal words |  |
| Hazard statements | H290 – May be corrosive to metals  H412 - Harmful to aquatic life with long lasting effects |
| Precautionary statements | P102 - Keep out of reach of children  P273 -Avoid release to the environment |

**Meta SPC 7**

The following classification applies to all products within Meta SPC 7:

(GMP 43 – Proactive/Iobac RTU)

| **Classification** | |
| --- | --- |
| Hazard category | Metal corrosive 1  Aquatic Chronic 3 |
| Hazard statement | H290 – May be corrosive to metals  H412 - Harmful to aquatic life with long lasting effects |
|  | |
| **Labelling** | |
| Signal words |  |
| Hazard statements | H290 – May be corrosive to metals H412 - Harmful to aquatic life with long lasting effects EUH208 - Contains sodium iodate. May produce an allergic reaction. |
| Precautionary statements | P102 - Keep out of reach of children  P273 -Avoid release to the environment |

### Authorised use

The family contains 7meta-SPC’s, of which meta-SPC 1-4 and 6-7 only contain ready-to-use products while meta-SPC 5 contains a concentrated product. The uses in all meta-SPC’s are identical, however, there are some small differences that make it necessary to divide the use instruction into different uses.

- Not all products will be used for both spraying and dipping, therefore, the use instructions for dipping and spraying need to be separated (use# 1 and 3 for dipping, use# 2 and 4 for spraying).

- The concentrated product needs to be diluted before use, which is a specific use instruction (use #3 and 4).

#### Use description

Meta SPC 1 to 4 and 6-7

Table 1. Use # 1 – Teat disinfection; Ready-to-use dip products applied manually

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for post-milking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking teat disinfection of udder teats with ready-to-use products.  The product is applied after milking on the teats by manual dipping using a dip cup. |
| **Application rate(s) and frequency** | To be applied after milking, 2 times per day. The products can be used all year during the lactation period.  Dose: ca. 5 ml per cow; ca. 2.5 ml per sheep or goat  Dilution: 0% |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Please see 2.1.7 |

#### Use-specific instructions for use #1

|  |
| --- |
| The products are ready-to-use products and are used undiluted.  The product must be brought to a temperature above 20°C before use.  **Directions for use**:  It is recommended to wear gloves during milking and application to protect the skin and ensure hygienic milking condition. For manual application: use a clean dip cup.  Ensure that teats are clean before use. Apply the ready-to-use solution of the product on each teat immediately after milking:  DIP: dip every teat in the product. Ensure that the teat is covered to at least three quarters length and replenish the dip cup as necessary;  Allow teats to dry after application for at least 5 min and keep the animals standing during this period. |

#### Use-specific risk mitigation measures for use #1

|  |
| --- |
| metaSPC1, 2, 3, 6 and 7:  There are no use specific risk mitigation measures.  metaSPC4:  Use eye/face protection during post-milking teat disinfection by manual dipping.  See 2.1.5 for general instructions. |

#### Where specific to the use #1, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #1, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #1, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| See 2.1.5.5 |

#### Use description

Meta SPC 1 to 4 and 6-7

Table 2. Use # 2 – Teat disinfection; Ready-to-use spray products applied manually

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for post-milking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking teat disinfection of udder teats with ready-to-use products.  The product is applied after milking manually on the teats by spraying using a spray container. |
| **Application rate(s) and frequency** | To be applied after milking, 2 times per day. The products can be used all year during the lactation period.  Dose: ca. 5 ml per cow; ca. 2.5 ml per sheep or goat  Dilution: 0% |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Please see 2.1.7. |

#### Use-specific instructions for use #2

|  |
| --- |
| The products are ready-to-use products and are used undiluted.  The product must be brought to a temperature above 20°C before use.  **Directions for use**:  For manual application: use a clean applicator.  Ensure that teats are clean before use. Apply the ready-to-use solution of the product on each teat immediately after milking:  1) MANUAL TRIGGER SPRAY: spray every teat 1 sec. with the product. Ensure that the teat is covered to at least three quarters length and replenish the spray container as necessary;  2) AUTOMATIC SPRAYER: spray every teat 1 sec. with the product.  Allow teats to dry after application for at least 5 min and keep the animals standing during this period. |

#### Use #2-specific risk mitigation measures

|  |
| --- |
| metaSPC1, 2, 3, 6 and 7:  Use chemical resistant gloves (glove material to be specified by the authorisation holder within the product information) during post-milking teat disinfection by manual spraying.  metaSPC4:  Use chemical resistant gloves (glove material to be specified by the authorisation holder within the product information) and eye/face protection during post-milking teat disinfection by manual spraying.  See 2.1.5 for general instructions. |

#### Where specific to the use #2, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #2, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #2, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| See 2.1.5.5 |

#### Use description

Meta SPC 5

Table 3. Use # 3 – Teat disinfection; concentrated dip products applied manually

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for post-milking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking disinfection of udder teats with diluted concentrate.  The product is applied manually after milking on the teats by manual dipping using a dip cup. |
| **Application rate(s) and frequency** | To be applied after milking, 2 times per day. The products can be used all year during the lactation period.  Dilution: 20% : Use concentration: 0.15 % w/w iodine.  Dose: ca. 5 ml per cow; ca. 2.5 ml per sheep or goat |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Please see 2.1.7 |

#### Use-specific instructions for use #3

|  |
| --- |
| **Directions for use**:  It is recommended to wear gloves during milking and application to protect the skin and ensure hygienic milking condition.  A 20% dilution should be made with clean water. Take 200 ml of the concentrated product and make up to 1 L with water to obtain an end concentration of 0.15% iodine.  The use solution must be brought to a temperature above 20°C before use.  It is possible that foaming occurs while preparing the ready-to-use solution. In that case it is strongly recommended to only start the treatment after the foam level has sufficiently decreased  For manual application: use a clean dip cup  Ensure that teats are clean before use. Apply the diluted product on each teat immediately after milking:  DIP: dip every teat in the product. Ensure that the teat is covered to at least three quarters length and replenish the dip cup as necessary;  Allow teats to dry after application for at least 5 min and keep the animals standing during this period. |

#### Use-specific risk mitigation measures for use #3

|  |
| --- |
| .  Use eye/face protection during post-milking teat disinfection by manual dipping.  See 2.1.5 for general instructions. |

#### Where specific to the use #3, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #3, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #3, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| See 2.1.5.5 |

#### Use description

#### Meta SPC 5

#### Table 4. Use # 4 – Teat disinfection; concentrated spray products applied manually

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for post-milking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking disinfection of udder teats with diluted concentrate.  The product is applied manually after milking on the teats by spraying using a spray container.. |
| **Application rate(s) and frequency** | To be applied after milking, 2 times per day. The products can be used all year during the lactation period.  Dilution: 20% : Use concentration: 0.15 % w/w iodine.  Dose: ca. 5 ml per cow; ca. 2.5 ml per sheep or goat |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | See 2.1.7 |

#### Use-specific instructions for use #4

|  |
| --- |
| **Directions for use**:  A 20% dilution should be made with clean water. Take 200 ml of the concentrated product and make up to 1 L with water to obtain an end concentration of 0.15% iodine.  The use solution must be brought to a temperature above 20°C before use.  It is possible that foaming occurs while preparing the ready-to-use solution. In that case it is strongly recommended to only start the treatment after the foam level has sufficiently decreased.  For manual application: use a clean applicator.  Ensure that teats are clean before use. Apply the diluted product on each teat immediately after milking:  1) MANUAL TRIGGER SPRAY: spray every teat 1 sec. with the product. Ensure that the teat is covered to at least three quarters length and replenish the spray container as necessary;  2) AUTOMATIC SPRAYER: spray every teat 1 sec. with the product.  Allow teats to dry after application for at least 5 min and keep the animals standing during this period. |

#### Use #4-specific risk mitigation measures

|  |
| --- |
| Use chemical resistant gloves (glove material to be specified by the authorisation holder within the product information) and eye/face protection during post-milking teat disinfection by manual spraying.  See 2.1.5 for general instructions. |

#### Where specific to the use #4, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #4, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #4, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| See 2.1.5.5 |

#### Use description

Meta SPC 1 to 4 and 6-7

Table 2. Use # 5 – Teat disinfection; Read–to-use dip or spray products applied automatically

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for post-milking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking teat disinfection of udder teats with ready-to-use products.  The product is applied automatically by milking machines after milking on the teats by integrated dipping or spraying device. |
| **Application rate(s) and frequency** | To be applied after milking, 3 times per day. The products can be used all year during the lactation period.  Dose: ca. 5 ml per cow; ca. 2.5 ml per sheep or goat  Dilution:- 0% for RTU products |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Please see 2.1.7. |

#### Use-specific instructions for use #5

|  |
| --- |
| Ready-to-use products and are used undiluted.  The product must be brought to a temperature above 20°C before use. |

#### Use #5-specific risk mitigation measures

|  |
| --- |
| metaSPC1, 2, 3, 6 and 7:  There are no use specific risk mitigation measures.  metaSPC4:  Use eye/face protection during post-milking teat disinfection by automated dipping or spraying.  See 2.1.5 for general instructions. |

#### Where specific to the use #5, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #5, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #5, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| See 2.1.5.5 |

Meta SPC 5

Table 2. Use # 6 – Teat disinfection; Concentrated dip or spray products applied automatically

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for post-milking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking teat disinfection of udder teats with ready-to-use products.  The product is applied automatically by milking machines after milking on the teats by integrated dipping or spraying device. |
| **Application rate(s) and frequency** | To be applied after milking, 3 times per day. The products can be used all year during the lactation period.  Dilution: 20% : Use concentration: 0.15 % w/w iodine.  Dose: ca. 5 ml per cow; ca. 2.5 ml per sheep or goat |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Please see 2.1.7. |

#### Use-specific instructions for use #6

|  |
| --- |
| A 20% dilution should be made with clean water. Take 200 ml of the concentrated product and make up to 1 L with water to obtain an end concentration of 0.15% iodine.  The use solution must be brought to a temperature above 20°C before use.  It is possible that foaming occurs while preparing the ready-to-use solution. In that case it is strongly recommended to only start the treatment after the foam level has sufficiently decreased |

#### Use #6-specific risk mitigation measures

|  |
| --- |
| Use eye/face protection during post-milking teat disinfection by automated dipping or spraying.  See 2.1.5 for general instructions. |

#### Where specific to the use #6, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #6, the instructions for safe disposal of the product and its packaging

|  |
| --- |
| There are no use specific instructions. See 2.1.5 for general instructions. |

#### Where specific to the use #6, the conditions of storage and shelf-life of the product under normal conditions of storage

|  |
| --- |
| See 2.1.5.5 |

### General directions for use

#### Instructions for use

|  |
| --- |
| There are no general instructions for use. See 2.1.4 for use specific instructions for use # 1 to 6. |

#### 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

|  |
| --- |
| **- Direct/Indirect effects:**  According to our experience and to the information provided to us, the product does not have any adverse effects if it is used and handled as specified.  **- First aid measures:**  Eye contact: Rinse thoroughly with plenty of water for at least 15 minutes. If eye irritation persists: Get medical advice/attention.  Skin contact: Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes.  Ingestion: Wash out mouth with water. Seek medical advice immediately if symptoms occur and/or large quantities have been ingested. Inhalation: Move to fresh air.  **- Emergency measures to protect the environment:**  Prevent further leakage or spillage if safe to do so.  Methods and materials for containment and cleanup: Dam up. Soak up with inert absorbent material. Prevent product from entering drains. Keep in suitable and closed containers for disposal. |

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

|  |
| --- |
| At the end of the treatment, dispose unused product and the packaging in accordance with local requirements. Used product can be flushed to the municipal sewer or disposed to the manure deposit depending on local requirements. Avoid release to an individual waste water treatment plant. |

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

|  |
| --- |
| Storage: Store upright in the tightly closed original container. Protect from direct light, temperatures above 30°C and frost.  Shelf-life: 2 years for concentrates (Meta SPC 5) and 1 year for ready-to-use products (Meta SPC 1-4). |

### Other information

|  |
| --- |
| Application codes: not applicable |

### 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)** |
| Bottle | 1 L | HDPE | HDPE screw caps and seals | professional | YES |
| Can | 5 L | HDPE | HDPE screw caps and seals | professional | YES |
| Can | 10 L | HDPE | HDPE screw caps and seals | professional | YES |
| Can | 20 L | HDPE | HDPE screw caps and seals | professional | YES |
| Can | 60 L | HDPE | HDPE screw caps and seals | professional | YES |
| Drum | 200 L | HDPE | HDPE screw caps and seals | professional | YES |
| IBC | 1000 L | HDPE | HDPE screw caps and seals | professional | YES |

### Documentation

#### Data submitted in relation to product application

See reference list in **Appendix 1**.

#### Access to documentation

The applicant, DeLaval NV, is owner of all data submitted with regard to the tests performed on the products within this family. Therefore no letter of access is submitted.

DeLaval NV is a member of the Iodine Registration Group (IRG) consortium that submitted the active substance dossier of Iodine for PT 1, 3, 4 and 22 to the Raporteur Member State Sweden. Also, DeLaval NV is listed as active substance supplier for iodine on the Article 95 list. Therefore a letter of access (LoA) to the active substance dossier is not required in this case. A declaration on ownership of data and access rights to the complete iodine substance dossier is provided.

## Assessment of the biocidal product family

### Intended use as applied for by the applicant

The uses below are the ones applied for by the applicant after the first evaluation, without any changes by the e-CA. These uses are assessed in the following chapters.

[See 2.1.4 for the authorised uses, after assessment of the dossier.]

Table 1. Intended Use # 1 – Teat disinfection; Ready-to-use dip products

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for postmilking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking teat disinfection of udder teats with ready-to-use products  The product is applied after milking on the teats by manual dipping using a dip cup. |
| **Application rate(s) and frequency** | To be applied after milking, usually 2 times per day. The products can be used all year during the lactation period.  Use concentration: 0.15 – 0.25 % w/w iodine. |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Type Material Size  Can Plastic: HDPE 5L  Can Plastic: HDPE 10L  Can Plastic: HDPE 20L  Can Plastic: HDPE 60L  Drum Plastic: HDPE 200L  IBC Plastic: HDPE 1000L |

Table 2. Intended Use # 2 – Teat disinfection; Ready-to-use spray products

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for postmilking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking teat disinfection of udder teats with ready-to-use products.  The product is applied after milking on the teats by spraying using a spray container. Alternatively, milking machines with integrated automated spraying are being used. |
| **Application rate(s) and frequency** | To be applied after milking, usually 2 times per day. The products can be used all year during the lactation period.  Use concentration: 0.15 – 0.25 % w/w iodine. |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Type Material Size  Can Plastic: HDPE 5L  Can Plastic: HDPE 10L  Can Plastic: HDPE 20L  Can Plastic: HDPE 60L  Drum Plastic: HDPE 200L  IBC Plastic: HDPE 1000L |

Table 3. Intended Use # 3 – Teat disinfection; concentrated dip products

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for postmilking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking disinfection of udder teats with diluted concentrate.  The product is applied after milking on the teats by manual dipping using a dip cup. |
| **Application rate(s) and frequency** | To be applied after milking, usually 2 times per day. The products can be used all year during the lactation period.  Use concentration: 0.15 – 0.25 % w/w iodine. |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Type Material Size  Bottle Plastic: HDPE 1L  Can Plastic: HDPE 5L  Can Plastic: HDPE 10L  Can Plastic: HDPE 20L  Can Plastic: HDPE 60L  Drum Plastic: HDPE 200L  IBC Plastic: HDPE 1000L |

#### Table 4. Use # 4 – Teat disinfection; concentrated spray products

|  |  |
| --- | --- |
| **Product Type** | 3 |
| **Where relevant, an exact description of the authorised use** | Teat disinfectant |
| **Target organism (including development stage)** | Bacteria  Yeasts  Viruses |
| **Field of use** | Indoor  All products within the product family are intended for postmilking teat disinfection. The products are applied directly after milking on the teats of lactating animals. |
| **Application method(s)** | Post-milking disinfection of udder teats with diluted concentrate.  The product is applied after milking on the teats by spraying using a spray container. Alternatively, milking machines with integrated automated spraying are being used. |
| **Application rate(s) and frequency** | To be applied after milking, usually 2 times per day. The products can be used all year during the lactation period.  Use concentration: 0.15 – 0.25 % w/w iodine. |
| **Category(ies) of users** | Professional |
| **Pack sizes and packaging material** | Type Material Size  Bottle Plastic: HDPE 1L  Can Plastic: HDPE 5L  Can Plastic: HDPE 10L  Can Plastic: HDPE 20L  Can Plastic: HDPE 60L  Drum Plastic: HDPE 200L  IBC Plastic: HDPE 1000L |

### Physical, chemical and technical properties

The products within the family have the following development codes:

|  |  |  |
| --- | --- | --- |
| Sorted in alphabetical order of the development code:Product code | Trade name | Meta SPC |
| F-2506 | TriActive | 1 |
| GMP34 | Dipal RTU | 3 |
| GMP36 | Dipal Plus | 4 |
| GMP42 | Proactive Plus | 6 |
| GMP43 | Proactive | 7 |
| GMP44 | Blockade | 2 |
| GMP48 | Dipal Conc | 5 |
| GMP51 | Tri-Fender | 1 |
| GMP54 | IodoFence | 2 |
| GMP56 | Fortex | 2 |

Sorted per meta SPC:

|  |  |  |
| --- | --- | --- |
| Meta SPC | Product code | Trade name |
| 1 | F-2506 | TriActive |
|  | GMP51 | Tri-Fender |
| 2 | GMP44 | Blockade |
|  | GMP54 | IodoFence |
|  | GMP56 | Fortex |
| 3 | GMP34 | Dipal RTU |
| 4 | GMP36 | Dipal Plus |
| 5 | GMP48 | Dipal Conc |
| 6 | GMP42 | Proactive Plus |
| 7 | GMP43 | Proactive |

In the table below, the physical and chemical data of the family was summarised. The eCA has made remarks, where deemed necessary. It should be noted that the evaluation may be based on 5 meta SPCs, where the application contains 7. Meta SPCs 1 and 2 needed to be split based on classification and labelling related issues (H290). The conclusions with regard to meta SPC 1 also apply to meta SPC 6. Conclusions with regard to meta SPC 2 also apply to meta SPC 7.

| **Property** | **Guideline and Method** | **Purity of the test substance (% w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Physical state at 20 °C and 101.3 kPa | Visual | Undiluted product | Liquid | Certificates of analysis of the products |
| Colour at 20 °C and 101.3 kPa | Visual | Undiluted product | Brown | Certificates of analysis of the products |
| Odour at 20 °C and 101.3 kPa | Smelling | Undiluted product | Iodine | Certificates of analysis of the products |
| **eCA remark**  Acceptable. All products within the family are brown liquids with an iodine-like odour. | | | | |
| Acidity / alkalinity | CIPAC MT 75.3 | Undiluted product  F-2506:  0.217%  GMP34:  0.149%  GMP36:  0.155%  GMP42:  0.159%  GMP43: 0.171%  GMP44: 0.261%  GMP48:  0.753%  GMP51:  0.272%  GMP54:  0.258%  GMP56:  0.249% | pH 4 – 6 (25°C)  F-2506: 5.78  GMP34: 4.06  GMP36: 4.83  GMP42: 5.61  GMP43: 5.53  GMP44: 5.72  GMP48: 4.39  GMP51: 5.88  GMP54: 5.52  GMP56: 4.75 | FR 2014-PC-002, 004, 006, 007, 009, 013, 014, 016, 018, 019 |
| **eCA remark**  Acceptable. All products within the family have a pH in the range of 4 to 6. This limitation should apply to future products as well to ensure the necessary stability. | | | | |
| Relative density / bulk density | USP Test Method 841, Specific Gravity (densitometer) | Undiluted product  F-2506:  0.217%  GMP34:  0.149%  GMP36:  0.155%  GMP42:  0.159%  GMP43: 0.171%  GMP44: 0.261%  GMP48:  0.753%  GMP51:  0.272%  GMP54:  0.258%  GMP56:  0.249% | 1.00 – 1.08 (25°C)  F-2506: 1.009  GMP34: 1.014  GMP36: 1.016  GMP42: 1.030  GMP43: 1.013  GMP44: 1.025  GMP48: 1.076  GMP51: 1.010  GMP54: 1.024  GMP56: 1.068 | FR 2014-PC-002, 004, 006, 007, 009, 013, 014, 016, 018, 019 |
| **eCA remark**  The data provided is considered representative for the family. As all products are aqueous, the density is generally at least 1.0 and depending on the co-formulants, may increase to approximately 1.1. | | | | |
| Storage stability test – **accelerated storage** | / | / | DATA WAIVING  Labels of all products contain the sentence: "Protect from temperatures above 30°C". Therefore accelerated storage stability tests were not performed. | / |
| **eCA remark**  The restriction with regard to storage conditions, necessary to allow waiving accelerated data, is storage equal to or below 30°C. The SPC includes recommendations for storage accordingly. | | | | |
| Storage stability test – **long term storage at ambient temperature** | **pH:** Ph. Eur. monograph 2.2.3 “Potentiometric determination of pH”.  **Density**: 2.2.5. Relative density, Eur. Ph. VII  **Iodine:** Ph. Eur. monograph 31 „Iodine“ | Undiluted product | Stability data of 1 batch per product (supporting at least the claimed shelf-life) are summarized below:   |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **F-2506** (Batch A344950300) | | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%)  Pot iodine\* (%) | | **TOM**  Conf  1.0072  5.27  0.21  0.389 | | **2 Y**  Conf  1.0072  5.45  0.22  0.297 | | | | **GMP 34** (Batch 3724502) | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%) | **TOM**  Conf  1.0128  3.91  0.14 | | **1 Y**  Conf  1.0129  3.70  0.13 | | | | **GMP 36** (Batch A343640400) | | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%) | | **TOM**  Conf  1.0137  4.65  0.15 | | **1 Y**  Conf  1.0136  4.19  0.14 | | | | **GMP 42** (Batch 31107202) | | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%)  Pot iodine\* (%) | | **TOM**  Conf  1.0278  5.14  0.15  0.394 | | **1 Y**  Conf  1.0281  5.58  0.17  0.313 | | | | **GMP 43** (Batch 3811402) | | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%)  Pot iodine\* (%) | | **TOM**  Conf  1.011  4.83  0.15  0.61 | | **1 Y**  Conf  1.011  5.42  0.17  0.54 | | | | **GMP 44** (Batch A3124120300) | | | | | | **Property**  Appearance  Density (g/ml)  pH  Viscosity (cP)  Av iodine (%)  Pot iodine\* | | **TOM**  Conf  1.023  5.1  194  0.25  0.80 | | **2 Y**  Conf  1.023  5.6  203  0.28  0.63 | | **GMP 48** (Batch 3603301 06A18) | | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%) | | **TOM**  Conf  1.076  3.62  0.74 | | **2.5 Y**  Conf  1.074  3.24  0.71 | | | | **GMP 51** (Batch 31119404) | | | | | | | | **Property**  Appearance  Density (g/ml)  pH  Av iodine (%) | | **TOM**  Conf  1.0075  5.42  0.25 | | **3 Y**  Conf  1.0075  5.23  0.24 | | | | **GMP 54** (Batch 3123840200) | | | | | | **Property**  Appearance  Density (g/ml)  pH  Viscosity (cP)  Av iodine (%)  Pot iodine\* | | **TOM**  Conf  1.0207  5.33  310  0.24  0.63 | | **1 Y**  Conf  1.022  5.15  289.6  0.27  0.44 | | **GMP 56** (Batch A332220200) | | | | | | **Property**  Appearance  Density (g/ml)  pH  Viscosity (cP)  Av iodine (%)  Pot iodine\* | | **TOM**  Conf  1.0673  4.42  1024  0.24  0.59 | | **2 Y**  Conf  1.0652  4.79  1072  0.26  0.28 |   All parameters remain within set specifications for all products for the duration of the study. The provided ambient stability data (25°C/60%R.H.) support a shelf life of 2 years at ambient storage conditions in HDPE cans for the following products:   * Blockade (GMP 44) * Fortex (GMP 56) * Tri-Fender (GMP 51) * TriActive (F-2506) * Dipal Conc (GMP 48)   For   * IodoFence (GMP 54) * Proactive (GMP 43) * Proactive Plus (GMP 42) * Dipal RTU (GMP 34) * Dipal Plus (GMP 36),   data support a shelf life of 1 year under normal conditions. | RA130196c  RA150000c  RA130197c  RA130216d  RA130515e  RA130198d  RA130203c  RA130184c  RA150180c  RA160174b |
| **eCA remark** All studies were performed in HDPE packaging.  The shelf-lives of the various products are not consistent throughout the family. Based on the data provided, a shelf-life of 12 months needs to be assigned to all ready-to-use products within the family, although some products tested may be stored for much longer periods of time. Considering meta SPCs need to have a set of common storage conditions and shelf-life, and all products appear to be stable for at least 12 months, the shelf-life for Meta SPC’s 1-4, 6 and 7 is set to 1 year / 12 months. Since the concentrate Dipal Conc (GMP 48) is presented in a separate Meta SPC 5, a 2 year shelf-life can be assigned for this product.  Dilution stability was addressed for meta SPC5 (see dilution stability entry below). | | | | |
| Storage stability test – **low temperature stability test for liquids** | / | / | DATA WAIVING  Labels of all products contain the sentence: "Protect from frost". Therefore low temperature stability tests were not performed. | / |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** | / | / | DATA WAIVING  All iodine-based teat disinfectants are packaged in UN-approved High-Density Polyethylene (HDPE) cans closed with HDPE screw caps. The packaging materials are standard containers for the packaging of pharmaceutical products and foodstuffs. These packaging materials have been approved and commercially used for over 10 years for the packaging and storage of iodine-containing teat dips. The cans are grey (5L, 10L, 20L, 60L, 200L) or white (1000L) and protect the product from exposure to light (UV light protected). It is also indicated on the labels that products should be stored in the tightly closed original container, protected from direct light. | / |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** | / | / | Not applicable (Labels of all products state that products should be stored upright in the tightly closed original container, protected from temperatures above 30°C and frost"). |  |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** | / | / | All materials used for packaging of the finished products are made of high-density polyethylene (HDPE) including the cans/drums/IBC, screw caps and seals. These packaging materials have been approved and commercially used for over 10 years for the packaging and storage of iodine-containing teat dips. All cans are UN-approved. The packaging materials are standard containers for the packaging of pharmaceutical products and foodstuffs and are chemically compatible with halogen containing aqueous solutions. Ambient stability studies on the products of this family are provided in IUCLID under 3.4.1. These were all performed using the same containers (identical composition and manufacturing process) as those used for commercial purposes. The smallest commercial container size was used for these studies, representing a worst-case scenario with respect to package-to-product ratio and relative headspace volume. There were no signs of interaction between the packaging materials and the product (no leakage, no ballooning or other deformations). | / |
| Wettability | n/a | n/a | n/a | n/a |
| Suspensibility, spontaneity and dispersion stability | n/a | n/a | n/a | n/a |
| Wet sieve analysis and dry sieve test | n/a | n/a | n/a | n/a |
| Emulsifiability, re-emulsifiability and emulsion stability | n/a | n/a | n/a | n/a |
| Disintegration time | n/a | n/a | n/a | n/a |
| Particle size distribution, content of dust/fines, attrition, friability | n/a | n/a | n/a | n/a |
| **eCA remark**  The MMAD of spray droplets was not determined as none of the products are equipped with a trigger sprayer and tox and efficacy do not require the droplet size for their assessments. | | | | |
| Persistent foaming | CIPAC MT 47.2 | 1+4 dilution (20%) dilution of Dipal Conc (GMP 48) | The level of foam generated when diluting Dipal Conc (GMP 48) - under the conditions of CIPAC method MT47.2 - is >100 ml after 1 minute.  The amount of foam decreases in time and after 12 min the level of foam is 50 ml. The RTU solution is not classified as hazardous and the generated foam will not lead to a risk for the operators following use of the preparation. | Persistent foaming test – Dipal Conc (GMP 48) diluted 1+4 -NB 590-36 |
| **eCA remark:**  The products are used in relatively low volumes in dipping cups. In addition, when diluting / applying the product manually, the operator is wearing PPE (gloves, protective clothing and eye/face protection) due to the product’s classification (H319). If the operator is made aware of possible foam formation, this should suffice to conclude that there is no unacceptable risk to the operator.  The following risk mitigation measure was therefore added to the SPC: *„It is possible that foaming occurs while preparing the ready-to-use solution. In that case it is strongly recommended to only start dipping or spraying after the foam level has sufficiently decreased.“* | | | | |
| Flowability/Pourability/Dustability | n/a | n/a | n/a | n/a |
| Burning rate — smoke generators | n/a | n/a | n/a | n/a |
| Burning completeness — smoke generators | n/a | n/a | n/a | n/a |
| Composition of smoke — smoke generators | n/a | n/a | n/a | n/a |
| Spraying pattern — aerosols | n/a | n/a | n/a | n/a |
| Physical compatibility | / | / | DATA WAIVING  This data requirement is not relevant to the product family and the intended uses. Products are not to be used with other substances, mixtures or biocidal or non-biocidal products (e.g. dyes). | / |
| Chemical compatibility | / | / | DATA WAIVING  This data requirement is not relevant to the product family and the intended uses. Products are not to be used with other substances, mixtures or biocidal or non-biocidal products (e.g. dyes). | / |
| Degree of dissolution and dilution stability | CIPAC MT41 | 1+4 dilution (20%) of Dipal Conc (GMP48) | Both a fresh sample of Dipal Conc (GMP 48) as well as product at the end of its shelf-life (>2 years old) and stored in a 5L HDPE can have been tested according to CIPAC MT 41. No sediment or separation was observed at the end of the test duration (18 hrs), tested at 20%v/v in CIPAC C water. | -Report dilution stability of Dipal Conc (GMP 48) – Oct 2015  Additional: Dilution stability Dipal Conc (GMP 48) - NB 525-96 |
| **eCA remark**  The dilution stability was not tested in any of the existing stability studies. Therefore, the only concentrate in the family (GMP 48, meta SPC5) was tested for dilution stability. To address storage stability, an older batch was analysed as well. As may be expected, the product can be adequately diluted. Although using two different batches does not formally allow a comparison between before and after storage, the eCA does not believe it is justified to require an entirely new study for this endpoint as it can be expected the product will remain stable upon dilution (generally the products contain readily soluble components). | | | | |
| Surface tension | EC method A.5 | Undiluted (RTU products) or 1+4 dilution (20%) of Dipal Conc (GMP48) | According to test method A.5, the surface tension of tested products lies between 33 - 43 mN/m at 20°C. | reports: 201503427 - 201503432 |
| **eCA remark**  Considering the products within the family are all based on surfactant complexed iodine (iodophor 1), the products within the family are all surface active. The RTU products were tested undiluted and the concentrate at 20%. The data is considered sufficiently representative. | | | | |
| Viscosity | OECD Test Guideline 114, Cipac L/MT 192 | Undiluted | For the more viscous products within the DeLaval iodine-based product family viscosity at 20°C is part of the release specifications:  -Blockade (GMP 44): 150–250 mPa.s (50 rpm);  -IodoFence (GMP 54): 275 – 350 mPa.s (50 rpm);  -Fortex (GMP 56): 1000-1500 mPa.s (20 rpm).  When measured with a rotational viscometer (spindle 2, 50 rpm and 20 rpm for Fortex), allproducts within this family have a dynamic viscosity at 20°C at time of manufacturing between 9.2 mPa.s (Dipal RTU, GMP 34) and 1118 mPa.s (Fortex, GMP 56).  Similarly, at 40°C the reported viscosity ranged from 7.2 mPa.s (Dipal RTU, GMP 34) to 1008 mPa.s (Fortex, GMP 56). | reports Eurofins: S‑2015‑02503 – S‑2015‑02508 |
| **eCA remark**  Acceptable. Representative viscosity data was provided. The products within meta SPC 1, 2 and 4 are thickened. Products within Meta SPCs 3 and 5 are not. | | | | |

*\* pot iodine is an abbreviation for potential iodine, taking into account the iodine (I2) concentration in addition to the amount of iodine that may be generated by iodate. As can be seen in some of the studies, the potential iodine concentration decreases whereas the actual iodine concentration remains the same. This means that degradation has occurred, but that this was compensated by the redox agent, iodate.*

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| **Conclusion on the physical, chemical and technical properties of the product** |
| **Appearance** at 20°C and 101.3 kPa (physical state, color and odor) is part of the release specifications of the products within this product family. All products are brown liquids, with an iodine odor.  **Acidity, alkalinity:** The pH is part of the release specifications. At time of manufacturing (and for the stability studies), the pH is measured according to the Ph. Eur. monograph 2.2.3 “Potentiometric determination of pH”. All products within this family have a pH at time of manufacturing between 4-6.  **Relative density:** The relative density is part of the release specifications. At time of manufacturing, the relative density is measured according to the 2.2.5. Relative density, Eur. Ph. VII. All products within this family have a relative density at time of manufacturing between 1.00 – 1.09 g/ml.  **Stability:** The provided stability data support a shelf life of two years at ambient storage conditions for the following products: Blockade (GMP 44), Fortex (GMP 56), Tri-Fender (GMP 51), Dipal Conc (GMP 48) and TriActive (F-2506). For IodoFence (GMP 54), Proactive (GMP 43), Proactive Plus (GMP 42), Dipal RTU (GMP 34) and Dipal Plus (GMP 36) a 1-year shelf-life under normal storage conditions is justified.  As for meta SPC 1-4, each meta SPC contains products with a shelf-life of 1 year, the overall shelf-life of each of these meta SPC’s is set to 1 year. The shelf-life of meta SPC 5 (Dipal Conc (GMP 48)) is set to 2 years. For meta SPCs 6 and 7, the shelf-life is 1 year.  Considering no accelerated storage data or low temperature stability studies were provided, products are to be stored protected from frost and at temperatures equal to or below 30 °C. These storage conditions are included in the SPC.  **Viscosity:** When measured with a rotational viscometer (spindle 2, 50 rpm and 20 rpm for Fortex), allproducts within this family have a dynamic viscosity at 20°C at time of manufacturing between 9.2 mPa.s (Dipal RTU, GMP 34) and 1118 mPa.s (Fortex, GMP 56).  **Surface tension:** The surface tension of 6 products within the product family was determined and for all products the surface tension was around 33 – 43 mN/m at 20°C.  **Technical properties**  The family contains one concentrate, included in meta SPC5. Data shows that foaming may be excessive. A warning and instructions were included in the SPC to address this. Dilution stability was acceptable before and after storage. |

### Physical hazards and respective characteristics

Based on the data provided, none of the representative products is classified with regard to their physical and chemical properties.

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Explosives |  |  | DATA WAIVING  Data requirement is not relevant to the products in this product family. None of the components of the biocidal products in this product family has explosive properties. |  |
| Flammable gases | n/a | n/a | n/a | n/a |
| Flammable aerosols | n/a | n/a | n/a | n/a |
| Oxidising gases | n/a | n/a | n/a | n/a |
| Gases under pressure | n/a | n/a | n/a | n/a |
| Flammable liquids | ASTM 3278 (similar to ISO methods 3679 and 3680) | Undiluted product | Of the constituents used in the formulations of the product family only one ingredient is classified as flammable. This ingredient is present in the products Proactive Plus (GMP 42), Fortex (GMP 56), Tri-Fender (GMP 51) and TriActive (F-2506). The concentration the flammable ingredient is only 0.05% in each of the four products, which is very low. In addition, the flashpoints of Fortex (GMP 56), Proactive Plus (GMP 42) and Tri-Fender (GMP 51) were determined to be > 80°. From these data it can be concluded that none of the products within the product family are classified as flammable. | Flashpoint reports:  - NB 423-23 (Tri-Fender)  -Fortex (GMP 56)  -Proactive Plus (GMP 42) |
| Flammable solids | n/a | n/a | n/a | n/a |
| Self-reactive substances and mixtures | / | / | DATA WAIVING  Data requirement is not relevant to the products in this product family. None of the components of the biocidal products in this product family has self-reactive properties | / |
| Pyrophoric liquids | / | / | DATA WAIVING  Data requirement is not relevant to the products in this product family. None of the components of the biocidal products in this product family has pyrophoric properties. | / |
| Pyrophoric solids | n/a | n/a | n/a | n/a |
| Self-heating substances and mixtures | n/a | n/a | n/a | n/a |
| Substances and mixtures which in contact with water emit flammable gases | n/a | n/a | n/a | n/a |
| Oxidising liquids | / | / | DATA WAIVING  Data requirement is not relevant to the products in this product family. None of the constituents used in the products of these product family are classified as oxidising except from sodium iodate. The highest concentration of sodium iodate is 0.14% w/w which is too low to conclude that Blockade has oxidising properties. Therefore and according to the information available to DeLaval NV we conclude that Blockade is unlikely to cause hazards arising from oxidation. None of the products in the product family is therefore classified as oxidising. | / |
| Oxidising solids | n/a | n/a | n/a | n/a |
| Organic peroxides | n/a | n/a | n/a | n/a |
| Corrosive to metals | Part III, sub-section 37.4 of the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria | Undiluted product | Corrosion tests with 7 product family members were performed with the required test according to the CLP regulation (EC 1272/2008). From the test results it is concluded that no product within this product family meets the criteria to be classified as corrosive for metals. | Corrosion test reports Blockade (11/266f), Dipal Conc (11/266e), Dipal RTU (11/266g), Fortex (13/422-3), Proactive (11/266c), Proactive Plus (11/266d) and Tri-Fender (11/266h) |
| **eCA remark**  7 day tests were performed tests according to the UN test method and the weight loss was monitored. The following data was provided (maximum weight loss for steel and aluminium respectively):  **Uniform corrosion**Dipal RTU (GMP34): weight losses 4.99% and 3.98%  Proactive Plus (GMP 42): weight losses 9.56% and 6.28%  Proactive (GMP 43): weight losses 4.48% and 7.25%.  Blockade (GMP 44): weight losses 5.04% and 4.95%.  Dipal Conc (GMP48): weight losses 4.74% and 6.94%  Fortex (GMP 56): weight losses 2.34% and 0.82%  Tri-Fender (GMP51): Weight losses of 3.44% and 11.43%.  None of the products meets the classification criteria for uniform corrosion (mass loss >13.5%). The product with the lowest pH is Dipal RTU (GMP34), meta SPC 3. The product with the highest iodine concentration is Dipal Conc (GMP48), meta SPC5. These are not the products showing the highest weight losses during the 7 day tests, meaning the worst-cases are not easy to identify.  **Localised corrosion**  Localised corrosion was not observed for all but two products. In the studies with the products Proactive (GMP 43) and Proactive Plus (GMP 42), localised corrosion was observed at 171µm and 133µm respectively, exceeding the 120µm classification threshold (7 day exposure). These two products also showed an above average uniform corrosion.  The other products did not have localised corrosion exceeding 120µm after a 7 day study.  **Conclusion**  Two products within the family exceeded the classification thresholds in a 7 day study. These products were therefore assigned to their own meta SPCs: Proactive Plus in meta SPC 6, Proactive in meta SPC 7.  The remainder of the products did not show uniform or localised corrosion exceeding the classification thresholds. Therefore, meta SPC 1 – 5 are not classified as metal corrosive. | | | | |
| Auto-ignition temperatures of products (liquids and gases) | n/a | n/a | n/a | n/a |
| Relative self-ignition temperature for solids | n/a | n/a | n/a | n/a |
| Dust explosion hazard | n/a | n/a | n/a | n/a |

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| **Conclusion on the physical hazards and respective characteristics of the product** |
| Based on the data provided, the products within the family do not require classification with regard to physical and chemical hazards, with the exception of the products within meta SPCs 6 and 7: Proactive Plus and Proactive. Meta SPCs 6 and 7 are classified as metal corrosive (H290). None of the products within the family are explosive, oxidising or flammable. |

### Methods for detection and identification

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Analytical methods for the analysis of the product as such including the active substance, impurities and residues** | | | | | | | | | |
| **Analyte (type of analyte e.g. active substance)** | **Analytical method** | **Fortification range / Number of measurements** | **Linearity** | **Specificity** | **Recovery rate (%)** | | | **Limit of quantification (LOQ) or other limits** | **Reference** |
| Range | Mean | RSD |
| Iodine in starting material of products | Titration (acc to Eur. Ph Iodine) | / | Ok, validated | Ok, validated | 98 - 102 | / | / | 0.02% w/w | -European Pharmacopoeia - iodine  -Iodine assay method validation |
| Iodine in GMP 54 (IodoFence) | titration | n = 3x2  Fortified at 120%, 130% and 150% of nominal concentration. | ok, r = 0.9999  Slope 0.7792  Intercept  0.385  50 – 150% of nominal concentration | ok | 98.09-99.74 | 99 | 1.06 | n/a | S-2014-02413 AMi |
| Iodine in GMP 56 (Fortex) | titration | n = 3x2  Fortified at 120%, 130% and 150% of nominal concentration. | ok, r = 0.999  Slope  1.3337  Intercept  -0.063  50 – 150% of nominal concentration | ok | 95.5 – 101.9 | 98.7 | 3.09 | n/a | S-2014-00964 AMi |
| Iodine in GMP 51 (Tri-Fender) | titration | n = 3x2  Fortified at 120%, 130% and 150% of nominal concentration. | ok, r = 0.9999  Slope  0.7958  Intercept  -0.514  50 – 150% of nominal concentration | ok | 99.21-99.57 | 99.52 | 0.29 | n/a | S-2014-02412AMi |
| **Methods for substances of concern:**  No methods are deemed to be required for the SoC alcohol ethoxylate as it cannot be formed during storage. A potential increase in its contents is not expected.  Sodium iodide is also considered a SoC in this family as it contributes to the classification on a total (elemental) iodine basis. Also, the iodide concentration can increase upon storage, although the total (elemental) iodine concentration, the driving factor for the risk assessment, will not be affected.  The eCA considers that, given the fact that the total iodine concentration is taken into account in the risk assessment, the effect of iodide increase during storage is not relevant to the risk assessment and does not need to be monitored (the risk assessment assumes a 100% conversion from all iodine species to iodide), which means no validated method should be necessary.  Still, several published methods are available for iodide determinations. In the presence of iodine, however, such methods are not always specific to iodide as methods for iodide are often based on first oxidising iodide to iodine, then titrating with thiosulphate (as the methods used in this dossier). Alternatively, ICP is used, which is also a method which does not distinguish between the various forms of iodine.  To be able to use the method available in the dossier, the following steps are required:   1. iodate is converted to iodine using sulphuric acid (the presence of iodide is required for this reaction) 2. Remaining iodide is oxidised to iodine using bromine or hydrogen peroxide, followed by neutralisation of residual bromine or hydrogen peroxide.   When conversion/neutralization is complete, the titration method for iodine can be used as described above, using thiosulfate and starch indicator. | | | | | | | | | |

The pharmacopoeia method is mainly intended for determination of the purity of iodine (crystals). The method description aims at 0.2g of iodine in 50mL (4 g/L or 0.4%) of water and titration with sodium thiosulfate and a starch indicator. The products within the family contain less than 0.4% iodine.

Specific validation for three products was performed, using a method comparable to the pharmacopoeia published method. These methods are also based on thiosulphate titrations with starch indicators and show the method can be adequately applied at concentrations relevant to the representative products within the family.

**eCA remark**

The pharmacopoeia method is commonly used for iodine determinations and the eCA considers it to be acceptable. The analytical methods are titration methods, not chromatographic. A titration method is not specific by default, but there are no compounds in the formulations that may be expected to react to the titrant. Thiosulphate and starch indicators are commonly used for iodine determinations by reduction of iodine to iodide. Within the formulations, there does not seem to be (a significant amount of) other compounds that will be reduced by thiosulphate.

This is confirmed by the data provided by the applicant, although the validation is not performed exactly according to the guidance with regard to accuracy. The accuracy should preferably be addressed by spiking a blank product. However, in this case the product was spiked at 120, 130 and 150% of its nominal active substance concentration by standard addition. No accuracy data was provided at the specified active substance concentration.

The RSD reported is not that of the accuracy determinations, but of the precision of 6 independently prepared samples.

Linearity was addressed using 5 calibration solutions over an appropriate range.

As the method is not chromatographic, specificity is not addressed using a blank, standard and spiked blank. Considering the method showed to be accurate, it is not expected there is any interference from other components in the products.

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| **Analytical methods for monitoring of active substances and residues in food and feeding stuff** | | | | | | | | | |
| **Analyte (type of analyte e.g. active substance)** | **Analytical method** | **Fortification range / Number of measurements** | **Linearity** | **Specificity** | **Recovery rate (%)** | | | **Limit of quantification (LOQ) or other limits** | **Reference** |
| Range | Mean | RSD |
| Iodide in milk | HPLC (ISO 14378) | / | / | / | / | / | / | Whole milk: 0.03 µg/g to 1 µg/g | AS dossier |
| Iodide in milk | Ion-selective electrode (AOAC 992.24) | / | / | / | / | / | / | Applicable to ready-to-feed milk-based in fant formula containing 75–150 µg/L io dide. | AOAC 992.24 |

**eCA remark**

The AOAC method could not be fully evaluated. It is a published method for the determination of iodide in ready-to-feed milk formulae, intended for infants (pre-registration data generation method). The method was ring validated according to the publication with an RSD < 20 at 75 – 150 µg/L. In the corresponding operating procedure, a calibration plot was included (mV was plotted against the 10log iodide concentration, at four concentrations), with an r2 of 0.9994 (y=-65.667x-49.043).

For this type of method, the validation is considered sufficient to conclude that a determination of the iodide content in milk can be adequately performed at the proposed concentrations (75 – 150µg/L).

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| **Conclusion on the methods for detection and identification of the product** |
| The analytical methods for monitoring purposes of iodine are adequately covered in the active substance dossier. There are no other toxicologically relevant components to be monitored since none of the components used in the formulations of the biocidal products in this product family are classified as toxic or very toxic. Also, there are no other ecotoxicologically relevant components to be monitored, since none of the components used in the formulations of the biocidal products in this product family are classified as dangerous for the environment.  **Analytical methods for the analysis of the product:** The method published in the European Pharmacopoeia is common standard method for the determination of Iodine in formulations. This method is routinely used to determine iodine concentration in the iodine based teat disinfectants of this product family at time of manufacturing and for stability studies. An internal validation report is also provided, showing accuracy, specificity, linearity, precision and robustness of the method.  **Analytical methods for monitoring of iodide in milk:** AOAC Method 992.24, is an official method for the determination of iodide in ready-to-feed (RTF) milk-based infant formula by ion selective electrode. A modification of this method (modified AOAC official method 992.24) can be used to determine soluble iodide content in liquid milk by ion selective electrode (ISE) method. This method has been used in residue studies with teat dip disinfectants of the product family. |

### Efficacy against target organisms

#### Function and field of use

PT03 - Veterinary hygiene (Disinfectants)

All products within the product family are intended for post-milking teat disinfection.

The products are applied directly after milking on the teats of lactating animals.

The products are used indoors by professional users only.

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

Organisms to be controlled are bacteria, yeasts and viruses.

The organism to be protected is the lactating animal (dairy cattle).

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

Disinfection of teats after milking by dipping them in or spraying them with a solution of iodine containing disinfectant, kills bacteria, yeasts and viruses.

#### Mode of action, including time delay

BIOCHEMICAL AND PHYSIOLOGICAL MECHANISMS

It is the free molecular I2 that is the biocidal agent in iodine-based teat dips. Elemental iodine is capable of rapidly and completely killing microorganisms upon contact. Numerous references describe the efficacy of iodine products towards relevant mastitis organisms supported by results from *in vitro* studies performed under standardized or modified conditions.

Iodine is bactericidal, yeasticidal and virucidal. Although the exact mechanism of antimicrobial action of iodine is still incompletely understood, it is associated with the rapid penetration of the cell wall of micro-organisms. Molecular I2 can freely enter cells and works via a variety of pathways to eliminate microorganisms in a non-specific manner. It attacks key groups of proteins (in particular the free sulfur amino acids cysteine and methionine), nucleotides, and fatty acids, thus affecting the structure and functions of enzymes and cell proteins, which culminates in rapid cell death. These multiple modes of action ensure the rapid death of microorganisms and help prevent the development of bacterial resistance.

TIME DELAY

The rapid penetration of iodine into microorganisms and its mode of action indicates 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.

#### Efficacy data

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| **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** | |
| bacterici-dal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | *E. coli, S. aureus, S. uberis, P. aeruginosa, E. hirae, P. vulgaris (= P. hauseri)* | EN 1656 (Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics for use in the veterinary field - Test method and requirements (Phase 2, Step 1)) | Dilution rates: 80, 20 and 1% of the ready-to-use product  Interfering substance: 1% milk  Temperature: 30°C  Contact time:  5 min | All products present bactericidal activity against the reference strains at a concentration of 80% of the ready-to-use solution.  The products no longer present bactericidal activity against the reference strains at a concentration of 1% of the ready-to-use solution. | | FR TSR 2014-09-182, 187 | |
| IodoFence  (GMP 54)  Meta SPC 2  0.25% a.s. | FR TSR 2014-09-183, 188 | |
| Proactive (GMP 43)  Meta SPC 2  0.15% a.s. | FR TSR 2014-09-156, 160 | |
| Proactive Plus  (GMP 42)  Meta SPC 6  0.15% a.s. | FR TSR 2014-09-186, 181 | |
| Fortex  (GMP 56)  Meta SPC 2  0.23% a.s. | FR TSR 2014-09-185, 190 | |
| Tri-Fender (GMP 51)  Meta SPC 1  0.25% a.s. | FR TSR 2014-09-153, 157 | |
| TriActive  (F-2506)  Meta SPC 1  0.21% | FR TSR 2015-01-016, 018 | |
| Dipal RTU (GMP 34)  Meta SPC 3  0.15% a.s. | FR TSR 2014-09-154, 158 | |
| Dipal Plus (GMP 36)  Meta SPC 4  0.15% a.s. | FR TSR 2015-01-015, 017 | |
| Dipal Conc (GMP 48)  Meta SPC 5  0.75% a.s. | FR TSR 2014-09-155, 159 | |
| yeasticidal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | *C. albicans* | EN 1657 (Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants and antiseptics for use in the veterinary field - Test method and requirements (Phase 2, Step 1)) | Dilution rates: 80, 20 and 0.1% of the ready-to-use product  Interfering substance: 1% milk  Temperature: 30°C  Contact time:  5 min | All products present yeasticidal activity against the reference strains at a concentration of 20% of the ready-to-use solution.  The products no longer present yeasticidal activity against the reference strains at a concentration of 0.1% of the ready-to-use solution. | | FR TSR-2014 -09 -192 | |
| IodoFence (GMP 54)  Meta SPC 2  0.25% a.s. | FR TSR-2014 -09 -193 | |
| Proactive (GMP 43)  Meta SPC 2  0.15% a.s. | FR TSR-2014 -09 -164 | |
| Proactive Plus  (GMP 42)  Meta SPC 6  0.15% a.s. | FR TSR-2014 -09 -196 | |
| Fortex  (GMP 56)  Meta SPC 2  0.23% a.s. | FR TSR-2014 -09 -195 | |
| Tri-Fender (GMP 51)  Meta SPC 1  0.25% a.s. | FR TSR-2014 -09 -161 | |
| TriActive  (F-2506)  Meta SPC 1  0.21% a.s. | FR TSR-2015 -01 -036 | |
| Dipal RTU (GMP 34)  Meta SPC 3  0.15% a.s. | FR TSR-2014 -09 -162 | |
| Dipal Plus (GMP 36)  Meta SPC 4  0.15% a.s. | FR TSR-2015 -01 -035 | |
| Dipal Conc (GMP 48)  Meta SPC 5  0.75% a.s. | FR TSR-2014 -09 -163 | |
| yeasticidal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | *C. albicans* | EN 1657 (Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants and antiseptics for use in the veterinary field - Test method and requirements (Phase 2, Step 1)) | Dilution rates: 80, 20 and 0.1% of the ready-to-use product  Interfering substance: 10g/L Bovine albumin+10g/L yeast extract\*  Temperature: 10°C  Contact time:  30 min  \*this soiling is not relevant for post-milking teat disinfection, therefore, these tests are only considered as additional information. | All products present yeasticidal activity against the reference strains at a concentration of 80% of the ready-to-use solution.  The products no longer present yeasticidal activity against the reference strains at a concentration of 0.1% of the ready-to-use solution. | | FR TSR-2014 -09 -197 | |
| IodoFence (GMP 54)  Meta SPC 2  0.25% a.s. | FR TSR-2014 -09 -198 | |
| Proactive (GMP 43)  Meta SPC 2  0.15% a.s. | FR TSR-2014 -09 -168 | |
| Proactive Plus  (GMP 42)  Meta SPC 6  0.15% a.s. | FR TSR-2014 -09 -201 | |
| Fortex  (GMP 56)  Meta SPC 2  0.23% a.s. | FR TSR-2014 -09 -200 | |
| Tri-Fender (GMP 51)  Meta SPC 1  0.25% a.s. | FR TSR-2014 -09 -165 | |
| TriActive  (F-2506)  Meta SPC 1  0.21% a.s. | FR TSR-2015 -01 -034 | |
| Dipal RTU (GMP 34)  Meta SPC 3  0.15% a.s. | FR TSR-2014 -09 -166 | |
| Dipal Plus (GMP 36)  Meta SPC 4  0.15% a.s. | FR TSR-2015 -01 -033 | |
| Dipal Conc (GMP 48)  Meta SPC 5  0.75% a.s. | FR TSR-2014 -09 -167 | |
| virucidal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | *Bovine enterovirus Type 1 (ECBO)* | EN 14675 (Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of virucidal activity of chemical disinfectants and antiseptics used in veterinary area - Test method and requirements (Phase 2, Step 1)) | Dilution rates: 80, 40 and 20% of the ready-to-use product  Interfering substance: 1% milk  Contact time: 5 min +/- 10 sec  - Temperature: 30°C +/- 1°C | Blockade (GMP 44) and Proactive (GMP 43) cause a reduction >4Log against *Bovine enterovirus Type 1 (ECBO) ATCC VR-248* at the test concentration of 80.0%. | | S-2014-02106 Ami | |
| Proactive  (GMP 43)  Meta SPC 2  0.15% a.s. | S-2014-02107 AMi | |
| bacterici-dal | Teat disinfection | Dipal Conc (GMP 48)  Meta SPC 5  0.75% a.s. | *S. aureus, E. coli, S. uberis* | Modified EN16437 : Surface bactericidal activity for the veterinary area using Vitroskin carriers as per DROP-DIP method | Carrier: Vitroskin  Dilution rates: 100, 80 and 20% of the ready-to-use product  Interfering substance: 1% milk  Contact time:  5 min  Temperature: 30°C +/- 1°C | | All three products cause a >4Log reduction against all the tested strains at the test concentration of 100%. | | S-2015-2790 AMi |
| Proactive (GMP 43)  Meta SPC 2  0.15% a.s. | S-2015-2791 AMi |
| Fortex  (GMP 56)  Meta SPC 2  0.23% a.s. | S-2015-2792 AMi |
| bacterici-dal | Teat disinfection | Dipal Conc (GMP 48)  Meta SPC 5  0.75% a.s. | *S. aureus, E. coli, S. uberis* | Modified EN16437 : Surface bactericidal activity for the veterinary area using Vitroskin carriers as per DROP-DROP method | Carrier: Vitroskin  Dilution rates: 100, 80 and 20% of the ready-to-use product  Interfering substance: 1% milk  Contact time:  5 min  Temperature: 30°C +/- 1°C | | Dipal Conc (GMP 48) causes a >5Log reduction against all the tested strains at the test concentration of 100%. Proactive (GMP 43) causes a >5Log reduction against *E. coli* and *S. uberis* and a >3Log reduction against *S. aureus* at the test concentration of 100%. | | S-2015-2785 AMi |
| Proactive (GMP 43)  Meta SPC 2  0.15% a.s. | S-2015-2786 AMi |
| bacterici-dal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | *S. aureus, E. hirae, E. coli, P. aeruginosa* | AFNOR NF T72-190 (Water miscible contact disinfectants used in liquid form - Germ carrier method - Determination of the bactericidal, fungicidal and sporicidal activity) | Carrier: non-porous (glass)  Interfering substance: none  Temperature: 20°C  Contact time: 15 min | | Blockade (GMP 44), tested undiluted was bactericidal against the referenced strains at 20°C and a contact time of 15 minutes. | | Norme NF T 72-190 - Blockade 00G06 |

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| bacteri-cidal | Teat disinfection | Proactive (GMP 43)  Meta SPC 2  0.15% a.s. | *S. aureus,*  *P. aeruginosa, E. hirae,*  *P. vulgaris* | EN 14349:2012 (Quantitative surface test for the evaluation of bactericidal activity of chemical disinfectant and antiseptics used in veterinary area on non-porous surfaces without mechanical action (phase 2/step2) | Dilution rates: 80, 40 and 20% of the ready-to-use product  Interfering substance: 0.3% Bovine Albumin  Contact time: 30 min  Temperature: 10°C +/- 1°C | Proactive (GMP 43) presents bactericidal activity against the referenced strains at the test concentrations of 80 and 40% after 30 minutes, using a 0.3% final concentration of bovine albumin. | | S-2015-00838 |
| bacterici-dal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | Mastitis pathogens | Field trial (evaluation udder health status of cows) | Duration: 4 weeks.  Product applied after each milking  20 cows on 2 farms  Analysis: Microbial culturing and SCC of aseptic quarter milk samples at the beginning and the end of the trial to monitor udder health status. | On both farms, in the Blockade treated cows, there was a reduction in the number of quarter milk samples that cultured positive for bacteria when comparing between day one and the end of the trial. These results indicate that Blockade has an bactericidal effect under *in vivo* conditions. | Blockade and Alfa Blue + Teat dips Winter Field Trials: Teat Skin Evaluation (ALACAT 99/14) | |
| bacterici-dal | Teat disinfection | Dipal Conc (GMP 48)  Meta SPC 5  0.75% a.s. | Mastitis pathogens | Field trial (evaluation udder health status of cows) | Duration: 12 weeks  Product applied after each milking (3x/day)  40 cows treated / 40 cows untreated  Analysis: Detection of pathogenic bacteria in quarterly milk samples at week 0 and week 12. | In the Dipal Conc group there was a reduction in the number of quarter milk samples and individual cows that cultured positive for pathogenic bacteria when comparing between day one and the end of the trial and also when comparing with the untreated group at week 12. These results indicate that Dipal Conc has a bactericidal effect under *in vivo* conditions. | Clinical trial report of Dipal Conc 1+4 | |
| bacterici-dal | Teat disinfection | Blockade (GMP 44)  Meta SPC 2  0.25% a.s. | *S. aureus, S. uberis, S. dysgalacticiae* | Field trial (evaluation udder health status of cows) | Duration: 4 months  Product applied after each milking  10 animals  Analysis: At the start of the trial and each 2 weeks during the trial, bacteriological study of quarterly milk samples. There was a quantification of the different species. | In all Blockade treated quarters that were positive for pathogens in the beginning of the trial, there was a reduction in the number of pathogenic bacteria detected by the end of the trial. The quarters that were negative for pathogens in the beginning of the trial were again negative at the end of the treatment period. These results confirm that the product Blockade disinfects the teats after milking. | Field trial new teat dip: "Blockade" Test report | |

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| **Conclusion on the efficacy of the product** |
| For efficacy testing and defining worst-case products only the initial (free) iodine concentration in the tested products was considered and not the maximum theoretical total iodine content (i.e. iodine + iodine from sodium iodide + iodine from sodium iodate). The iodine formed from iodide and iodate is only very slowly released in such a way that a constant concentration of available (free) iodine is guaranteed. Therefore in practice the other iodine species will not play a significant role in efficacy and only the initial (free) iodine concentration that is measured is relevant.  Bactericidal efficacy of the products within this product family has been demonstrated *in vitro* in EN1656 efficacy tests run under standard conditions for teat disinfection (1% milk, 5min, 30°C). Also, EN1657 studies are presented, demonstrating *in vitro* yeasticidal efficacy of all products within this product family, using teat disinfection conditions (1% milk, 5 min and 30°C). Since these products contain a range of concentrations of the co-formulants, these tests demonstrated that the possible variation in co-fomulants in this family will not influence the efficacy of the products.  In addition, both Blockade (GMP 44; 0.25% w/w iodine) and Proactive (GMP 43; 0.15% w/w iodine) show *in vitro* virucidal activity (EN 14675) under simulated teat disinfection conditions (1% milk, 5min, 30°C) at a concentration of 80% of the ready-to-use solution. Since all products in the iodine-based teat disinfectant family contain minimal 0.15% w/w iodine and maximal 0.25% w/w iodine, we conclude that the results can be extrapolated and virucidal activity can be claimed for all products within the biocidal product family.  Proactive (GMP 43; 0.15% w/w iodine), Dipal Conc (GMP 48; 0.15% w/w iodine in RTU solution) and Fortex (GMP 56; 0.24% w/w iodine) were also shown to be bactericidal in a modified EN16437 phase 2/ step 2 test developed by the Iodine Registration Group (IRG), with Vitroskin as a carrier. Modifications of EN 16437 that were made allow the use of a standardized synthetic skin surface (Vitroskin) to simulate the use on teat skin. The test organism (*S. aureus, E. coli* and *S. uberis*) as well as test temperature (30°C), contact time (5 min) and soiling (1% milk) have been adapted according to EN 1656 for teat disinfection. Two different application methods of the test item have been selected in order to cover different application scenarios:   * the drop/drop method, in which a drop of bacterial suspension is dried on the skin, after which a drop of teat disinfectant is added, * the drop/dip method, in which a drop of bacterial suspension is dried on the skin, after which the skin is dipped in teat disinfectant.   Dipal Conc (GMP 48) and Proactive (GMP 43) were tested using both the drop/drop and the drop/dip method. Fortex (GMP 56) was tested with the drop/dip method only since it is a viscous product typically applied by dipping. In summary, when using the drop/dip method Fortex (GMP56), Dipal Conc (GMP 48) and Proactive (GMP 43) all cause a >4Log reduction against all the tested strains at the test concentration of 100%. Furthermore, when using the drop/drop method Dipal Conc (GMP 48) causes a >5Log reduction against all the tested strains at the test concentration of 100%. Proactive (GMP 43) causes a >5Log reduction against *E. coli* and *S. uberis* and a Log reduction of 3.1 against *S. aureus* at the test concentration of 100%. This lower log reduction might be due to the variation in this drop/drop test, since the test is not standardised nor validated yet. Proactive (GMP 43) did pass the drop/dip test and can therefore be considered efficacious.  Since all products in the iodine-based teat disinfectant family contain minimal 0.15% w/w iodine in the RTU solution, we conclude that the phase 2/ step 2 results are representative for all products within the biocidal product family.    To further support the bactericidal claim of the teat disinfectants within this family, three field trials are presented: two with Blockade (GMP 44; 0.25% w/w iodine) and one with Dipal Conc (GMP 48: 0.15% w/w iodine in the RTU solution). Before and during each of these trials, a bacteriological study of milk samples of treated animals was performed. The results of these studies clearly demonstrated the *in vivo* bactericidal properties of Blockade and Dipal Conc. Together, the presented results clearly demonstrate that teat disinfectants of this product family - all containing 0.15 - 0.25% w/w iodine in the ready-to-use solution - have bactericidal properties under *in vivo* conditions.  It can be concluded that the products in this family are efficacious, after at least 5 min contact time, as post-milking teat disinfectants against bacteria, yeasts and viruses. |

#### Occurrence of resistance and resistance management

Iodine has been used for medicinal purposes for almost 200 years and despite this prolonged use, the reports of iodine resistant strains are extremely rare. One or two reports on iodine resistance were questionable from a study design validity point of view. The broad antimicrobial spectrum is due to the mode of action of iodine. As mentioned earlier, it is believed that the antimicrobial efficacy of iodine is due to its ability to penetrate the cell walls of microorganisms, to damage the bacterial membrane structure as well as to affect the structure and functions of enzymes and cell proteins. These multiple modes of action help prevent the development of bacterial resistance to iodine, unlike antibiotics that function through a specific molecular pathway. Many *in vitro* studies demonstrated that iodine does not induce resistance in clinically relevant bacteria species.

#### Known limitations

No known limitations.

#### Evaluation of the label claims

General post-milking teat disinfection is claimed on the labels of all products within this product family. Although the main target organisms are bacteria, *in vitro* efficacy studies have been provided demonstrating bactericidal, yeasticidal and virucidal efficacy of the products, after at least 5 min contact time.

The label claims as stated in the SPC reflect the efficacy of the biocidal product.

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

Not applicable, the products are not to be used with other biocidal products.

### Risk assessment for human health

#### Assessment of effects on Human Health

***Skin corrosion and irritation***

*In vivo* skin corrosion/irritation studies according to OECD guidelines 404 were performed on 8 out of 10 products within the product family. These studies were not performed on TriActive (F-2506) and Dipal Plus (GMP 36) due to the high degree of similarity with respectively Tri-Fender (GMP 51) and Dipal RTU (GMP 34) (expert judgement).

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| **Summary table of animal studies on skin corrosion /irritation** | | | | | |
| **Method, Guideline,**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance, Vehicle, Dose levels,  Duration of exposure** | **Results**  *Average score**(24, 48, 72h)/*  *observations and time point of onset, reversibility; other adverse local / systemic effects, histopathological*  *findings* | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 404, GLP, reliable without restriction | Rabbit, New Zealand white, 3 rabbits | Blockade (GMP 44), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0.3, 1.0, 2.0; Edema: Average score (24, 48 and 72h): 1.3, 0.3, 0.0; time of onset: 1h; fully reversible (D3 – D7); no other adverse effects | n/a | Gomond, P., 2000 (OECD 404 Blockade, Tg314 / 00-1588) |
| IodoFence (GMP 54), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0,0,0; Edema: Average score (24, 48 and 72h): 0,0,0; no other adverse effects | n/a | Colas, S., 2011 (OECD 404 IodoFence-GMP54, IC-OCDE-PH-11/0566) |
| Proactive (GMP 43), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0,0,0; Edema: Average score (24, 48 and 72h): 0,0,0; no other adverse effects | n/a | Fagette, S. 2010 (OECD 404 Proactive, Tq521/10-3365) |
| Proactive Plus (GMP 42), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0,0,0; Edema: Average score (24, 48 and 72h): 0,0,0; no other adverse effects | n/a | Canguilhem, B., 2010 (OECD 404 Proactive Plus, Tq 143/10-1156) |
| Fortex (GMP 56), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0,0,0; Edema: Average score (24, 48 and 72h): 0,0,0; no other adverse effects | n/a | Richeux F., 2013 (OECD 404 Fortex, IC-OCDE-PH-13/0541) |
| Tri-Fender (GMP 51), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0,0.7,1.0; Edema: Average score (24, 48 and 72h): 0, 0.7, 0.3; time of onset: 1h; fully reversible (D2 – D3); no other adverse effects | n/a | Richeux F., 2011 (OECD 404 Tri-Fender, IC-OCDE-PH-11/0097) |
| Dipal RTU (GMP 34), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 0,0,0; Edema: Average score (24, 48 and 72h): 0,0,0; no other adverse effects | n/a | Canguilhem, B., 2010 (OECD 404 Dipal RTU, Tq142/10-1157) |

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|  |  | Dipal Conc (GMP 48), 0.5 ml undiluted, 4h exposure | Erythema: Average score (24, 48 and 72h): 1.0.1.0.1.0; Edema: Average score (24, 48 and 72h):0.0.0; time of onset: 1h; fully reversible (D5-6); no other adverse effects | n/a | Fagette, S. 2011 (OECD 404 Dipal Conc, Tq519/10-3362) |

No human data are available on the products of this product family.

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| **Conclusion used in Risk Assessment – Skin corrosion and irritation** | |
| Value/conclusion | *In vivo* skin corrosion/irritation studies according to OECD guidelines 404 were performed on 8 out of 10 products within the product family.  In accordance with the Regulation EC No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the products must not be classified. No signal word or hazard statement is required. |
| Justification for the value/conclusion | Available *in vivo* test results were conclusive and did not lead to classification. No studies were performed on TriActive (F-2506) and Dipal Plus (GMP 36) but due to the high degree of similarity with respectively Tri-Fender (GMP 51) and Dipal RTU (GMP 34) it seems justified to conclude that both products are also not classified.  It is noted that except for Dipal Plus and TriActive (not tested), the products in the BPF were already on the market for several years across the EU, before BPR legislation became effective. In addition, some of the products are also marketed outside the EU and in vivo toxicity tests were therefore also performed for the purpose of other regulations. An example is Fortex ,that justifies the study for this product performed after 2012. |
| Classification of the product according to CLP and DSD | Not classified. |

***Eye irritation***

*In vivo* eye corrosion/irritation studies according to OECD guidelines 405 were performed on 9 out of 10 products within the product family. These studies were not performed on TriActive (F-2506) due to the high degree of similarity with Tri-Fender (GMP 51) (expert judgement). An OECD 405 study was performed on Dipal Plus (GMP 36) since it contained more alcohol ethoxylate, classified as Eye Dam 1 (H318) than Dipal RTU (GMP 34) and based on the study outcome product needs to be classified as Eye Irrit Cat 2 (H319).

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| **Summary table of animal studies on serious eye damage and eye irritation** | | | | | |
| **Method, Guideline,**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance,Dose levels, Duration of exposure** | **Results**  *Average score (24, 48, 72h)/*  *observations and time point of onset, reversibility* | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 405, GLP, reliable without restriction | Rabbit, New Zealand white, 3 rabbits | Blockade (GMP 44), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0;0;0; **Redness:** Average score (24, 48 and 72h):0.3;0;0; **Iris:** Average score (24, 48 and 72h): 0;0;0; **Cornea:** Average score (24, 48 and 72h): 0;0;0 time of onset: 1-24 h; fully reversible (D2); no other adverse effects | n/a | Fagette, S. 2011 (OECD 405 Blockade,Tq 527 / 10-3367) |
| IodoFence (GMP 54), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h):>= 0.3;0.3;0; **Redness:** Average score (24, 48 and 72h):0.7;0.3;0.3 **Iris:** Average score (24, 48 and 72h): 0;0;0; **Cornea:** Average score (24, 48 and 72h): 0;0;0; time of onset: 1h; fully reversible (D1-3); no other adverse effects | n/a | Colas, S., 2011 (OECD 405 IodoFence, IO-OCDE-PH-11/0566) |

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|  |  | Proactive (GMP 43), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0;0;0; **Redness:** Average score (24, 48 and 72h): 0.3;0.3;0.3; **Iris:** Average score (24, 48 and 72h): 0;0;0; **Cornea:** Average score (24, 48 and 72h): 0;0;0; time of onset: 1h; fully reversible (D2); no other adverse effects | n/a | Fagette, S. 2010 (OECD 405 Proactive, Tq 525 / 10-3365) |
| Proactive Plus (GMP 42), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0;0.3;0.3; **Redness:** Average score (24, 48 and 72h): 0.7;0.7;1; **Iris:** Average score (24, 48 and 72h): 0;0;0; **Cornea:** Average score (24, 48 and 72h): 0;0;0; time of onset: 1h; fully reversible (D3-5); no other adverse effects | n/a | Canguilhem, B., 2010 (OECD 405 Proactive Plus, Tq 145 / 10-1156) |
| Fortex (GMP 56), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0.3;0.3;03;; **Redness:** Average score (24, 48 and 72h): 0.3;0.7;0.7; **Iris:** Average score (24, 48 and 72h): 0;0;0; **Cornea:** Average score (24, 48 and 72h): 0;0;0; time of onset: 1h; fully reversible (D2-3); no other adverse effects | n/a | Richeux F., 2013 (OECD 405 Fortex, IO-OCDE-PH-13/0541) |

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|  |  | Tri-Fender (GMP 51), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0;0;0; **Redness:** Average score (24, 48 and 72h): 0.3;0;0; **Iris:** Average score (24, 48 and 72h): 0;0;0; **Cornea:** Average score (24, 48 and 72h): 0;0;0; time of onset: 1h; fully reversible (D2); no other adverse effects | n/a | Richeux F., 2011 (OECD 405 Tri-Fender, IO-OCDE-PH-11/0097) |
|  |  | Dipal RTU (GMP 34), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0; 1; 0.3 ; **Redness:** Average score (24, 48 and 72h): 1;1.3;1; **Iris:** Average score (24, 48 and 72h): 0.3;0.3;0.3; **Cornea:** Average score (24, 48 and 72h): 1.0;0.7;0.7; time of onset: 1h; fully reversible (D1-5); no other adverse effects | n/a | Canguilhem, B., 2010 (OECD 405 Dipal RTU, Tq 144 / 10-1157) |
| Dipal Plus (GMP 36), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 0;0.7;07; **Redness:** Average score (24, 48 and 72h): 0;1.3;1; **Iris:** Average score (24, 48 and 72h): 0;0.3;0.3; **Cornea:** Average score (24, 48 and 72h): 0.3;1.7;1.3; time of onset: 1h; fully reversible (D1-7); no other adverse effects  Furthermore,  in at least in 2 of 3 tested animals, a positive response of: corneal opacity of ≥1. | n/a | Richeux F., 2015 (OECD 405 Dipal Plus, IO-OCDE-PH-15/0021) |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | Dipal Conc (GMP 48), 0.1 ml undiluted, no washing, 72 h observation | **Chemosis:** Average score (24, 48 and 72h): 1.3, 1.3, 1.3; **Redness:** Average score (24, 48 and 72h):2.7, 2.7, 3.0; **Iris:** Average score (24, 48 and 72h): 0.3, 0.3, 0.3; **Cornea:** Average score (24, 48 and 72h):2.0, 1.3, 2.0; time of onset: 1h; fully reversible (D2-9); no other adverse effects  Furthermore,  in at least in 2 of 3 tested animals, a positive response of: conjunctival redness, and conjunctival oedema ≥2, and iritis ≥1.  Furthermore, corneal opacity of ≥1, however the individual average scores were 2,1.3 and 2. Therefore, H319 needs to be assigned. | n/a | Gomond, P., 2004 (OECD 405 GMP 40/Dipal Conc: Dipal Conc, Tk 335 / 04-2102) |

No human data are available on the products of this product family.

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| --- | --- |
| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | *In vivo* eye damage/irritation studies according to OECD guidelines 405 were performed on 9 out of 10 products within the product family.  In accordance with the Regulation EC No. 1272/2008 on classification, labelling and packaging of substances and mixtures, based on the study outcome, the products Dipal Plus (GMP 36) and Dipal Conc (GMP 48) must be classified in category 2 "Irritating to eyes". The signal word "Warning" and hazard statement H319 "Causes serious eye irritation" are required. These products (GMP36 and GMP48) are grouped in Meta SPC 4&5. No signal word or hazard statement is required for the 8 products in Meta SPC 1,2, 3, 6 and 7. |
| Justification for the value/conclusion | Available *in vivo* test results were conclusive and did not lead to classification for the following products (grouped in **Meta SPC 1,2, 3, 6 &7**): Blockade (GMP 44), IodoFence (GMP 54), Proactive/Iobac RTU (GMP 43), Proactive Plus (GMP 42), Fortex (GMP 56), Tri-Fender (GMP 51) and Dipal RTU (GMP 34). No studies were performed on TriActive (F-2506) but due to the high degree of similarity with Tri-Fender (GMP 51) it seems justified to conclude that the product is also not classified.  According to the *in vivo* tests on Dipal Plus (GMP 36) and Dipal Conc (GMP 48), products of **Meta SPC 4&5** must be classified in category 2 "Irritating to eyes".  It is noted that except for Dipal Plus and TriActive (not tested), the products in the BPF were already on the market for several years across the EU, before BPR legislation became effective. In addition, some of the products are also marketed outside the EU and in vivo toxicity tests were therefore also performed for the purpose of other regulations. An example is Fortex ,that justifies the study for this product performed after 2012. |
| Classification of the product according to CLP and DSD | **Meta SPC 1,2, 3, 6&7 products:** Not classified  **Meta SPC 4&5 products:** Eye Irrit Cat 2 (H319) (CLP) |

***Respiratory tract irritation***

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| **Conclusion used in the Risk Assessment – Respiratory tract irritation** | |
| Justification for the conclusion | Two of the components used in the formulations are classified as Specific target organ toxicity — Single exposure, Hazard Category 3 for respiratory tract irritation (H335). However, their concentrations are below the concentration limit for classification of the products with H335. |
| Classification of the product according to CLP and DSD | Not classified. |

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| **Data waiving** | |
| Information requirement | Respiratory tract irritation |
| Justification | No studies have been performed on the products of this product family. Two of the components in the mixtures are classified for respiratory tract irritation, but individually and summed up present in the BPF <<20% classification limit. |

***Skin sensitization***

Of the components in the products in the DeLaval iodine-based teat-disinfectant family only sodium iodate is classified for skin sensitisation (Cat 1 - H317). *In vivo* skin sensitisation studies according to OECD guidelines 406 were performed on 7 out of 10 products within the product family. These studies were not performed on Tri-Fender and TriActive (F-2506) and Dipal Plus (GMP 36).

| **Summary table of animal studies on skin sensitisation** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline, GLP status, . Reliability** | **Species, Strain, Sex, No/group** | **Test substance, Vehicle,**  **Dose levels,  duration of exposure Route of exposure** *(topical/intradermal, if relevant)* | **Results**  *(EC3-value or amount of sensitised animals at induction dose); evidence for local or systemic toxicity (time course of onset)* | **Remarks**  *(e.g. major deviations)* | **Reference** |
| OECD 406 (Maximization test), GLP, reliable without restriction | Guinea pig, Hartley, male, 10 animals in test group and 5 in control group | Blockade (GMP 44); Vehicle: distilled water; Doses: MIC topical and MIC intradermal; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in test group and control group. | n/a | Fagette, S. 2011 (OECD 406 Blockade, Tq 536 / 10-3367) |
| Guinea pig, Dunkin-Hartley, male, 10 animals in test group and 5 in control group | IodoFence (GMP 54); Vehicle: distilled water (topical) or isotonic salt (intradermal); Doses: topical at 100% and intradermal at 12.5%; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in control group. A very slight erythema was recorded in 10% (1/10) of the animals from the treated group, 24 hours  after the challenge phase, on the treated area with the test item at 100% or 50%. No cutaneous reaction was recorded at 48 hours after the challenge phase. | n/a | Colas, S., 2012 (OECD 406 IodoFence, SMK-PH-11/0566) |
| Guinea pig, Hartley, male/female, 10 animals in test group and 5 in control group | Proactive (GMP 43); Vehicle: distilled water; Doses: MIC topical and MIC intradermal; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in test group and control group. | n/a | Fagette, S. 2011 (OECD 406 Proactive, Tq 534 / 10-3365) |
| Guinea pig, Hartley, male/female, 10 animals in test group and 5 in control group | Proactive Plus (GMP 42); Vehicle: distilled water; Doses: MIC topical and MIC intradermal; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in test group and control group. | n/a | Canguilhem, B., 2010 (OECD 406 Proactive Plus, Tq 149 / 10-1156) |
| Guinea pig, Dunkin-Hartley, female, 10 animals in test group and 5 in control group | Fortex (GMP 56); Vehicle: distilled water (topical) or isotonic salt (intradermal); Doses: topical at 100% and intradermal at 2%; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in test group and control group. | n/a | Richeux F., 2014 (OECD 406 Fortex, SMK-PH-13/0541) |
| Guinea pig, Hartley, male/female, 10 animals in test group and 5 in control group | Dipal RTU (GMP 34); Vehicle: distilled water; Doses: MIC topical and MIC intradermal; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in test group and control group. | n/a | Canguilhem, B., 2010 (OECD 406 Dipal RTU, Tq 148 / 10-1157) |
| Guinea pig, Hartley, male/female, 11 animals in test group and 5 in control group | Dipal Conc (GMP 48); Vehicle: distilled water; Doses: MIC topical and MIC intradermal; Route: topical + intradermal; Duration topical exposure: 48 h | No reactions after challenge exposure (undiluted and 50%) in control group. In the test group, the application of the test element undiluted induced discrete or moderate erythema in 3 animals at the 24 and 48 hours' readings and in 2 animals for at the 72 hours' reading.  => Percentage of reactive treated animals : 27 %;  A second challenge test was performed under the same conditions.  Again, no reactions after challenge exposure (undiluted and 50%) in control group. In the test group, the application of the test element undiluted induced discrete or moderate erythema in 3 animals at the 24 and 48 hours' readings and in 2 animals at the 72 hours' reading.  = > Percentage of reactive treated animals : 27 % | n/a | Fagette, S. 2011 (OECD 406 Dipal Conc, Tq 531 / 10-3362) |

No human data are available on the products of this product family.

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| --- | --- |
| **Conclusion used in Risk Assessment – Skin sensitisation** | |
| Value/conclusion | *In vivo* skin sensitisation studies according to OECD guidelines 406 were performed on 7 out of 10 products within the product family. In accordance with the Regulation EC No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the products must not be classified in category 1. No signal word or hazard statement is required. |
| Justification for the value/conclusion | Available *in vivo* test results were conclusive and did not lead to classification. No studies were performed on Tri-Fender (GMP 51), TriActive (F-2506) and Dipal Plus (GMP 36) but since these formulations contain no or less sodium iodate (the only component classified for skin sensitisation) compared to the 7 tested products and given the negative results for the other products within this family, it seems justified to conclude that these products are also not classified.  Due to the presence of sodium iodate in concentrations higher or equal to 0.1%, the following products however require the hazard statement EUH208 and are therefore grouped in a separate Meta SPC 2: Blockade (GMP 44), IodoFence (GMP 54), Proactive (GMP 43) and Fortex (GMP 56).  It is noted that except for Dipal Plus and TriActive (not tested), the products in the BPF were already on the market for several years across the EU, before BPR legislation became effective. In addition, some of the products are also marketed outside the EU and in vivo toxicity tests were therefore also performed for the purpose of other regulations. An example is Fortex ,that justifies the study for this product performed after 2012.  Note CA NL:  During commenting phase the similarity was not sufficiently addressed to justify bridging for products tested and metaSPC level. Based on the classification rules as included in CLP, no classification for this endpoint is considered necessary for products included in metaSPC1, 3, 4, 5 & 6.  Products included in metaSPC 2 and 7 need to be classified with:  EUH208 - Contains sodium iodate. May produce an allergic reaction.  More specific information included in the confidential PAR, section 3.6.7. |
| Classification of the product according to CLP and DSD | Not classified.  However, H317 classified co-formulants could be present <1% but > 0.1%. Therefore, metaSPC2 and metaSPC7 needs to be classified with: EUH208 – Contains sodium iodate. May produce an allergic reaction. |

***Respiratory sensitization (ADS)***

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| **Conclusion** **used in Risk Assessment – Respiratory sensitisation** | |
| Justification for the conclusion | None of the components used in the formulations is classified as for respiratory sensitisation Category 1 (H334). |
| Classification of the product according to CLP and DSD | Not classified. |

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| **Data waiving** | |
| Information requirement | IUCLID 8.4 Respiratory sensitisation |
| Justification | No studies have been performed on the products of this product family. None of the components in the mixtures is classified as Category 1 for respiratory sensitisation (H334). |

***Acute toxicity***

*Acute toxicity by oral route*

Acute oral toxicity studies according to OECD guidelines 423 (or OECD guideline 401) were performed on 8 out of 10 products within the product family. These studies were not performed on TriActive (F-2506) and Dipal Plus (GMP 36) due to the high degree of similarity with respectively Tri-Fender (GMP 51) and Dipal RTU (GMP 34) (expert judgement).

| **Summary table of animal studies on acute oral toxicity** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Method Guideline**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance**  **Dose levelsType of administration** *(gavage, in diet, other)* | **Signs of toxicity** *(nature, onset, duration, severity, reversibility)* | **Value LD50** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 401, GLP, reliable without restriction | Rat, Sprague-Dawley, male/female, 5 animals per sex | Blockade (GMP 44), 1 dose of 2000 mg/kg per body weight by oral gavage | Nothing to report | >2000 mg/kg bw | n/a | Gomond, P., 2000 (OECD 401 Blockade, Tg 315 / 00-1588) |
| OECD 423, GLP, reliable without restriction | Rat, Sprague-Dawley, female, 6 animals per dose | IodoFence (GMP 54), 1 dose of 2000 mg/kg per body weight by oral gavage | Nothing to report | >2000 mg/kg bw | n/a | Colas, S., 2011 (OECD 423 IodoFence, TAO423-PH-11/0566) |
| Rat, Sprague-Dawley, female, 6 animals per dose | Proactive (GMP 43), 1 dose of 2000 mg/kg per body weight by oral gavage | A slight piloerection was observed in all animals just after treatment and during the first 4 hours of observation. Then, no clinical signs were noted anymore till the end of the observation period (D15). | >2000 mg/kg bw | n/a | Fagette, S. 2011 (OECD 423 Proactive, Tq 510 / 10-3365) |
| Rat, Sprague-Dawley, female, 6 animals per dose | Proactive Plus (GMP 42), 1 dose of 2000 mg/kg per body weight by oral gavage | A slight piloerection was observed in all animals just after treatment and during 30 minutes. Then, no clinical signs were noted anymore till the end of the observation period (D15). | >2000 mg/kg bw | n/a | Canguilhem, B., 2010 (OECD 423 Proactive Plus, Tq 138 / 10-1156) |
| Rat, Sprague-Dawley, female, 6 animals per dose | Fortex (GMP 56), 1 dose of 2000 mg/kg per body weight by oral gavage | Nothing to report. | >2000 mg/kg bw | n/a | Richeux F., 2013 (OECD 423 Fortex, TAO423-PH-13/0541) |
| Rat, Sprague-Dawley, female, 6 animals per dose | Tri-Fender (GMP 51), 1 dose of 2000 mg/kg per body weight by oral gavage | Nothing to report. | >2000 mg/kg bw | n/a | Richeux F., 2011 (OECD 423 Tri-Fender, TAO423-PH-11/0097) |
| Rat, Sprague-Dawley, female, 6 animals per dose | Dipal RTU (GMP 34), 1 dose of 2000 mg/kg per body weight by oral gavage | A slight piloerection was observed in all animals just after treatment and during 30 minutes. Then, no symptoms were observed anymore till the end of the observation period (D15). | >2000 mg/kg bw | n/a | Canguilhem, B., 2010 (OECD 423 Dipal RTU, Tq 137 / 10-1157) |
| Rat, Sprague-Dawley, female, 6 animals per dose | Dipal Conc (GMP 48), 1 dose of 2000 mg/kg per body weight by oral gavage | A slight piloerection was observed in all animals just after treatment and during 30 minutes. Then, no symptoms were observed anymore till the end of the observation period (D15). | >2000 mg/kg bw | n/a | Gomond, P., 2007 (OECD 423 Dipal Conc, Tm 622 / 06-3019) |

No human data are available on the products of this product family.

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| **Value used in the Risk Assessment – Acute oral toxicity** | |
| Value | >2000 mg/kg body weight |
| Justification for the selected value | The LD50 of the 8 tested products is always higher than 2000 mg/kg body weight by oral route in the rat.  ln accordance with the Regulation EC No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the tested products must not be classified. No signal word or hazard statement is required. No studies were performed on TriActive (F-2506) and Dipal Plus (GMP 36) but due to the high degree of similarity with respectively Tri-Fender (GMP 51) and Dipal RTU (GMP 34) it seems justified to conclude that both products are also not classified.  It is noted that except for Dipal Plus and TriActive (not tested), the products in the BPF were already on the market for several years across the EU, before BPR legislation became effective. In addition, some of the products are also marketed outside the EU and in vivo toxicity tests were therefore also performed for the purpose of other regulations. An example is Fortex ,that justifies the study for this product performed after 2012. |
| Classification of the product according to CLP and DSD | Not classified. |

*Acute toxicity by inhalation*

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| **Value used in the Risk Assessment – Acute inhalation toxicity** | |
| Value | Not applicable |
| Justification for the selected value | Droplet size when u­sed by spraying is well above 50 µm. (C. Kingston, 2007) |
| Classification of the product according to CLP and DSD | Not classified : Iodine is classified for acute tox inhalation, but present below generic cut-off value (< 1%) in all products => does not contribute to classification acute tox inhalation of the products. |

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| **Data waiving** | |
| Information requirement | IUCLID 8.5.2 Acute toxicity: inhalation |
| Justification | It was considered scientifically unjustified to perform acute inhalation toxicity studies for several reasons:  First, testing on product/mixtures does not need to be conducted if there are valid data available on each of the components in the mixture, sufficient to allow classification according to the rules laid down in Regulation 1272/2008. When following these guidelines, none of the products within the iodine based teat disinfectant family needs to be classified for inhalation toxicity (Iodine is classified for acute tox inhalation, but present below generic cut-off value (< 1%) in all products => does not contribute to classification acute tox inhalation of the products).  Second, we provided in IUCLID section 8.5.1 and 8.5.3 respectively oral and dermal acute toxicity studies for all products. According to those tests, none of the products were classified for oral or dermal toxicity. According to the ECHA Guidance on information requirements for BPR, acute toxicity tests for 2 relevant exposure routes are sufficient. The risk for inhalation exposure is also considered to be unlikely, even for the products that are applied by spraying, since the particle size of sprayed droplets is well above 50 µm (Kingston, 2007). |

*Acute toxicity by dermal route*

Acute dermal toxicity studies according to OECD guidelines 402 were performed on 8 out of 10 products within the product family. These studies were not performed on TriActive (F-2506) and Dipal Plus (GMP 36) due to the high degree of similarity with respectively Tri-Fender (GMP 51) and Dipal RTU (GMP 34) (expert judgement).

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| --- | --- | --- | --- | --- | --- | --- |
| **Summary table of animal studies on acute dermal toxicity** | | | | | | |
| **Method, Guideline,**  **GLP status,**  **Reliability** | **Species, strain, Sex, No/group** | **Test substance, Vehicle, Dose levels, Surface area** | **Signs of toxicity** *(nature, onset, duration, severity, reversibility)* | **LD50** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 402, GLP, Reliable without restriction | Rat, Sprague-Dawley, male/female, 5 animals per sex | Blockade (GMP 44), undiluted, one dose of 2000 mg/kg body weight, Surface area: about 45 cm2 | Nothing to report | >2000 mg/kg bw | n/a | Fagette, S. 2011 (OECD 402 Blockade, Tq 518 / 10-3367) |
| IodoFence (GMP 54), undiluted, one dose of 2000 mg/kg body weight, at least 10% total body surface area. | Nothing to report | >2000 mg/kg bw | n/a | Colas, S., 2011 (OECD 402 IodoFence, TAD-PH-11/0566) |
| Proactive (GMP 43), undiluted, one dose of 2000 mg/kg body weight, Surface area: about 45 cm2 | Nothing to report | >2000 mg/kg bw | n/a | Fagette, S. 2011 (OECD 402 Proactive, Tq 516 / 10-3365) |
| Proactive Plus (GMP 42), undiluted, one dose of 2000 mg/kg body weight, Surface area: about 45 cm2 | Nothing to report | >2000 mg/kg bw | n/a | Canguilhem, B., 2010 (OECD 402 Proactive Plus, Tq 141/ 10-1156) |
| Fortex (GMP 56), undiluted, one dose of 2000 mg/kg body weight, at least 10% total body surface area | Nothing to report | >2000 mg/kg bw | n/a | Richeux F., 2013 (OECD 402 Fortex, TAD-PH-13/0541) |
| Tri-Fender (GMP 51), undiluted, one dose of 2000 mg/kg body weight, at least 10% total body surface area | Nothing to report | >2000 mg/kg bw | n/a | Richeux F., 2011 (OECD 402 Tri-Fender, TAD-PH-11/0097) |

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| --- | --- | --- | --- | --- | --- | --- |
|  |  | Dipal RTU (GMP 34), undiluted, one dose of 2000 mg/kg body weight, Surface area: about 45 cm2 | Nothing to report | >2000 mg/kg bw | n/a | Canguilhem, B., 2010 (OECD 402 Dipal RTU, Tq 140/ 10-1157) |
| Dipal Conc (GMP 48), undiluted, one dose of 2000 mg/kg body weight, Surface area: about 55 cm2 for males and 50 cm2 for females | Nothing to report | >2000 mg/kg bw | n/a | Gomond, P., 2007 (OECD 402 Dipal Conc, Tq 621/ 06-3019) |

No human data are available on the products of this product family.

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| **Value used in the Risk Assessment – Acute dermal toxicity** | |
| Value | >2000 mg/kg body weight |
| Justification for the selected value | The LD50 of the 8 tested products is always higher than 2000 mg/kg body weight by dermal route in the rat.  ln accordance with the Regulation EC No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the tested products must not be classified. No signal word or hazard statement is required. No studies were performed on TriActive (F-2506) and Dipal Plus (GMP 36) but due to the high degree of similarity with respectively Tri-Fender (GMP 51) and Dipal RTU (GMP 34) it seems justified to conclude that both products are also not classified.  It is noted that except for Dipal Plus and TriActive (not tested), the products in the BPF were already on the market for several years across the EU, before BPR legislation became effective. In addition, some of the products are also marketed outside the EU and in vivo toxicity tests were therefore also performed for the purpose of other regulations. An example is Fortex ,that justifies the study for this product performed after 2012. |
| Classification of the product according to CLP and DSD | Not classified. |

***Information on dermal absorption***

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| --- | --- | --- | --- |
| **Value(s) used in the Risk Assessment – Dermal absorption** | | | |
| Substance | Iodine | / | / |
| Value(s)\* | 12 % | / | / |
| Justification for the selected value(s) | The percutaneous absorption of total iodine from two biocide formulations through human skin membranes was examined, as part of the active substance dossier. The mean total absorption was respectively 11.3% and 12.0% of the dose applied. | / | / |

*\* please include the concentration range(s) the values are applicable for, if relevant*

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | IUCLID 8.6 Dermal absorption |
| Justification | No specific dermal absorption test has been performed with the iodine teat disinfectants within this product family. The Iodine Registration Group has submitted data on *in vitro* penetration studies where the percutaneous absorption of total iodine from two biocide formulations (0.26% and 0.66% w/w iodine) through human skin membranes was examined, as part of the active substance dossier. The results demonstrated that in the concentration range tested, the dermal penetration of total iodine was independent of the concentration of iodine in the biocidal formulations. Therefore, based on these results, a dermal penetration rate for iodine of 12% will be used for the human health exposure assessment and the subsequent risk characterisation of the products within this product family.  The composition of the BPF products are considered comparable to the tested formulations.  Note eCA: An justification for the dermal absorptions value of 12% based on read across, including an overview of the BPF and the tested formulation, is included in a separate document. This document is prepared by the eCA and is only available for the MSs, as it includes information from the confidential part of the CAR of iodine. |

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

Not applicable; The data available on each of the components of the products in this product family is sufficient to allow classification of the mixtures according to the rules laid down in Regulation (EC) No 1272/2008, and synergistic effects between any of the components are not expected. The first substance of concern for this product family is an alcohol ethoxylate Neodol 91-8 (CAS nr 68439-46-345-3) classified as Acute Tox. 4 (H302) and Eye Dam. 1 (H318) and present in maximal a concentration of 6.34% in Dipal Conc (GMP 48). At this concentration, the ethoxylated alcohol only presents a possible hazard for the eye (according to OECD 405 on Dipal Conc (GMP 48)). This local effect is considered sufficiently covered by classification and labelling of Dipal Conc (GMP 48) as Eye Irritation Cat 2 with a recommendation on the label to wear eye/face protection (P280). Therefore, exposure of the eye is very unlikely to occur and this SOC was not taken further into account for the exposure assessment.

Furthermore, sodium iodide is considered a SoC as this formulant contributes to the classification of metaSPC5 with H373- May cause damage to thyroid through prolonged or repeated exposure, oral route. H373 falls into Band C, for which a full risk assessment in indicated in the guidance. As the assessment for iodine is based on concentration total iodine which considers all iodine equivalents included in a metaSPC, exposure to sodium iodide is already covered by the risk assessment to iodine.

In the confidential annex more information is included.

***Other***

1. **Milk residue field trial (Reference: 2012-009)**

Considering that the intended use of the products is application to the teats of cows after milking, secondary exposure via residues in milk is potentially possible. The calculation of the livestock exposure according to DRAWG guidance indicates that for all products, the trigger value of 0.004 mg a.s/kg/day is exceeded for the intended use. This is interpreted as indicating that a more detailed consideration of the potential for residues in edible products is required and an estimation of the worst case consumer exposure (WCCE) needs to be undertaken and compared with the limit value. Therefore, potential secondary exposure of the general public to iodine in milk was considered. Consumer exposure to iodine from meat was not considered in accordance to the EFSA 2013 opinion on the safety and efficacy of iodine compounds (E2) as feed additives, in which it was concluded that the iodine level in edible tissues/products is generally found to be highest in milk and not in meat. Although according to the opinion of the Agency for Toxic Substances and Disease Registry (ATSDR), the major contribution to iodine content in milk is feed supplementation rather than the use of iodine dip/spray, a field residue trial was performed to quantify the respective contributions of feeding and teat disinfection to the iodide content in milk.

The trial was designed to monitor the effects of three iodine-based teat dips on milk iodide levels over a two week period. The trial farm was purged of all iodine based products for 21 days during a "washout period". Pre-treatment baseline iodide levels were determined. During the treatment period, iodine-based teat dips were introduced at post-dipping and the change in milk iodide residue levels for each teat dip was evaluated. A control group was treated with a non-iodine based teat dip to monitor background levels of iodide in milk. IodoFence (GMP 54) and Tri-Fender (GMP 51) were 2 of the products tested. Tri-Fender was applied either by dipping or manual spraying after each milking. The latter being worst-case, since the consumption per cow for this application type was shown to be the highest compared to dipping and automatic spraying. The cows were milked 3x/day which is again a worst-case situation for monitoring of residues since in Europe most cows are milked only 2x/day. The method used for the determination of soluble iodide in milk in the residue study is based on the internationally recognised AOAC standard: AOAC Official Method AOAC 992.24 "Iodide in Ready-to-feed milk-based Infant formula (Ion-selective Electrode Method)".

The trial determined that the introduction of iodine-based teat dips increased iodide residue content in milk relative to a non-iodine treated control group however, the residues were within the same range as reported values from bulk sample analysis in various European studies (60 - 250 ppb) (EFSA Journal 2013; 11(2): 3099).

The trial also showed that a higher concentration of iodine in the disinfectant (0.5% in Bovidip) increased milk iodide levels by 20.2 ppb compared to the lower concentration of 0.25% iodine (Tri-Fender, dip).

Also, the method of product application to the teats appears to influence iodide residue content in milk. Spray application increased milk iodide residue levels more than dip cup application by an amount of 20.7 ppb. ln this trial, spray application utilized approximately 23% more teat dip compared to dip cup application.

The table below outlines the least square mean milk iodide concentration in the milk of cows treated with each of the test products and the contribution of each iodine product relative to the control disinfectant.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Test product | Percent iodine | application | Iodide in milk (ppb) | Standard error | Teat dip Milk iodide contribution (ppb) |
| Control | H2O2 | dip | 148,4 | 5,1 |  |
| Tri-Fender | 0,25% | dip | 156,9 | 5,1 | 8,48 |
| Tri-Fender | 0,25% | spray | 177,7 | 5,1 | 29,21 |
| Bovidip | 0,50% | dip | 177,1 | 5,1 | 28,64 |
| IodoFence | 0,25% | dip | 163,3 | 5,1 | 14,88 |

1. **Safety reports veterinary medicines:**

To demonstrate the safety of the iodine based teat disinfectants, we provide pharmacovigilance data that are available because some products of the product family are also registered as Veterinary Medicines in some EU countries. The method of application and frequency are the same as for the biocidal use. Periodic safety update reports for these products have to be submitted at defined timepoints during the post-authorisation phase by the marketing authorisation holder. These pharmacovigilance documents intend to provide a safety update to be able to evaluate the impact on the risk-benefit balance of a medicinal product.

PSUR Summary Bridging Report: Blockade 0.25% w/w iodine teat dip solution.

PSUR Summary Bridging Report: Proactive 0.15% w/w Teat Dip/Spray Solution.

PSUR Summary Bridging Report: Proactive Plus, tepeldip oplossing.

PSUR Summary Bridging Report: Dipal Conc 0.75% concentraat voor speendip of -spray oplossing.

For none of the 4 products reports were received of serious and non-serious suspected adverse events or lack of efficacy during this period in any species, including human beings.

***Assessment for endocrine disrupting properties***

According to the ED (endocrine disruptor) criteria with respect to humans established in the Commission Delegated Regulation (EU) 2017/2100, a substance shall be considered as having endocrine disrupting properties if it meets all of the following criteria:

a) it shows an adverse effect in [an intact organism or its progeny]/[non-target organisms], which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

b) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;

c) the adverse effect is a consequence of the endocrine mode of action.

Potentially an alert is identified by the eCA for two co-formulants, i.e. sodium iodide and sodium iodate. In CA-80, September 2018, the CA document on the subject: Implementation of scientific criteria to determine the endocrine-disrupting properties of already approved active substances (CA-March18-Doc.7.5.a-Final - EDs approved active substances) was endorsed. Iodine and PVP-iodine are mentioned as selected active substances for an early review of the approval in light of its potential ED properties and the renewal process for these substances does not take place before the end of 2020. As information for iodine and PVP-iodine on the ED assessment should be used for sodium iodide and sodium iodate, the outcome of the EU discussions on the actives should be awaited for these two co-formulants.

To examine if any of the other co-formulants contained in the product may possess ED properties, a screening was performed by examining the co-formulants are

* Classified as CMR or PBT;
  + Identified as ED in the DG Santé’s Impact Assessment study on Screening of available evidence on chemical substances for the identification of endocrine disruptors;
  + Identified as ED in the EU list of potential endocrine disruptors; or
  + Listed in CoRAP linked to ED concerns.

None of the co-formulants triggered an alert for ED property. See assessment included in the confidential annex.

Subsequently, it was examined if there are any concerns for adverse effect to meet the critaria a) as described above using ECHA REACH database. Furthermore, US databases EDSP21 and ToxCast were checked. This examination did not result in alerts, and therefore no further ED assessment was required

#### Exposure assessment

The following human exposure assessment is performed for the worst-case product within the DeLaval iodine-based teat disinfectant family. Within Meta SPC 5, **Dipal Conc (GMP 48)** is selected as the worst-case product for assessment of human exposure during Mixing & Loading, since this product is a concentrate containing 1.03 % w/w total iodine. For the exposure during application, **Blockade (GMP 44)** is selected as worst-case product (part of Meta SPC 2), since this product contains 0.43% w/w total iodine (see confidential part of the PAR).

**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 | n.a | Yes | n.a | n.a | No | n.a | n.a |
| Dermal | n.a | Yes | n.a | n.a | Yes | n.a | n.a |
| Oral | n.a | No | n.a | n.a | No | n.a | Yes |

As the products are only intended for professional use, primary oral exposure is considered to be negligible. The main routes of primary exposure are dermal and inhalation. Respiratory exposure is considered possible in view of the high vapour pressure of the active substance (iodine: 40.7 Pa at 25 ºC).

Only exposure towards aerosol was assessed for relevant scenarios as in the teat disinfection products the iodine is present as ionic and/or complex-bound species which are not prone to evaporation. A detailed justification as to why inhalation exposure towards vapour is negligible is provided in the confidential part of the PAR.

***List of scenarios***

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario**  (e.g. mixing/ loading) | **Primary or secondary exposure**  **Description of scenario** | **Exposed group**  (e.g. professionals, non-professionals, bystanders) |
| 1. | Mixing and loading | Primary exposure (dermal and inhalation): Exposure to the concentrate can occur during dilution of the disinfection solution while exposure to the ready-to-use solution can occur during the loading of the dip cups or spray applicators. | professionals |
| 2. | Application – manual dipping | Primary exposure (dermal and inhalation): Exposure to the ready-to-use solution can occur during the application by manual dipping.  Secondary exposure of professional users might occur by rubbing against the teats or from drops dripping from the teat on the hand. Bystander exposure is considered negligible. | professionals |
| 3. | Application – manual spraying | Primary exposure (dermal and inhalation): Exposure to the ready-to-use solution can occur during the application by manual spraying.  Secondary exposure of professional users might occur by rubbing against the teats or from drops dripping from the teat on the hand. Bystander exposure is considered negligible. | professionals |
| 4. | Post-application -cleaning of teats by wiping with cloth | Primary exposure (dermal and inhalation): Exposure to residues of the ready-to-use solution may occur in the post-application phase during cleaning of teats post-milking. | professionals |
| 5. | Post-application – cleaning of equipment | Primary exposure (dermal and inhalation): Exposure to the ready-to-use solution may occur in the post-application phase during cleaning of equipment materials or emptying of containers. | professionals |

***Industrial exposure***

Not applicable, no industrial exposure is foreseen.

***Professional exposure***

*Scenario 1*

| **Description of Scenario 1– Mixing and loading** | | |
| --- | --- | --- |
| In line with HEAdhoc recommendation no. 13: Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3) (Agreed at the Human Health Working Group I on 19 January 2017), for mixing and loading of concentrated product for dermal exposure, mixing and loading model 4 is used.  For the dermal exposure, the total amount of the required solution that is needed per day is of importance. Manually, cows are miked twice a day, however, for robotic milking, cows can be milked three times a day. Only, *meta*SPC5 contains concentrated products (Worst-case product: Dipal Conc (GMP 48)), and can be used post-milking and the max amount used for cows is 10 ml (assumption). Therefore, as worst case the amount needed for one day is: 10ml diluted product x 3 times a day = 30 ml.  As the product is used at max 20% (v/v) dilutions, max (30 ml x20% = ) 6 ml concentrated product per cow/day is used. Considering 82 cows, this results in a total amount of product per day of 6 ml x 82 cows = 492 ml ≈ 0.5 liter product/day.  For mixing and loading model 4, the indicative hand exposure for handling 1 L is 0.01 ml/treatment.  In case of loading of electronic sprayer, automated dipping/foaming-system or robotic milking device (for automated spraying) the sucking lance of the electronic sprayer, automated dipping/foaming-system or robotic milking device is inserted in a can containing the RTU product. Therefore, the exposure for the manual scenario is considered worst-case, and therefore used in the exposure calculation.    As iodine in the product is complex-bound in the formulation, no evaporation is expected and therefore no inhalation exposure is assessed.  In HEAdhoc recommendation no 13. 2 for mixing and loading of concentrates and RTUs, the same model is included. The difference is the amount handled. If the same assumption is used (10 ml per cow per treatment), and considering 82 cows, this results in a total amount of product per day of 20 ml x 82 cows = 1.6 L product/day. Based on this amount, the indicative hand exposure for handling of 5 L is 0.2 ml/treatment of mixing and loading model 4 should be used.  Worst-case concentrate: Dipal Conc (GMP 48)(part of *meta*SPC5)  Total Concentration of active substance: **1.03 % w/w**  Worst-case RTU: Blockade (GMP 44) (part of *meta*SPC2)  Total Concentration of active substance: **0.43 % w/w**  Exposure from (re)-filling of dipping cups or sprayer with the diluted concentrate is assumed to be covered by the overall M/L step of the concentrate. | | |
|  | Parameters | Value |
| Tier 1 – | Total iodine (available iodine and iodide) | Concentrate: 1.03%  RTU: 0.43% |
| Dermal penetration | 12% |
| Body weight | 60 kg |
| indicative dermal exposure value (mixing and loading model 4) | Concentrate: 0.01 ml/event  RTU: 0.2 ml/event |
| No PPE |  |
| Tier 2 | gloves | 90% protection |

**Calculations for Scenario [1] – Mixing and loading**

In the following, the results of the calculations are provided for scenario 1 performed twice a day when using a **concentrate 1.03% total iodine (*meta*SPC5)**.

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake**  **(mg/kg bw/d)** | **Estimated oral uptake** | **Estimated total uptake**  **(mg/kg bw/d)** |
| Scenario [1.1] – M/L model 4– | Tier 1/ none | - | 2.06E-04 | - | 2.06E-04 |
| Tier 2/  gloves | - | 2.06E-05 | - | 2.06E-05 |

In the following, the results of the calculations are provided for scenario 1 performed twice a day when using a **RTU 0.43% total iodine (*meta*SPC2)**.

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake**  **(mg/kg bw/d)** | **Estimated oral uptake** | **Estimated total uptake**  **(mg/kg bw/d)** |
| Scenario [1.2] – M/L model 4 | Tier 1/ none | - | 1.72E-03 | - | 1.72E-03 |
| Tier 2/  Gloves | - | 1.72E-04 | - | 1.72E-04 |

The exposure calculations are included in Annex 3.2.

*Scenario 2*

| **Description of Scenario 2 – application by dipping** |
| --- |
| *Application by manual dipping, scenario 2.1*  Dermal exposure during use of the dip cups, based on the design of the dipping cup, is not expected. Any possible spillage exposure is considered covered by the dermal exposure as calculated by the scenario of mixing and loading. This is in line with HEAdhoc recommendation no. 13: Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3) (Agreed at the Human Health Working Group I on 19 January 2017)  Additionally, as iodine in the product is complex-bound in the formulation, no evaporation is expected and therefore no inhalation exposure is assessed.  *Application by automated dipping, scenario 2.2*  No exposure of professionals occurs during automated dipping. |

*Scenario 3*

| **Description of Scenario 3.1 – application by manual spraying** | | |
| --- | --- | --- |
| After milking, the teats are sprayed with the disinfectant using a trigger sprayer or electronic sprayer making sure that each teat is covered with the disinfectant.  In line with HEAdhoc recommendation no. 13: Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3) (Agreed at the Human Health Working Group I on 19 January 2017), for application by spraying (both manual trigger spraying and electronic spraying (not with robot)) Hand-held trigger spray model (consumer product spraying and dusting model 2, Biocides Human Health Exposure Methodology) is used.  The following assumptions are considered in the calculations:   * The farmer milks 82 cows twice a day * The spraying time per cow/event is 10 seconds * Results in (10 seconds \*82 cows)/60 = 13.7 min exposure time per milking event   Worst-case product: Blockade (GMP 44) (part of *meta* SPC2)  Total Concentration of active substance: **0.43 % w/w** | | |
|  | Parameters | Value |
| Tier 1 – | Total iodine (available iodine and iodide) | 0.43% |
| Dermal penetration | 12% |
| Body weight | 60 kg |
| Inhalation rate (short- and long-term;  acc. to HEEG opinion “Default human factor values for use in exposure assessments  for biocidal products”, 2013) | 1.25 m³/h (0.021 m³/min) |
| Exposure duration | 13.7 min |
| Number of applications per day | 2 |
| No PPE |  |
| Tier 2 | gloves | 90% protection |

**Calculations for Scenario [3.1] - Application of teat disinfectant by manual spraying**

In the following, the results of the exposure calculations of scenario 3 are provided for 82 animals disinfected after each milking, i.e. twice a day.

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake**  **(mg/kg bw/d)** | **Estimated oral uptake**  **(mg/kg bw/d)** | **Estimated total uptake**  **(mg/kg bw/d)** |
| Scenario [3] – Consumer spraying and dusting Model 2. Hand-held trigger spray | Tier 1/ none | 4.29E-04 | 1.08E-02 | - | 1.12E-02 |
| Tier 2/  Inside gloves | 4.29E -04 | 3.13E-03 | - | 3.56E-03 |

**Further information and considerations on scenario [3.1] - Application of teat disinfectant by spraying: Local exposure concentration of iodine in air**

| **Summary table: estimated exposure from professional uses** | |
| --- | --- |
| **Exposure scenario** | **Iodine in air inhaled (mg/m³)** |
| Scenario [3] – Consumer spraying and dusting model 2, Hand-held trigger spray | 4.52E-02 |

The calculation sheets are provided in **Annex 3.2**.

| **Description of Scenario 3.2 – application by automated spraying** |
| --- |
| No exposure of professionals occurs during automated spraying. |

*Scenario 4*

| **Description of Scenario 4 – cleaning of teats by wiping with cloth (post-milking)** |
| --- |
| In line with HEAdhoc recommendation no. 13: Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3) (Agreed at the Human Health Working Group I on 19 January 2017), no exposure calculation is necessary as the exposure during cleaning of teats, removal of dried residues for post-milking applications is considered limited. |

*Scenario 5*

| **Description of Scenario 5-cleaning of equipment** | | |
| --- | --- | --- |
| In line with HEAdhoc recommendation no. 13: Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3) (Agreed at the Human Health Working Group I on 19 January 2017), for cleaning of equipment, RISKOFDERM ‘Loading liquid, automated or semi-automated’ for the cleaning phase of different equipment (dipping cup, spraying nozzle etc.) is used. The indicative value is 0.92 mg/min and a duration of is 5 minutes is considered.  Additionally, as iodine in the product is complex-bound in the formulation, no evaporation is expected and therefore no inhalation exposure is assessed.  Worst-case product: Blockade (GMP 44)  Total Concentration of active substance: **0.43 % w/w** (= sum of all iodine equivalents, see confidential annex) | | |
|  | Parameters | Value |
| Tier 1 | Total iodine (available iodine and iodide) | 0.43% |
| Dermal penetration | 12% |
| Body weight | 60 kg |
|  | indicative value of RISKOFDERM ‘Loading liquid, automated or semi-automated’ | 0.92 mg/min |
|  | Exposure duration | 5 min per day |
|  | No PPE |  |
| Tier 2 | Gloves | 90% protection |

**Calculations for Scenario [5] – Cleaning of equipment**

In the following, the results of the calculations are provided for scenario 5 performed twice a day

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake**  **(mg/kg bw/d)** | **Estimated oral uptake** | **Estimated total uptake**  **(mg/kg bw/d)** |
| Scenario [5] – ‘Loading liquid, automated or semi-automated’ | Tier 1/ none | - | 3.96E-05 | - | 3.96E -05 |
| Tier 2/  Gloves | - | 3.96E -06 | - | 3.96E -06 |

The calculation sheets are provided in **Annex 3.2**.

**Calculations for Scenario 1-5**

In the summary table below only the values for the worst-case products for each scenario are represented which is Dipal Conc (GMP 48) (part of *meta*SPC5) for scenario 1.1 (covering also scenario 2) and Blockade (GMP 44) for scenario 1.2 (covering also scenario 2), 3, 4 and 5.

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake**  **(mg/kg bw/d)** | **Estimated oral uptake** | **Estimated total uptake**  **(mg/kg bw/d)** |
| Scenario 1.1- mixing and loading : concentrate | Tier 1 / no PPE | n.a | 2.06E-04 | n.a | 2.06E-04 |
| Scenario 1.1- mixing and loading : concentrate | Tier 2 / gloves | n.a | 2.06E-05 | n.a | 2.06E-05 |
| Scenario 1.2- mixing and loading : RTU | Tier 1 / no PPE | n.a | 1.72E-03 | n.a | 1.72E-03 |
| Scenario 1.2- mixing and loading : RTU | Tier 2 / gloves | n.a | 1.72E-04 | n.a | 1.72E-04 |
| Scenario 2 – application by manual dipping | )  Exposure is considered covered by the mixing and loading scenario. | | | | |
| Scenario 2 – application by automated dipping | No exposure of professionals occurs during automated dipping. | | | | |
| Scenario 3 – application by spraying | Tier 1 / no PPE | 4.29E-04 | 1.08E-02 | n.a | 1.12E-02 |
| Scenario 3 – application by spraying | Tier 2 / gloves | 4.29E-04 | 3.13E-03 | n.a | 3.56E-03 |
| Scenario 3 – application by automated spraying | No exposure of professionals occurs during automated spraying. | | | | |
| Scenario 4 – cleaning of teats by wiping with cloth (post-milking) | Exposure of professionals considered to be negligible during cleaning of teats by wiping with cloth: removal of dried residues from post-milking treatment. | | | | |
| Scenario 5 – cleaning of equipment | Tier 1 / no PPE | n.a | 3.96E-05 | n.a | 3.96E -05 |
| Scenario 5 – cleaning of equipment | Tier 2 / gloves | n.a | 3.96E -06 | n.a | 3.96E -06 |

**Further information and considerations on scenario 1-5**

Local effects of the products in the family are not expected since skin irritation studies (OECD 404) have shown that the products are not classified as irritant or corrosive by dermal application.

For inhalation, no risk for local effects was found. The local inhalation exposure to Blockade (GMP 44) (worst-case) during application by spraying was well below the AECinh (1 mg/m3) for iodine (calculations available in **Annex 3.2**).

| **Task/**  **Scenario** | **Iodine in air inhaled (mg/m³)** | **% OEL (1 mg/m³)** | **Acceptable**  **(yes/no)** |
| --- | --- | --- | --- |
| [3] – Application of teat disinfectant by spraying | 4.52E -02 | 5 | yes |

*Combined scenarios*

When the product is applied by manual dipping or spraying the professional user will be exposed during all use phases (mixing and loading, application and post-application phase). The combination of these scenarios (1+2+4+5 and 1+3+4+5) will be taken into account for the exposure assessment, as a worst-case. When the product is applied by automatic spraying, the professional user is only exposed during the mixing and loading phase (scenario 1).

The two possible combined exposure scenarios are presented for the ready-to-use product (Blockade, GMP 44, from *meta*SPC2). Calculations with this product delivered the highest estimated exposure values for all individual scenario’s - including scenario 1 for mixing and loading - and combined exposure to this product is therefore a worst-case representative for the entire product family.

**Blockade (GMP 44) - RTU**

| **Summary table: combined systemic exposure from professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake (mg/kg bw/d)** | **Estimated oral uptake (mg/kg bw/d)** | **Estimated total uptake (mg/kg bw/d)** |
| **Manual teat dip application**  Scenarios 1.2 + 2.1 + 4 + 5 for, Tier 1 (no PPE) | n.a | 1.76E-03 | n.a | 1.76E-03 |
| **Manual teat dip application**  Scenarios 1.2 + 2.1 + 4 + 5 for manual teat dip application, Tier 2 (gloves) | n.a | 1.76E-04 | n.a | 1.76E-04 |
| **Manual spraying using a trigger sprayer or automated sprayer**  Scenarios 1.2+3.1 + 4 + 5 for, Tier 1 (no PPE) | 4.29E-04 | 1.26E-02 | n.a | 1.30E-02 |
| **Manual spraying using a trigger sprayer or automated sprayer**  Scenarios 1.2+3.1 + 4 + 5 for manual teat spray application, Tier 2 (gloves) | 4.29E-04 | 3.31-03 | n.a | 3.73E-03 |

The calculation sheet is included in annex 3.2 (which also includes the combined scenarios for the concentrate)

***Non-professional exposure***

Not applicable, non-professional exposure is not foreseen.

***Exposure of the general public***

Not applicable, no exposure of the general public is foreseen during mixing and loading or application phase.

***Monitoring data***

There are no monitoring data available on the products.

***Dietary exposure***

*List of scenarios*

| **Summary table of main representative dietary exposure scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Type of use1** | **Description of scenario** | **Subject of exposure2** |
| 2. | Professional use | Application-manual dipping of teats after milking (see scenario professional exposure) | Milk |
| 3. | Professional use | Application-manual spraying of teats after milking (see scenario professional exposure) | Milk |
| 6. | Professional use | Application-automatic spraying of teats after milking (additional scenario, no professional exposure) | Milk |

1 e.g. animal husbandry, food industry, professional use, residential use.

2 e.g. chicken, milk, beer

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

Not applicable since this is an application for biocidal products.

For the sake of completeness, additional sources of iodine with possibility of milk residues are listed in the table below.

| **Summary table of other (non-biocidal) uses** | | | |
| --- | --- | --- | --- |
|  | **Sector of use** | **Intended use** | **Reference value(s)** |
| 1. | Veterinary use | Teat disinfection | Inappropriate to elaborate Maximum Residue Levels for iodine and that iodine should therefore be included in Annex II of Council Regulation (EEC) 2377/90 (currently replaced by EU 37/2010) (EMEA)(1) |
| 2. | Food & Feed additive | Iodine containing salts in animal feedingstuff | Inappropriate to elaborate Maximum Residue Levels for iodine and that iodine should therefore be included in Annex II of Council Regulation (EEC) 2377/90 (currently replaced by EU 37/2010) (EMEA)(1) |

1. EMEA summary report on iodine (CVMP)

**Note regarding need to set MRLs:** Since the direct treatments of cows with iodine-containing veterinary hygiene products may lead to residues in milk, the need to set new maximum residue limits (MRLs) should be investigated according to the “Proposed decision for Iodine” of 31 January 2014. However, it should be acknowledged that iodine-based teat dips and sprays have a long history as veterinary medicines for the prevention of mastitis all over Europe and worldwide and that veterinary and biocidal uses are quite similar (if not identical) with respect to application frequency, iodine use concentration and product composition. The European Agency for the Evaluation of Medicinal Products (EMA) concluded in their summary report on iodine that it would be inappropriate to elaborate maximum residue levels (MRLs) for iodine. Therefore, iodine was included in Annex II of Council Regulation (EEC) 2377/90 (now repealed by Regulation (EC) No 470/2009) comprising the list of substances not subject to maximum residue limits. Commission Regulation (EU) No 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin lists iodine (including inorganic compounds) in Table 1 “Allowed substances” of the Annex with a “no MRL required” entry for all food producing species and all target tissues (including milk).

*Estimating Livestock Exposure to Active Substances used in Biocidal Products*

Livestock exposure estimates are required for the risk assessment on animal health as well as for determining the worst-case human exposure estimate (WCCE). However, according to the EMEA (European Agency for the Evaluation of Medicinal Products) summary report on iodine-containing products used for veterinary medicine, only small increases in serum iodine concentration have been found after teat dipping indicating that the procedure has a negligible effect on tissue iodine concentrations. These results suggest limited livestock exposure and no-detailed risk assessment was therefore performed for animal health.

This is supported by the EFSA 2013 opinion on the safety and efficacy of iodine compounds (E2) as feed additives, in which it was concluded that the iodine level in edible tissues/products is generally found to be highest in milk and not in meat. Meat was therefore not considered to be the major source of dietary iodine for the consumer.

As iodine is excreted in milk, and iodine-based teat disinfection does result in increased iodine levels in milk, a worst-case dietary exposure assessment from possible residues in milk is performed. The evaluation of exposure to iodine from milk, is based on a study on iodine measurements in milk using products included in the applications (see “Estimating transfer of biocidal active substances into foods as a result of professional and/or industrial application(s)”)**.**

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

**Consumer exposure**

Iodine-based post-milking teat dip solutions are used worldwide for the disinfection of lactating animals’ teats in order to reduce contamination with mastitis pathogens between cows or from the environment. The iodine level of these products may vary greatly, between 1000 and 10000 ppm iodine (the iodine level of DeLaval teat disinfectants is between 1500 - 2500 ppm available iodine). The level of iodine residues in milk from the use of these products was assessed to address any potential issues related to elevated residue levels in milk, with special emphasis on the risk assessment for milk consumption by children. A complete risk assessment report is added in **Appendix 2**, included in the confidential part of the PAR.

A field trial was conducted to monitor the effect of three iodine-based teat dips on milk iodine levels over a two week period. IodoFence and Tri-Fender were 2 of the products tested. Tri-Fender was applied either by dipping or manual spraying after each milking. The cows were milked 3x/day which is a worst-case situation for monitoring of residues. The highest levels were found in the Tri-Fender spray group, which had a mean milk iodine level of 177.7 ppb. However, mean milk iodine levels in the control group (non-iodine teat dip) where 148.4 ppb so it can be concluded that the contribution of Tri-Fender (applied by spraying), to the milk iodine levels was only about 29.21 ppb. The contribution of IodoFence to the milk iodine levels was only about 14.88 ppb in that same study.

It must also be noted that for the field study, milk iodine levels have been measured in raw milk samples. Several publications indicate that milk pasteurization results in an approximate reduction in the iodine concentration of at least 27% (EFSA, 2013, 11(2):3099). During discussions in the human health working group and WebEx meetings for eCA with iodine based union authorisations applications, the assumptions that could be considered for the exposure to residues via milk were discussed. Among other them the effect of pasteurisation. Reduction due to pasteurisation were considered not applicable for the risk assessment.

Note of eCA - dietary exposure is discussed in various human health working group meetings and WebEx meetings for eCA evaluating iodine based union authorisations application. The assumptions that could be considered for the exposure to residues via milk were that needs to be considered:

* Exposure in accordance to intended use (WGIII 2017). The submitted field trial is based on post-application use as included in the BPF.
* For exposure to residues the following was concluded by eCAs from iodine based union authorisation applications (Secure Webex meeting (3-10-2017)): “The expected iodine residues in milk from two milking events per day for manual milking and from three events per day for automatic milking are considered comparable”. For exposure of the residues the submitted field trial is used. For this field trial the cows were milked 3x/day which is a worst-case situation for monitoring of residues.
* 50% reduction due to bulking of milk is not allowed (WGII 2017).
* 27% reduction due to pasteurisation of the milk is not allowed. (WGII 2017)
* At WGIV 2017 it was agreed that for daily milk consumption to use 0.45 L/day for adults (EFSA PRIMo version 2, based on highest mean for Dutch populations) and 0.46 L/day for infant/toddlers (EFSA PRIMo version 2, based on highest mean for French population).
* For exposure of the residues the submitted field trial is used. For this field trial the cows were milked 3x/day and resulted in 183 µg iodine L in milk of the control animals which were treated with an non-iodine based teat disinfectant and in maximally 258 µg iodine L in milk in animals treated with an iodine based teat disinfectant (0.25% available iodine applied by spraying; Tri-Fender). Therefore, for the addition of iodine due to teat disinfection 258-183 = 75 µg iodine L in milk is taken into account for the dietary exposure calculation. This information can be found in Table 3 of the pdf document included in the confidential annex, section dietary exposure. More specific information on the trial is included in the document entitled annex 2 (confidential annex, section dietary exposure).
* The inclusion from other sources in the consumer risk assessment was discussed at WGIV, and the following was concluded:

Iodine exposure from all sources will be included in the assessment.

The assessment will include exposure to iodine coming from:

1. Teat treatment

2. Teat treatment + background from milk (= total milk intake)

3. Teat treatment + background from milk + dietary intake from other sources (= total dietary intake)

* Background in milk is variable due to differences in iodine concentrations in natural sources (drinking water and grass) and due to feed (supplemented with various amounts of iodine). The background was discussed in the Secure Webex meeting (3-10-2017), in which was concluded by eCAs from iodine based union authorisation applications: “General support was given to the derivation of an EU harmonised value. The value of 200 µg/L iodine in milk was considered appropriate as an EU harmonised value, based on the monitoring data from EFSA 2013 (EFSA Journal 2013;11(2):3101) and the O’Brien study.”
* Iodine dietary intake from other sources than milk was also discussed in the Secure WebEx meeting (3-10-2017), in which was concluded by eCAs from iodine based union authorisation applications: “The values from the UK survey were considered adequate to represent the EU iodine dietary intake from sources other than milk. Rounding of the values to 185 µg/day for adults and 96 µg/day for toddler was agreed.” It should be noted that these values excluded iodine intake from milk. Furthermore, within this UK study (UK retail survey of iodine in UK produced dairy foods, FSIS 02/08, 16 June 2008) 350 samples of dairy and seaweed products were purchased from eight areas of the UK. Levels of iodine found were generally in similar ranges to those reported from previous surveys (MAFF iodine in milk), Furthermore the reported values are in agreement with an EFSA scientific opinion on the use of iodine in feeding stuffs. It is noted that in the UK study report for the calculations for body weights 76 for adults and 14.5 kg for infants are considered, whereas 70 kg and 12 kg are used in the consumption calculations. Moreover, during the discussion at the Secure WebEx meeting it was noted that comparable values could be obtained from French and German monitoring studies.

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 depicted in the table below. Intakes which exceed the respective UL are highlighted in red in the table below. Calculations are included in annex 3.2 (DeLaval residues).

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.

**Comparison of estimated daily iodine intakes compared to upper limit of post-milking teat-disinfection**

|  |  |  |
| --- | --- | --- |
|  | **Adults (0.45 L/day)** | **Infants (0.46 L/day)** |
|  | **Estimated daily intake (µg/day)**  **[% ofUL]** | **Estimated daily intake (µg/day)**  **[% ofUL]** |
| **3x post-milking teat-disinfection by manual spraying using a trigger sprayer (based on 0.25% available iodine)** | | |
| **Intake from milk due to teat treatment** | 34  6 | 35  17 |
| **Total milk intake\*** | 124  21 | 127  63 |
| **Total dietary intake\*\*** | 309  51 | 223  111 |

\* Total milk intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based on the submitted field trial) and the background milk value of 200 µg/L (EFSA 2013)

\*\* Total dietary intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based on the submitted field trial), the background milk value of 200 µg/L (EFSA 2013) and 185 µg/d for adult or 96 µg/d for infant based on UK data (2008).

**Conclusion: Post-milking teat-disinfection**

For adults, the estimated daily intake of iodine resulting from biocidal product use is maximally 6% of the UL. When background values for iodine in milk is added, the iodine intake from milk consumption is maximally 21% of the UL. Finally, a total dietary intake of iodine resulting from milk consumption and from other dietary sources lead to maximally 51% of the UL.

For infants, the estimated daily intake of iodine resulting from biocidal product use is maximally 17% of the UL. When background values for iodine in milk is added, the iodine intake from milk consumption is maximally 63% of the UL. Finally, a total dietary intake of iodine resulting from milk consumption and from other dietary sources lead to maximally 111% of the UL.

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

Not applicable: products are not intended for non-professional use.

***Summary of exposure assessment***

In the summary table below only the values for the worst-case product for each scenario is represented which is Blockade – RTU for scenario 1, 3 and 5 (Note: for scenario 2, exposure is assumed to be covered by scenario 1; for scenario 4 exposure is considered negligible).

| **Scenarios and values to be used in risk assessment** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Exposed group**  **(e.g. professionals, non-professionals, bystanders)** | **Tier/PPE** | **Estimated total uptake**  **(mg/kg bw/d)** |
| 1. mixing and loading - RTU | Professionals | Tier 1 / no PPE | 1.72E-03 |
|  |  | Tier 2 / gloves | 1.72E-04 |
| 2.1 application by manual dipping | Professionals | Exposure is considered covered by the mixing and loading scenario. | |
| 2.2 application by automated dipping | Professionals | No exposure of professionals occurs during automated dipping. | |
| 3. 1application by manual spraying | Professionals | Tier 1 / no PPE | 1.12E-02 |
|  |  | Tier 2 / gloves | 3.56E-03 |
| 3.2 application by automated spraying | Professionals | No exposure of professionals occurs during automated spraying. | |
| 5. | Professionals | Tier 1 / no PPE | 3.96E-05 |
|  |  | Tier 2 / gloves | 3.96E-06 |

| **Summary table: combined systemic exposure from professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Estimated inhalation uptake (mg/kg bw/d)** | **Estimated dermal uptake (mg/kg bw/d)** | **Estimated oral uptake (mg/kg bw/d)** | **Estimated total uptake (mg/kg bw/d)** |
| **Manual teat dip application**  Scenarios 1.2 + 2.1 + 4 + 5 for, Tier 1 (no PPE) | n.a | 1.76E-03 | n.a | 1.76E-03 |
| **Manual teat dip application**  Scenarios 1.2 + 2.1 + 4 + 5 for manual teat dip application, Tier 2 (gloves) | n.a | 1.76E-04 | n.a | 1.76E-04 |
| **Manual spraying using a trigger sprayer or automated sprayer**  Scenarios 1.2+3.1 + 4 + 5 for, Tier 1 (no PPE) | 4.29E-04 | 1.26E-02 | n.a | 1.30E-02 |
| **Manual spraying using a trigger sprayer or automated sprayer**  Scenarios 1.2+3.1 + 4 + 5 for manual teat spray application, Tier 2 (gloves) | 4.29E-04 | 3.31-03 | n.a | 3.73E-03 |

#### Risk characterisation for human health

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

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF** | **Correction for oral absorption** | **Value** |
| AELshort-term | Not derived in the CAR and not relevant for HHRA. | | | | |
| AELmedium-term | Not derived in the CAR and not relevant for HHRA. | | | | |
| AELlong-term = Upper Intake Level (UL) | Human data |  |  |  | Adult: 600 µg/day  (0.01 mg/kg bw/d)  Toddler: 200 µg/day |
| ARfD | According to CAR, not applicable. Substance is not acute toxic or harmful. | | | | |
| ADI | Not derived in the CAR and not relevant for HHRA. Instead of an ADI, a Recommended daily intake of 150-200 µg/day is given in the CAR. | | | | |
| AEC = OEL (Occupational exposure limit) | Human data |  |  |  | 0.1 ppm / 1 mg/m3 |

**Maximum residue limits or equivalent**

Since the direct treatments of cows with iodine-containing veterinary hygiene products may lead to residues in milk, the need to set new maximum residue limits (MRLs) should be investigated according to the “Proposed decision for Iodine” of 31 January 2014. However, it should be acknowledged that iodine-based teat dips and sprays have a long history as veterinary medicines for the prevention of mastitis all over Europe and worldwide and that veterinary and biocidal uses are quite similar (if not identical) with respect to application frequency, iodine use concentration and product composition. The European Agency for the Evaluation of Medicinal Products (EMA) concluded in their summary report on iodine that it would be inappropriate to elaborate maximum residue levels (MRLs) for iodine. Therefore, iodine was included in Annex II of Council Regulation (EEC) 2377/90 (now repealed by Regulation (EC) No 470/2009) comprising the list of substances not subject to maximum residue limits. Commission Regulation (EU) No 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin lists iodine (including inorganic compounds) in Table 1 “Allowed substances” of the Annex with a “no MRL required” entry for all food producing species and all target tissues (including milk).

***Risk for industrial users***

Not applicable, no exposure of industrial users is foreseen.

***Risk for professional users***

**Systemic effects**

Intakes which exceed the UL are highlighted in red in the table below.

| **Task/**  **Scenario** | **Tier/**  **PPE** | **Estimated total uptake**  **(mg/kg bw/d)** | | **% UL (0.01 mg/kg bw/day) due to biocidal use** | **% UL (0.01 mg/kg bw/day) due to biocidal use + iodine from milk due to teat treatment1** | **% UL (0.01 mg/kg bw/day) due to biocidal use + total milk intake2** | **% UL (0.01 mg/kg bw/day) due to biocidal use + total dietary intake3** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Mixing and loading of concentrate – scenario 1.1 | 1/  none | 2.06E-04 | | 2 | 8 | 23 | 54 |
| 2/  Gloves | 2.06E -05 | | 0 | 6 | 21 | 52 |
| Mixing and loading of RTU – scenario 1.2 | 1/  none | 1.72E-03 | | 17 | 23 | 38 | 69 |
| 2/  Gloves | 1.72E-04 | | 2 | 7 | 22 | 53 |
| Application of teat disinfectant by manual dipping– scenario 2.1 | Exposure is considered covered by the mixing and loading scenario. | | | | | | |
| Application by automated dipping –  Scenario 2.2 | No exposure of professionals occurs during automated dipping. | | | | | | |
| Application of teat disinfectant by manual spraying – scenario 3.1 | 1/  none | | 1.12E-02 | 112 | 118 | 133 | 164 |
| 2/  Gloves | | 3.56E-03 | 36 | 41 | 56 | 87 |
| Application of teat disinfectant by automated spraying – scenario 3.2 | No exposure of professionals occurs during automated spraying. | | | | | | |
| Cleaning of teats by wiping with cloth (removal of dried product) – scenario 4 | Exposure of professionals considered to be negligible. | | | | | | |
| Cleaning of equipment – scenario 5 | 1/  none | 3.96E-05 | | 0 | 6 | 21 | 52 |
| 2/  Gloves | 3.96E-06 | | 0 | 6 | 21 | 51 |

1 as worst case, maximal values derived from post-application field trial are included.

2 Total milk intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based the submitted field trial) and the background milk value of 200 µg/L (EFSA 2013)

3 Total dietary intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based the submitted field trial), the background milk value of 200 µg/L (EFSA 2013) and 185 µg/d for adult or 96 µg/d for toddler based on UK data (2008).

Calculation sheet is included in annex 3.2.

**Local effects**

No AELdermal is available for iodine but local effects of Dipal Conc (or any of the other products within this product family) are not expected since skin irritation studies (OECD 404) have shown that the product is not classified as irritant or corrosive by dermal application.

For inhalation, no risk for local effects was found. The local inhalation exposure to Blockade (GMP 44) (worst-case) during application by spraying was well below the AECinh (1 mg/m3) for iodine (calculations available in **Annex 3.2**).

However, due to the classification as H319 of the products in Meta SPC 4-5(Dipal Conc (GMP 48) and Dipal Plus (GMP 36)), P280; wear eye/face protection is included in the label.

| **Task/**  **Scenario** | **Iodine in air inhaled (mg/m³)** | **% OEL (1 mg/m³)** | **Acceptable**  **(yes/no)** |
| --- | --- | --- | --- |
| [3] – Application of teat disinfectant by spraying | 4.52E -02 | 5 | yes |

**Combined scenarios**

Two possible combined exposure scenarios are represented starting from the ready-to-use product (Tri-Fender, GMP 51) as this is the worst-case product, leading to the highest exposure for all scenario’s.

Intakes which exceed the UL are highlighted in red in the table below.

| **Scenarios combined** | **Tier / PPE** | **Estimated uptake**  **mg/kg bw/d** | **% UL (0.01 mg/kg bw/day) due to biocidal use** | **% UL (0.01 mg/kg bw/day) due to biocidal use + iodine from milk due to teat treatment1** | **% UL (0.01 mg/kg bw/day) due to biocidal use + total milk intake2** | **% UL (0.01 mg/kg bw/day) due to biocidal use + total dietary intake3** |
| --- | --- | --- | --- | --- | --- | --- |
| **Manual dipping –** Scenarios 1.2 + 2.1 + 4 + 5 | 1/  none | 1.76E-03 | 18 | 23 | 38 | 69 |
| 2/  gloves | 1.76E-04 | 2 | 7 | 22 | 53 |
| **Manual spraying –** Scenarios 1.2 + 3.1 + 4 + 5 | 1/  none | 1.30E-02 | 130 | 136 | 151 | 181 |
| 2/  gloves | 3.73E-03 | 37 | 43 | 58 | 89 |
| **Automated dipping/spraying –** Scenarios 1.2 + 2.2/3.2 + 4 + 5 | 1/  none | 1.72E-03 | 17 | 23 | 38 | 69 |
| 2/  gloves | 1.72E-04 | 2 | 7 | 22 | 53 |

1 as worst case, maximal values derived from post-application field trial are included.

2 Total milk intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based the submitted field trial) and the background milk value of 200 µg/L (EFSA 2013)

3 Total dietary intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based the submitted field trial), the background milk value of 200 µg/L (EFSA 2013) and 185 µg/d for adult or 96 µg/d for toddler based on UK data (2008).

Calculation sheet, which also includes the combined scenario for concentrates, is included in annex 3.2.

It is noted that the combined assessment when using a concentrate would lead to the same conclusions as for using RTUs (see annex 3.2 Delaval combined prof exposure including residues). Therefore the conclusion below, based on the RTU assessment also covers the assessment for the concentrate.

**Conclusions Post-milking application**

**Assessment according to HEAdhoc Recommendation no. 13 (Jan. 2017), and taken into account iodine from other dietary sources (WG agreement WGIV 2017):**

Tier 1:

When using the RTU product (**exposure from biocidal use,** without considering PPE (Tier 1) results in 18% of the UL for manual dipping, 130% of the UL for manual spraying, and 17% of the UL for automated dipping/spraying.

**Exposure from biocidal use, including iodine from milk consumption due to teat treatment**, without considering PPE (Tier 1) results in 23% of the UL for manual dipping, 136% of the UL for manual spraying, and 23% of the UL for automated dipping/spraying.

**Exposure from biocidal use, including iodine from milk consumption**, without considering PPE (Tier 1) results in 38% of the UL for manual dipping, 151% of the UL for manual spraying and 38% of the UL for automated dipping/spraying.

**Exposure from biocidal use, including iodine from milk consumption and iodine from other dietary sources**, without considering PPE (Tier 1) results in 69% of the UL for manual dipping, 181% of the UL for manual spraying, and 69% of the UL for automated dipping/spraying.

Tier 2:

When using the RTU product (**exposure from biocidal use,** considering PPE (Tier 2: gloves) results in 2% of the UL for manual dipping, 37% of the UL for manual spraying, and 2% of the UL for automated dipping/spraying.

**Exposure from biocidal use, including iodine from milk consumption due to teat treatment**, considering PPE (Tier 2: gloves) results in 7% of the UL for manual dipping, 43% of the UL for manual spraying, and 7% of the UL for automated dipping/spraying.

**Exposure from biocidal use, including iodine from milk consumption**, considering PPE (Tier 2: gloves) results in 22% of the UL for manual dipping, 58% of the UL for manual spraying, and 22% of the UL for automated dipping/spraying.

**Exposure from biocidal use, including iodine from milk consumption and iodine from other dietary sources**, considering PPE (Tier 2: gloves) results in 53% of the UL for manual dipping, 89% of the UL for manual spraying, and 53% of the UL for automated dipping/spraying.

Furthermore, the OEL of 1 mg/m³ for iodine is not reached in the application scenario “Application of teat disinfectant by spraying using a trigger sprayer”. The maximum value was 5 % of the OEL.

**Overall conclusions post-milking application:**

metaSPC1, 2, 3, 6 and 7:

For manual dip applications and automated dipping/spraying, no PPE is needed for safe use.

For manual spray applications, chemical resistant gloves (90% protection) are needed for safe use.

metaSPC 4 and 5:

For manual dip applications and automated dipping/spraying, wear eye face protection.

For manual spray applications, chemical resistant gloves (90% protection) and eye face protection are needed for safe use.

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

Not applicable, no exposure of non-professional users is foreseen.

***Risk for the general public***

Not applicable, no exposure of the general public is foreseen.

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

**Note regarding need to set MRLs:** Since the direct treatments of cows with iodine-containing veterinary hygiene products may lead to residues in milk, the need to set new maximum residue limits (MRLs) should be investigated according to the “Proposed decision for Iodine” of 31 January 2014. However, it should be acknowledged that iodine-based teat dips and sprays have a long history as veterinary medicines for the prevention of mastitis all over Europe and worldwide and that veterinary and biocidal uses are quite similar (if not identical) with respect to application frequency, iodine use concentration and product composition. The European Agency for the Evaluation of Medicinal Products (EMA) concluded in their summary report on iodine that it would be inappropriate to elaborate maximum residue levels (MRLs) for iodine. Therefore, iodine was included in Annex II of Council Regulation (EEC) 2377/90 (now repealed by Regulation (EC) No 470/2009) comprising the list of substances not subject to maximum residue limits. Commission Regulation (EU) No 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin lists iodine (including inorganic compounds) in Table 1 “Allowed substances” of the Annex with a “no MRL required” entry for all food producing species and all target tissues (including milk).

**Dietary Risk Assessment**

Iodine-based post-milking teat dip solutions are used worldwide for the disinfection of lactating animals’ teats in order to reduce contamination with mastitis pathogens between cows or from the environment. The iodine level of these products may vary greatly, between 1000 and 10000 ppm iodine (the iodine level of DeLaval teat disinfectants is between 1500 - 2500 ppm available iodine). The level of iodine residues in milk from the use of these products was assessed to address any potential issues related to elevated residue levels in milk, with special emphasis on the risk assessment for milk consumption by children. A complete risk assessment report is added in **Appendix 2**, included in the confidential part of the PAR.

A field trial was conducted to monitor the effect of three iodine-based teat dips on milk iodine levels over a two week period. IodoFence and Tri-Fender were 2 of the products tested. Tri-Fender was applied either by dipping or manual spraying after each milking. The cows were milked 3x/day which is a worst-case situation for monitoring of residues. The highest levels were found in the Tri-Fender spray group, which had a mean milk iodine level of 177.7 ppb. However, mean milk iodine levels in the control group (non-iodine teat dip) where 148.4 ppb so it can be concluded that the contribution of Tri-Fender (applied by spraying), to the milk iodine levels was only about 29.21 ppb. The contribution of IodoFence to the milk iodine levels was only about 14.88 ppb in that same study.

It must also be noted that for the field study, milk iodine levels have been measured in raw milk samples. Several publications indicate that milk pasteurization results in an approximate reduction in the iodine concentration of at least 27% (EFSA, 2013, 11(2):3099). During discussions in the human health working group and WebEx meetings for eCA with iodine based union authorisations applications, the assumptions that could be considered for the exposure to residues via milk were discussed. Among other them the effect of pasteurisation. Reduction due to pasteurisation were considered not applicable for the risk assessment.

Note of eCA - dietary exposure is discussed in various human health working group meetings and WebEx meetings for eCA evaluating iodine based union authorisations application. The assumptions that could be considered for the exposure to residues via milk were that needs to be considered:

* Exposure in accordance to intended use (WGIII 2017). The submitted field trial is based on post-application use as included in the BPF.
* For exposure to residues the following was concluded by eCAs from iodine based union authorisation applications (Secure Webex meeting (3-10-2017)): “The expected iodine residues in milk from two milking events per day for manual milking and from three events per day for automatic milking are considered comparable”. For exposure of the residues the submitted field trial is used. For this field trial the cows were milked 3x/day which is a worst-case situation for monitoring of residues.
* 50% reduction due to bulking of milk is not allowed (WGII 2017).
* 27% reduction due to pasteurisation of the milk is not allowed. (WGII 2017)
* At WGIV 2017 it was agreed that for daily milk consumption to use 0.45 L/day for adults (EFSA PRIMo version 2, based on highest mean for Dutch populations) and 0.46 L/day for infant/toddlers (EFSA PRIMo version 2, based on highest mean for French population).
* For exposure of the residues the submitted field trial is used. For this field trial the cows were milked 3x/day and resulted in 183 µg iodine L in milk of the control animals which were treated with an non-iodine based teat disinfectant and in maximally 258 µg iodine L in milk in animals treated with an iodine based teat disinfectant (0.25% available iodine applied by spraying; Tri-Fender). Therefore, for the addition of iodine due to teat disinfection 258-183 = 75 µg iodine L in milk is taken into account for the dietary exposure calculation. This information can be found in Table 3 of the pdf document included in the confidential annex, section dietary exposure. More specific information on the trial is included in the document entitled annex 2 (confidential annex, section dietary exposure).
* The inclusion from other sources in the consumer risk assessment was discussed at WGIV, and the following was concluded:

Iodine exposure from all sources will be included in the assessment.

The assessment will include exposure to iodine coming from:

1. Teat treatment

2. Teat treatment + background from milk (= total milk intake)

3. Teat treatment + background from milk + dietary intake from other sources (= total dietary intake)

* Background in milk is variable due to differences in iodine concentrations in natural sources (drinking water and grass) and due to feed (supplemented with various amounts of iodine). The background was discussed in the Secure Webex meeting (3-10-2017), in which was concluded by eCAs from iodine based union authorisation applications: “General support was given to the derivation of an EU harmonised value. The value of 200 µg/L iodine in milk was considered appropriate as an EU harmonised value, based on the monitoring data from EFSA 2013 (EFSA Journal 2013;11(2):3101) and the O’Brien study.”
* Iodine dietary intake from other sources than milk was also discussed in the Secure WebEx meeting (3-10-2017), in which was concluded by eCAs from iodine based union authorisation applications: “The values from the UK survey were considered adequate to represent the EU iodine dietary intake from sources other than milk. Rounding of the values to 185 µg/day for adults and 96 µg/day for toddler was agreed.” It should be noted that these values excluded iodine intake from milk. Furthermore, within this UK study (UK retail survey of iodine in UK produced dairy foods, FSIS 02/08, 16 June 2008) 350 samples of dairy and seaweed products were purchased from eight areas of the UK. Levels of iodine found were generally in similar ranges to those reported from previous surveys (MAFF iodine in milk), Furthermore the reported values are in agreement with an EFSA scientific opinion on the use of iodine in feeding stuffs. It is noted that in the UK study report for the calculations for body weights 76 for adults and 14.5 kg for infants are considered, whereas 70 kg and 12 kg are used in the consumption calculations. Moreover, during the discussion at the Secure WebEx meeting it was noted that comparable values could be obtained from French and German monitoring studies.

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 depicted in the table below. Intakes which exceed the respective UL are highlighted in red in the table below. Calculations are included in annex 3.2 (DeLaval residues).

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.

**Comparison of estimated daily iodine intakes compared to upper limit of post-milking teat-disinfection**

|  |  |  |
| --- | --- | --- |
|  | **Adults (0.45 L/day)** | **Infants (0.46 L/day)** |
|  | **Estimated daily intake (µg/day)**  **[% ofUL]** | **Estimated daily intake (µg/day)**  **[% ofUL]** |
| **3x post-milking teat-disinfection by manual spraying using a trigger sprayer (based on 0.25% available iodine)** | | |
| **Intake from milk due to teat treatment** | 34  6 | 35  17 |
| **Total milk intake\*** | 124  21 | 127  63 |
| **Total dietary intake\*\*** | 309  51 | 223  111 |

\* Total milk intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based on the submitted field trial) and the background milk value of 200 µg/L (EFSA 2013)

\*\* Total dietary intake is the sum of the estimated additional intake resulting from the transfer into milk following teat disinfection (based the submitted field trial ), the background milk value of 200 µg/L (EFSA 2013) and 185 µg/d for adult or 96 µg/d for infant based on UK data (2008).

**Conclusion: Post-milking teat-disinfection**

For adults, the estimated daily intake of iodine resulting from biocidal product use is maximally 6% of the UL. When background values for iodine in milk is added, the iodine intake from milk consumption is maximally 21% of the UL. Finally, a total dietary intake of iodine resulting from milk consumption and from other dietary sources lead to maximally 51% of the UL.

For infants, the estimated daily intake of iodine resulting from biocidal product use is maximally 17% of the UL. When background values for iodine in milk is added, the iodine intake from milk consumption is maximally 63% of the UL. Finally, a total dietary intake of iodine resulting from milk consumption and from other dietary sources lead to maximally 111% of the UL.

The UL for toddlers is (i.e. 111%) exceeded when taken into account teat disinfection and dietary intake.

Exposure to iodine via drinking water was not taken into account in the risk assessment. The use of the iodine teat treatments could potentially contribute to the levels found in groundwater. As part of the environmental risk assessment PEC have been estimated. However, the main issue with these estimated PEC is that they are significant over estimates as they are done as a porewater calculation so do not account for any means of dissipation at all i.e. binding to organic matter, plant uptake, lateral transfer. In addition, assuming that 100 % drinking water comes from groundwater could be an overestimate; the proportion of drinking water that is sourced from groundwater sources varies from region to region.

With no agreed background levels of iodine in water, no agreed proportion of water sourced as groundwater and with significantly overestimated PEC values for the iodine teat treatment uses then at this time a consumer risk assessment including water would be subject to a high level of uncertainty. However, this issue should be a part of the consideration by MS/ECHA/EFSA in obtaining more reliable information on the sources of iodine in the diet.

The consumer exposure evaluation shows exceedance of the UL for toddlers, however this is not a new issue. The ‘UK retail survey of iodine in UK product dairy foods’ (please note that this reference is also used for total dietary intake calculations) noted exceedances of the PMTDI (Provisional Maximum Tolerable Daily Intake = 0.017 mg/kg bodyweight/day). It was however noted that these exceedances result from worst case exposure scenarios and the occasional exceedance of the PMTDI would not be of concern.

Another notable example of exceedance of the UL was reported in an EFSA scientific opinion of the safety and efficacy of iodine compounds (2013). Please note that this report included the reference used for the background value for milk used in the residue calculations. In this paper it was stated that: ‘The iodine content of food of animal origin, if produced from animals receiving the currently authorised maximum contents of total iodine in complete feed for dairy cows and laying hens (5 mg/kg), would represent a substantial risk to consumers, mainly for high-consuming (95th percentile) adults and toddlers. The risk would originate primarily from the consumption of milk and, to some extent, from consumption of eggs. The ULs would for adults be exceeded by a factor of 2 (1230 vs. 600 μg I/day), and for toddlers by a factor of 4 (840 vs. 200 μg I/day).’ As a result of these exceedances the FEEDAP Panel recommended a reduction in the currently authorised maximum iodine contents in complete feed. The recommended reduced supplementation of 2 mg/kg would still result in an exceedance for the toddler (320 vs. 200 μg I/day).

Iodine can be consumed from many different sources, however in many countries, also the Netherlands, the natural iodine levels in the diet are insufficient to meet the requirements. Therefore, international and national legislation and guidelines exist to improve the iodine intake by e.g. addition of iodine to food or salt (e.g. the Netherlands) or advice to use iodine containing dietary supplements. Other EU countries (e.g. UK, Czech Republic) regulate adequate iodine intake through addition of iodine to cattle feed, which subsequently leads to increased iodine levels in milk, eggs and animal tissues (meat, fat, edible offal). Although it is recognised that both insufficient and excessive iodine intakes can cause diseases, it is generally considered that the benefits of the prevention of diseases from iodine deficiency far outweighs possible side-effects of oversupply.

Relevant sources of iodine outside the scope of the BPR are:

1. Feed supplementation
2. Food and salt supplementation
3. Dietary supplements

The risk assessment performed could be considered worst case/conservative, based on the following

1. For background in milk we have used a value of 200 µg/L based reported total levels in milk from monitoring data (100-200 µg/L, EFSA 2013). Using the higher value, consider to take into account the EU variation. However, as the higher value is used, and this value also take into account the effect of teat disinfection, the resulting milk intake from the assessment is considered worst case, as for the assessment the additional milk intake due to teat disinfection is also taken into account separately. It is noted that the background value in the provided trial study is within range as reported by EFSA 2013, i.e. 148 µg/L)
2. The UL used is based on the limit values in the CAR were taken from/in line with the report of The Scientific Committee on Food (SCF). SCF based the iodine tolerable upper intake (UL) on studies in humans (male/female). The studies showed an increased serum thyroid-stimulating hormone (TSH) level in response to iodine intake and an enhanced response of TSH concentrations to thyrotropin-releasing hormone (TRH) at 1700-1800 μg/day. However, these changes were considered marginal and not associated with any clinical adverse effects. An uncertainty factor of 3 was selected to derive the UL for adults. For nutrients, an UF of 3 is a relatively high uncertainty factor, and therefore the derived UL is considered conservative. An additional factor of 3 was used to derive an UL for toddlers of 200 μg/day, which is standard approach to compensate differences between adults and children. Exceedance of the UL was discussed in various WG meetings. It was acknowledged that the value itself could be considered conservative, taken in mind that the value based on marginal effects and taken in mind that WHO derived a value of 1000 μg/day. However, no agreement was reached what would be considered acceptable for exceedance, and also there was no support to change the limit value at this stage. Therefore, the limit value should be considered during active substance renewal.
3. Furthermore, it is noted that the estimated intakes are based on worst case theoretical levels of iodine in milk from a short term study. The intakes are compared to the UL, which is derived for chronic exposure. Furthermore, it is noted that SCF (from which the UL for adult and toddler are included in the CAR for iodine) also reports adapted UL values for older children. Taken this in consideration, as the estimated residue levels of iodine in milk are based on worst case assessments and the data are based on short term consumption studies, the intakes seen in reality may not be of concern if the lifelong exposures of varying sources of food and levels were considered.

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 cattle, iodine supplementation programs and other factors. The iodine intake that can be attributed to the use of iodine-containing teat disinfectants is only a minor part of the total iodine intake. Exceedances of the UL are reported when worst case consumption values are used in the human health risk assessment, but these exceedances can for the larger part be attributed to the iodine intakes arising from background levels. The additional burden arising from teat disinfection is considered of no significant impact. To ensure that the population's needs are met and not exceeded, a wider approach encompassing different regulatory regimes would need to be considered. Such a task can’t be handled in the context of the Biocidal Product Regulation alone, but requires an integrated concept.

Considering the above, we consider the exceedance of the UL for toddlers (i.e. 111%) taking into account teat disinfection and dietary intake acceptable.

***Risk characterisation from combined exposure to several active substances or substances of concern within a biocidal product***

Not applicable, no combined exposure.

### Risk assessment for animal health

There is no risk expected for the treated animal.

First, as already concluded in 2.2.6.1 (Assessment of effects on human health), the products within Meta SPC 1-3 of this product family are not classified as dangerous. Products included in metaSPC4 and 5 are classified for irritating effect on the eyes (H319). As the product will be applied to the teats of the udder, no exposure of the eyes of the animal is envisaged. Subsequently, no adverse effects due to local effects are expected for the animal due to the use of products included in the BPF.

Second, iodine-based teat-disinfection products have a long history as safe veterinary hygiene and medicinal products. To demonstrate the safety of the iodine based teat disinfectants, pharmacovigilance data for 4 products are provided in the application file. These data are available because some of the products of the product family are also registered as veterinary medicines in some EU countries. The method of application and frequency are the same as for the biocidal use. Periodic safety update reports for these products have to be submitted at defined timepoints during the post-authorisation phase by the marketing authorisation holder. These pharmacovigilance documents intend to provide a safety update to be able to evaluate the impact on the risk-benefit balance of a medicinal product.

PSUR Summary Bridging Report: Blockade 0.25% w/w iodine teat dip solution.

PSUR Summary Bridging Report: Proactive 0.15% w/w Teat Dip/Spray Solution.

PSUR Summary Bridging Report: Proactive Plus, tepeldip oplossing.

PSUR Summary Bridging Report: Dipal Conc 0.75% concentraat voor speendip of -spray oplossing.

For none of the 4 products reports were received of serious and non-serious suspected adverse events or lack of efficacy during this period in any species, including human beings.

Third, according to the EMEA (European Agency for the Evaluation of Medicinal Products) summary report on iodine-containing products used for veterinary medicine, only small increases in serum iodine concentration have been found after teat dipping indicating that the procedure has a negligible effect on tissue iodine concentrations. These results suggest limited livestock exposure and no-detailed risk assessment was therefore performed for animal health. This is supported by the EFSA 2013 opinion on the safety and efficacy of iodine compounds (E2) as feed additives, in which it was concluded that the iodine level in edible tissues/products is generally found to be highest in milk and not in meat.

### Risk assessment for the environment

#### Effects assessment on the environment

The products contain only one substance that needs to be considered for environmental risk assessment: the active substance iodine. All other ingredients in the product family do not pose an environmental risk as these are not classified regarding the environment. Therefore, these co-formulants cannot be regarded as substances of concern and do not need to be assessed. Note that classification was based on the total iodine contents in the products including iodine from possible other sources. Iodine is currently classified as H400 (harmonised classification according to ATP00). Chronic classification was not considered in ATP00, but needs in accordance to the CLP-directive addressed in the classification and labelling. Data provided in the assessment report justify H410 based on a NOEC of 0.25 mg/L (*Daphnia magna*).

|  |  |  |  |
| --- | --- | --- | --- |
| **Environmental compartment** | | **Iodine species** | **PNEC** |
| **Aquatic, freshwater** | Surface water | Iodine (I2) | 0.59 µg/L |
| Iodate (IO3-) | 58.5 µg/L |
| Iodide (I-) | 0.83 µg/L |
| Freshwater sediment | - | not used in risk assessment |
| **Terrestrial** | | Iodine (I2) | 0.0118 mg/kgwwt |
| Iodate (IO3-) | 0.304 mg/kg |
| Iodide (I-) | 0.0043 mg/kg |
| **STP** | | Iodine (I2) | 2.9 mg/L |

Iodine is a natural occurring substances for which background values are available. These will be considered as well. The background levels are summarised below.

|  |  |
| --- | --- |
| **Background concentration of iodine in the environment  (CAR, 2011 on iodine)** | |
| **Compartment** | **natural background concentration** |
| Air | - |
| STP | - |
| Surface water | 0.5 – 20 µg iodine/L |
| Fresh water sediment | typically 6 mg iodine/kg |
| Sea water | 45 - 60 µg iodine/L |
| Marine sediment | 3 - 400 mg iodine/kg |
| Soil | 0.5 – 20 mg/kgdwt  with extremes up to 98 mg/kgdwt (corresponding to 0.4 - 18 mg iodine/kgwwt with extremes up to 86 mg/kgwwt) depending on soil types and locations. Highest concentrations are found in peaty soils (18.7-98.2 mg/kg dwt). Concentrations in sandy and clayey soils are respectively 1.7-5.4 mg/kg dwt and 2.1-8.9 mg/kg dwt (source DOCIIIA, 7.2.1/01-03 and references therein). |
| Groundwater | mean concentration: 1 µg/L  < 1-70 μg iodine/L (with extremes up to 400 μg/L) depending on geographical location and local geology. Higher concentrations can be found in saline waters such as coastal and arid areas (source DOCIIIA, 7.2.3.2 and references therein). |

***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***

Iodine, classified as Aquatic Acute 1, is the only active substance for the environment in the formulations of this product family. According to EC1272/2008, the M-factor for iodine is 1 (0.1< L(EC)50 ≤ 1) (table 4.1.3).

However, in absence of chronic data, iodine is classified as Chronic 1 (H410) with an M-factor of one. Products containing ≥0.25% total iodine must be according to EC1272/2008 classified as H412.

***Further Ecotoxicological studies***

Not applicable, no studies have been performed on the products. The iodine-based teat disinfectants in this product family are all aqueous solutions in which the active substance iodine is dissolved. The solutions also contain surfactants, pH regulators, emollients and solubilizers for iodine while the main ingredient is water. Within these formulations, iodine classified as Aquatic Acute 1 and Chronic 1, is the only substance of concern for the environment whereas the other ingredients do not bear such a classification. The amount of active substance present in the formulations can be completely recovered by quantitative analysis (no more and no less). This indicates that there is no enhancement or inhibition of the active substance within the formulation and that there are no chemical interactions between the active substance and other components of the formulations. It can be concluded that the ecotoxicological properties of iodine in the formulations can be extrapolated from data on iodine. So for this section we refer to the active substance dossier.

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

Not applicable, no studies have been performed on the products. The iodine-based teat disinfectants in this product family are all aqueous solutions in which the active substance iodine is dissolved. The solutions also contain surfactants, pH regulators, emollients and solubilizers for iodine while the main ingredient is water. Within these formulation, iodine classified as Aquatic Acute 1 and Chronic 1, is the only substance of concern for the environment whereas the other ingredients do not bear such a classification. The amount of active substance present in the formulations can be completely recovered by quantitative analysis (no more and no less). This indicates that there is no enhancement or inhibition of the active substance within the formulation and that there are no chemical interactions between the active substance and other components of the formulations. It can be concluded that the ecotoxicological properties of iodine in the formulation can be extrapolated from data on iodine. So for this section we refer to the active substance dossier.

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

Not applicable, the biocidal product is not in the form of baits or granules.

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

Not applicable, the biocidal product is not in the form of baits or granules.

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

Not applicable.

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

The products are intended for use as teat-disinfectants for dairy cows. They are applied by dipping or spraying to the teats of the animals before or after milking. Exposure to the environment is predominantly secondary, i.e. via liquid manure to soils or to surface water via the municipal sewer. Exposure to air during application is not relevant due to the low vapour pressure of the active substance.

When applying the products to the animal teats by spraying, spray may not reach the animal teats or part of the product applied to the teats may be lost by drip formation. Drip formation may also occur when the products are applied by dipping. In both cases losses are possible into the liquid manure (release pathway via manure spreading on grassland or arable land) or the sewer system (release pathway via STP). If applied post-milking, the products will only partly remain on the animal teats between two milking events. The part which simply falls off or is lost due to contact with the surfaces (e.g. when the cows lie down for rest) will finally end up in the liquid manure. The part remaining on the teats will be removed before the next milking by wiping with a dry cloth or a single paper towel. If disposable tissues are used, the product will end up in the waste bin. Residues are also released to the environment during cleaning of the applied equipment such as milking cups and reusable milking cloths. Considering that most farms are not connected to the municipal sewer, waste water is often released to the manure depot instead. If present, residues may be released to individual sewage treatment plants as well when equipment is for instance rinsed above sinks. In all other cases release to the municipal sewer and subsequently to a sewage treatment plant (STP) is likely.

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

Not applicable, no studies have been performed on the products. We refer to the active substance dossier for available data.

***Leaching behaviour (ADS)***

Not applicable, data not relevant for the veterinary health disinfectants.

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

Not applicable, no studies have been performed on the products. We refer to the active substance dossier for available data.

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

Not applicable, no studies have been performed on the products. We refer to the active substance dossier for available data.

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

Not applicable, no studies have been performed on the products. We refer to the active substance dossier for available data.

***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 applicable, products are not sprayed near surface waters.

***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 applicable, product is used indoors.

#### Exposure assessment

The biocidal product family concerns six uses:

1. Manual teat dip with ready to use products (metas 1-4, 6, and 7);
2. Manual teat spray with ready to use products (metas 1-4, 6, and 7);
3. Manual teat dip with concentrated products (meta 5);
4. Manual teat spray concentrated products (meta 5);
5. Automated teat dip or spray with ready to use products (metas 1-4, 6, and 7);
6. Automated teat dip or spray with concentrated products (meta 5);

The recommended dose is for all intended uses about 5 mL/cow, but field trails demonstrated that actual consumption may up to 7 mL when sprayed in milking robots (see elsewhere). The product is applied manually two times a day, but three times in milking robots. Uses #5 and #6 are therefore worst-case. Use #5 in meta-SPC 2 results in the highest total iodine consumption (0.376-0.433%) and consequently applied in the environmental risk assessment.

**General information**

|  |  |
| --- | --- |
| Assessed PT | PT 3 |
| Assessed scenarios | Manual teat spraying |
| ESD(s) used | Emission Scenario Document for Product Type 3: Veterinary hygiene biocidal products, JRC Scientific and Technical Reports, Report nr. EUR 25116 EN, Publications Office of the European Union, Luxembourg |
| Approach | Average consumption by applying the scenario for non-medical teat disinfection |
| Distribution in the environment | Reference to active substance dossier |
| Groundwater simulation | The calculation of the concentrations in groundwater was performed according to the approach described in the guidance Vol IV, part B where the concentration in pore water of agricultural soil is used as a first indication for groundwater concentrations. |
| Confidential Annexes | No |
| Life cycle steps assessed | Production: No  Formulation No  Use: Yes  Service life: No |
| Remarks | PECs for surface water were calculated according to the ESD for PT18 ‘stable disinfection’ in which emission to surface water is included. Subsequent sorption onto sediments as well as concentration in pore and groundwater were calculated according to the guidance. Where necessary a reference is made to the CAR for iodine. |

***Emission estimation***

**Scenario [1]**

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | |
| **Input** | **Value** | **Unit** | **Remarks** |
| Scenario:**Teat spraying** | | | |
| Concentration of active substance in the product | 4.33 | g/kg |  |
| Amount of product to be used for one treatment of one animal | 7 | mL | Results consumption test with Tri-Fender |
| Dilution factor | 1 |  | Ready-to-use |
| Daily applications | 3 | /day | Products are applied post-milking (default) |

No default values for the amount of product per treatment are specified in the ESD. Therefore, the applicant did a survey amongst their customers. Products (n=6) were weighed and subsequently delivered to 16 farms. After 15.5-21.5 days the remaining products were weighed again. Meanwhile the farmers recorded the number of disinfection events and how the product was applied. Farmers that applied the product by dipping applied between 2.9 and 4.7 g/cow. In case of spraying between 4.5 and 6.8 g/cow was applied. Milking robots consumed between 4.3 and 7.0 g/treatment. Note that the amount of product is not necessarily the amount that is applied on the cow’ teats as it includes spillage during mixing and filling as well as residual fluids. The highest value for spraying was subsequently applied in the exposure assessment.

Calculations

The applied values results in the following iodine releases to the environment.

| **Resulting local emission to relevant environmental compartments** | | |
| --- | --- | --- |
| **Compartment** | **Local emission (Elocalcompartment)** | **Remarks** |
| STP | 3.47E-03 kg/d | Daily emission to the sewer system |
| Soil | 0.198 kg (after one manure application)  0.790 kg (after four manure applications) | Amount of active ingredient in manure or slurry after the relevant number of biocide applications for the manure application to grassland.  Since the manure for grassland is applied four times per year, the amount after 1 manure application ( 0.198 kg) is multiplied with the factor of 4. The emission of 0.790 kg was used for the environmental risk assessment on grassland. |
| 0.790 kg | Amount of active ingredient in manure or slurry after the relevant number of biocide applications for the manure application to arable land. |

According to the ESD for PT3, the deposition of active substances onto agricultural land (grassland) by manure/ slurry is estimated on the basis of emission standards for nitrogen or phosphor. Depending on the amount of nitrogen or phosphor in manure and the type of soil to which it is applied, these emission standards define the maximum amount of manure/slurry that can be applied per hectare and per year. The concentration in soil after manure/slurry application at maximum permissible rate (170 kg N/ha for both grassland and arable land and 110 kg P/ha for grassland and 85 kg P/ha for arable land) is calculated using the equations as proposed in the ESD for PT3. Note that dairy cows produce three times more nitrogen than phosphor (0.3389 vs. 0.1047 kg/animal/d), while the nitrogen emission standards are about a factor of two higher. Consequently, the phosphate emission standards combined with the dairy’s cows phosphate production allows more manure per hectare and therefore higher PECs. Although the PECs based on the phosphate emission standards are worst-case, one should realise that the nitrogen emission standards are already exceeded. In other words, the nitrogen emission standards limit the emission to the environment for dairy cows. Therefore, only the predicted environmental concentrations (PECs) based on the nitrogen emission standards are presented in the current PAR.

Emission to the manure and STP is according to the Technical Agreements on Biocides (version 2.0, entry ENV-63) based on 82 lactating cows, but manure production on 100 cows.

According to the assessment report for iodine (I2), iodate (IO3-) may be considered to be the dominant chemical form of iodine in the soil solution under aerobic non-flooded soil conditions, while iodide (I-) appears mainly under anaerobic conditions. In surface water, however, both species may appear depending on the acidity (pH) and oxygen concentrations (redox) of the receiving fresh water body. In general iodate is the dominant species in oxygen rich water, while iodide is present in water low in oxygen contents. Predicted environmental concentrations were therefore calculated assuming no transformation (100% iodine) and 100% transformation into iodide or iodate. Limited information on the behaviour of iodate and iodide in environmental compartments is available. Therefore, the physical-chemical properties for iodine were applied to these two transformation products as well. PECs for iodate were derived by multiplying those for iodine with 1.382 (differences in molar weight).

The PEC’s as calculated with the ESD represent the concentration after one manure application on arable land and one on grassland (Predicted Initial Environmental Concentrations, PIEC). However, agricultural soils are fertilised repeatedly and iodine may consequently accumulate in soils after successive years of manure applications. Therefore, the concentrations presented in the current assessment report are the concentrations after ten years, i.e. ten manure applications on arable land and forty on grassland. Concentrations in soils after ten years were calculated according to the addendum for PT18 (insecticide in stables), although the no-manure time was increased from 206 to 365 days. This approach has been meanwhile accepted by the BPC working group (WG-I-2018).

Although iodine being an element 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 and the active substance’s physical-chemical parameters as presented elsewhere. 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).

PECs in adjacent surface water due to runoff was derived from the concentration in the soil’s pore water according to the principles described in the ESD for PT18, but concentrations were additionally corrected for sorption onto suspended matter. PECs where therefore calculated according to formula 45 of the guidance by using an experimentally derived solids-water partition coefficient in suspended matter (Kp, susp) of 220 L/kg and a dilution of ten. Although this approach may largely overestimate the concentration in surface water, higher tier models such as SWASH were not applied as these were considered inaccurate for inorganic compounds such as iodine. PECs for sediments were not calculated as no predicted no effect concentrations (PNECs) are available. Although PNECs may be calculated using equilibrium partitioning, the same formulas are applied to derive PECsediment. Therefore, the PEC:PNEC ratios and risk for sediment is similar to that for water.

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

Two different emission pathways are described in the ESD for PT3 (2011):

* Release via sewage treatment plant or
* Release into slurry/manure

Therefore, both emission pathways are considered in the environmental risk assessment. The compartments exposed are summarised below.

| **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 | yes | yes | yes | no | yes | yes | no |
| Via slurry/manure | yes | yes | no | no | no | no | yes | yes | no |

The active substance’s properties applied for the risk assessment are summarised below.

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters (only set values) for calculating the fate and distribution in the environment** | | | |
| Input | Value | Unit | Remarks |
| Molecular weight | 253 | g/mol | Source: ECHAa, molweight for iodine (I2) |
| Melting point | 113.6 | °C | Source: ECHA |
| Boiling point | 184.4 | °C | Source: ECHA |
| Vapour pressure | 1.0E-06 | Pa | Source: ECHA Although iodide (I2) may evaporate as the vapour pressure is 40.7 Pa, it cannot be expected that ionised iodine species are volatile. Therefore, emission to air was not considered. |
| Water solubility (at 25°C) | 300 | g/L | Source: ECHA  Value for the environmental relevant iodine species iodate and iodide. Solubility of iodine is 0.3 g/L. |
| Henry’s law constant | 4.05E-07 | Pa  m3/mol | calculated |
| Log Octanol/water partition coefficient | - |  | Inorganic substance |
| Solids-water partition coefficient in soil (Kd) | 5.8 | l/kg | Source: ECHA |
| Solids-water partition coefficient in sediment (Kp, sed)\_ | 200 | l/kg | Source: ECHA |
| Solids-water partition coefficient in suspended matter (Kp, susp)\_ | 220 | l/kg | Source: ECHA |
| Biodegradability | Not readily biodegradable | - | Inorganic substanceb |

a Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products. Evaluation of active substances. Assessment Report for Iodine (including PVP-iodine) product types 1, 3, 4, and 22. 13 December 2013,

b Iodine is an inorganic substance, which cannot biodegrade. Depending on whether aerobic or anaerobic conditions prevail, iodine is present in the environment either as iodide or iodate (see CAR for iodine).

Distribution in the sewage treatment plants was not calculated according SimpleTreat, but based on laboratory and field tests. The values applied in the risks assessment are summarised below.

|  |  |  |
| --- | --- | --- |
| **Calculated fate and distribution in the STP *[if STP is a relevant compartment]*** | | |
| Compartment | Percentage [%] | Remarks |
| Air | Not relevant | Source: ECHAa, based on laboratory and field experiments |
| Water | 80% |
| Sludge | 20% |
| Degraded in STP | Not applicable |

a Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products. Evaluation of active substances. Assessment Report for Iodine (including PVP-iodine) product types 1, 3, 4, and 22. 13 December 2013,

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

***Calculated PEC values***

The PECs resulting from disinfection of cow’s teats are presented below. Concentrations are calculated after ten years of successive manure and sewage applications. Emission via manure is based on nitrogen emission standards.

| **Summary table on calculated PEC values for iodine and iodide** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PECSTP** | **PECwater** | **PECsed** | **PECseawater** | **PECseased** | **PECsoil** | **PECGW** | **PECair** |
| [µg/l] | [µg/l] | [mg/kgwwt] | [µg/l] | [mg/kgwwt] | [mg/kgwwt] | [μg/l] | [mg/m3] |
| ***via STP*** | | | | | | | | |
|  | 1.39 | 1.38E-01 | 6.72E-03 | - | - | 8.62E-03 | 1.65 | -- |
| ***via slurry/manure – concentrations after ten years. Leaching from the top soil layer between two applications is considered.*** | | | | | | | | |
| grassland | -- | 1.14 | 5.55E-02 | -- | -- | 6.09E-02 | 11.5 | -- |
| arable land | -- | 0.693 | 3.38E-02 | -- | -- | 3.67E-02 | 6.981 | -- |

| **Summary table on calculated PEC values for iodate** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PECSTP\*** | **PECwater** | **PECsed** | **PECseawater** | **PECseased** | **PECsoil** | **PECGW1** | **PECair** |
| [µg/l] | [µg/l] | [mg/kgwwt] | [µg/l] | [mg/kgwwt] | [mg/kgwwt] | [μg/l] | [mg/m3] |
| ***via STP*** | | | | | | | | |
|  | - | 1.92 | 9.29E-03 | - | - | 1.19E-02 | 2.28 | -- |
| ***via slurry/manure – concentrations after ten years. Leaching from the top soil layer between two applications is considered.*** | | | | | | | | |
| grassland | -- | 1.58 | 7.67E-02 | -- | -- | 8.42E-02 | 15.8 | -- |
| arable land | -- | 9.62 | 4.68E-02 | -- | -- | 5.07E-02 | 9.65 | -- |

\* No PEC has been calculated as PNEC values are not available.

***Primary and secondary poisoning***

Primary poisoning

The direct exposure of birds or mammals (other than the treated animal) to the biocidal product is considered negligible since there is no direct release of the product in the environment. In addition, none of the products within the product family is classified for oral toxicity according to OECD 423 (see 2.3.5A) and the active substance iodine is an essential nutrient. Organisms may be therefore able to regulate internal concentrations within small boundaries by passive uptake or elimination.

Secondary poisoning

As iodine is an essential element, internal concentrations are expected to be regulated within small boundaries. Moreover, because iodine is not hydrophobic (log Kow < 3), passive uptake by partitioning to lipid and other hydrophobic phases is not expected. Therefore, accumulation and biomagnification in higher tropic levels cannot be expected.

#### Risk characterisation

***Atmosphere***

Exposure to air is not considered as iodine is assumed to speciate into non-volatile iodide and iodate in the different compartments it is released to. It cannot be expected that airborne iodine will significantly increase the already high background values in air (1.10E-2 to 2.10E-2 µg/m³, according to the CAR on iodine). There are no indications that iodine contributes to depletion of the ozone layer as iodine or organic-bound iodine are not listed as ‘controlled substance’ in Annex I of Regulation (EC) No 1005/2009 of the European Parliament.

***Sewage treatment plant (STP)***

The risk assessment for sewage treatment plants resulted in a PEC/PNEC ratio of <0.001 for iodine. Although no PNECs are available for iodate and iodide, it cannot be expected that these iodine species will results in unacceptable risks. As a rule of thumb, the aquatic and terrestrial PNECs for iodide are similar to iodine, and iodate is about 25-100 less toxic. Therefore, the risks ratios are expected to be <0.001 as well and the risks for the STP are considered acceptable. However, dairy farms are not necessarily connected to the municipal sewer and domestic waste water may be purified on-site by individual sewage treatment plants. Considering that these systems are small (a few cubic meters), high loads of iodine may kill the microbial population therein instantly, resulting in malfunctioning of the plant. Therefore, a precautionary measure stating that residues must be discharged to the (liquid) manure depot or municipal sewer will be added to the SPC.

***Aquatic compartment***

The risk evaluation (PEC:PNEC ratios) for the aquatic compartment when residues are released to the STP or due to runoff from fertilised agricultural land is presented below. The risk ratios for sediment are not presented in the PAR. Because both PEC and PNEC are derived from the aqueous concentrations, risks ratios for sediment will be similar to water. The PECs in sediment will be therefore only compared to the background values.

| **Summary table on calculated PEC/PNEC values for iodine** | | |
| --- | --- | --- |
|  | **PEC/PNECwater** | **PEC/PNECsed** |
| ***via STP*** | | |
|  | 0.0.234 | 0.234 |
| ***via slurry/manure – PEC:PNEC ratios after ten years. Leaching from the top soil layer between two applications is considered.*** | | |
| grassland | 1.93 | 1.93 |
| arable land | 1.18 | 1.18 |

| **Summary table on calculated PEC/PNEC values for iodide** | | |
| --- | --- | --- |
|  | **PEC/PNECwater** | **PEC/PNECsed** |
| ***via STP*** | | |
|  | 0.167 | 0.167 |
| ***via slurry/manure – PEC:PNEC ratios after ten years. Leaching from the top soil layer between two applications is considered.*** | | |
| grassland | 1.38 | 1.38 |
| arable land | 0.839 | 0.839 |

| **Summary table on calculated PEC/PNEC values for iodate** | | |
| --- | --- | --- |
|  | **PEC/PNECwater** | **PEC/PNECsed** |
| ***via STP*** | | |
|  | 0.003 | 0.003 |
| ***via slurry/manure – PEC:PNEC ratios after ten years. Leaching from the top soil layer between two applications is considered.*** | | |
| grassland | 0.027 | 0.027 |
| arable land | 0.016 | 0.016 |

For the emission pathway via STP, the PEC/PNEC values for iodine, iodide and iodate in the aquatic compartment (surface water incl. sediment, marine water incl. sediment) are below the trigger value of 1 (max. 0.234). Therefore, unacceptable risk for the aquatic environment cannot be expected.

Although iodate is the dominant iodine specie in soils under aerobic conditions, it may be transformed to iodide once entering the aquatic environment depending on the acidity and redox potential (oxygen concentrations). The maximum PEC/PNEC value for iodide is 1.93 after ten years of successive manure applications, while iodate results in a PEC:PNEC ratio of 0.027 Unacceptable risks may be expected in surface water low in oxygen. Iodine is however a natural occurring compound for which aquatic background levels are reported between 0.5 and 20 µg/L. Moreover, many uncertainties exist as currently available higher tier modelling (FOCUS PEARL, SWASH) are not suitable for inorganic substances such as iodine. It was therefore agreed that the natural background concentration replaces the PNEC as environmental standard. The PECs in sediment are well below the typical natural background concentration of 6 mg/kg. The accompanied risks are consequently considered acceptable.

***Terrestrial compartment***

The risk evaluation (PEC:PNEC ratios) for the soil compartment when residues are released to the STP or due to runoff from fertilised agricultural land is presented below.

|  |  |
| --- | --- |
| **Calculated PEC/PNEC values for iodine** | |
|  | **PEC/PNECsoil** |
| ***via STP*** | |
|  | 0.731 |
| ***via slurry/manure*** | |
|  | **after ten years** |
| grassland | **5.16** |
| arable land | **3.11** |

|  |  |
| --- | --- |
| **Calculated PEC/PNEC values for iodide** | |
|  | **PEC/PNECsoil** |
| ***via STP*** | |
|  | 2.01 |
| ***via slurry/manure*** | |
|  | **after ten years** |
| grassland | **14.2** |
| arable land | **8.54** |

|  |  |
| --- | --- |
| **Calculated PEC/PNEC values for iodate** | |
|  | **PEC/PNECsoil** |
| ***via STP*** | |
|  | 0.039 |
| ***via slurry/manure*** | |
|  | **after ten years** |
| grassland | 0.280 |
| arable land | 0.169 |

Once released to soils, iodine will be transformed into iodide or iodate depending on the redox conditions. Iodine is therefore not relevant for the soil compartment. Unacceptable risks are expected for iodide in both arable and grassland, while the PECs remain below the PNEC in case of iodate. The highest risks are expected for the most toxic specie iodide. These risks are nevertheless hypothetical as iodide only occurs in anaerobic i.e. flooded soils which may happen only incidentally. The ecological impact of long-term flooding is more disastrous compared to the risks related to anthropogenic elevated iodine concentrations. Moreover, the PECs are based on 100% transformation into iodide, while 14% transformation was reported in the assessment report for iodine. Therefore, the estimated PEC:PNEC ratios are considered unrealistic for agricultural soils for cattle and crops.

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 in sandy and clayey soils vary between 1.7-5.4 and 2.1-8.9 mg/kg dwt, respectively, while peaty soils may contain 18.7-98.2 mg/kg dwt. The expected PECs after ten years (0.0609 mg iodine/kg wwt in grassland and 0.0367 mg iodine/kg wwt in arable land) are in the lower range and therefore a significant increase of the background concentration cannot be expected, although it should be realised that atmospheric deposition is double as anthropogenic imission to soils due to teat disinfection is 8.09 g/ha/y[[2]](#footnote-2) and natural atmospheric deposition 25.6 g/ha/y[[3]](#footnote-3). However, naturally occurring iodine may be less bioavailable due to strong sorption on organic material or complexation with e.g. metals. Unacceptable risks in soils are conclusively not expected.

***Groundwater***

The concentration in the soil’s pore water derived by equilibrium partitioning according to the guidance is expected to be 11.5 µg/L in grassland and 6.98 µg/L in arable land (iodine and iodide) 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 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.

***Primary and secondary poisoning***

Because the product is mainly applied indoors and not released to the environment directly, direct uptake by non-target organisms cannot be expected. Moreover, because iodine is an essential nutrient and its hydrophobicity does not exceed the trigger value for bioaccumulation, excessive passive uptake cannot be expected. Therefore, the PEC will not exceed the oral PNEC. No risks from primary and secondary poisoning are expected.

***Mixture toxicity***

Not relevant for this product family as the product only contains one active substance and no substances of concern.

***Aggregated exposure (combined for relevant emission 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. See the decision tree in Figure 1 for details.



*Figure 1: Decision tree on the need for estimation of aggregated exposure*

|  |
| --- |
| **Overall conclusion on the risk assessment for the environment of the product** |
| When residues are released to the sewer, no unacceptable risks are expected for micro-organisms in the sewage treatment plant, and aquatic organisms in surface water and sediment as all predicted environmental concentrations (PECs) are well below the predicted no-effect concentrations (PNECs). Distribution of sewage sludge on agricultural land does not result in unacceptable risks either considering that all iodine is transformed into iodate as soils are aerobic.  Release via manure results in a PEC:PNEC ration >1 for surface water adjacent to agricultural soils due to runoff and concentrations in groundwater >0.1 µg/L due to leaching. The expected concentrations are however within the natural background range. The accompanied risks are therefore considered acceptable. |

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

**RECOMMENDED METHODS AND PRECAUTIONS**

**Storage:** Store upright in the tightly closed original container. Keep away from direct light, temperatures above 30°C and frost.

**Handling:** Ensure adequate ventilation. Handle in accordance with good industrial hygiene and safety practice (e.g. when using, do not eat, drink or smoke; regular cleaning of equipment, work area and clothing).

Meta SPC 4-5: Wear protective gloves/protective clothing/eye protection/face protection.

**Transport:** not classified for transport.

**Fire:** The products in this family are not flammable.

As in every fire, firefighters should wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

**Suitable Extinguishing Media:** Dry chemical, Carbon dioxide (CO2), Water spray, alcohol-resistant foam.

**Disposal:** Waste from residues, unused product and its packaging should be disposed of in accordance with local regulations. To prevent malfunctioning of an individual wastewater treatment plant, possible residues containing the product must be discharged to the manure storage or to the municipal sewer

**IDENTITY OF RELEVANT COMBUSTION PRODUCTS IN CASES OF FIRE**

Not applicable as the products are not flammable.

The active substance iodine, is not combustible but upon heating, toxic iodide fumes are formed.

**SPECIFIC TREATMENT IN CASE OF AN ACCIDENT**

**First-aid measures:**

Eye contact: Immediately flush with plenty of water. After initial flushing, remove any contact lenses and continue flushing for at least 15 minutes. Keep eye wide open while rinsing. If symptoms persist, call a physician.

Skin contact: Immediate medical attention is not required. Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes. If skin irritation persists, call a physician.

Ingestion: Clean mouth with water and afterwards drink plenty of water. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person. Consult a physician.

Inhalation: Immediate medical attention is not required. Move to fresh air in case of accidental inhalation of vapours. If symptoms persist, call a physician.

**Emergency measures to protect the environment**

Prevent further leakage or spillage if safe to do so.

Methods and materials for containment and clean-up: Dam up. Soak up with inert absorbent material. Prevent product from entering drains. Keep in suitable and closed containers for disposal.

**POSSIBILITY OF DESTRUCTION OR DECONTAMINATION FOLLOWING RELEASE**

The ready to use preparations are not classified as hazardous for the environment according to Regulation EC 1272/2008. In addition, the products are not likely to lead to direct entry to the environment since the products are mainly used indoors in the milking parlour, above an impermeable floor. There is no direct release to air, soil or surface waters. The active substance iodine is a natural oligo-element, present in soil, water and air, at concentrations far in excess to the contributions that the teat disinfectants in this product family will make to the environment. Hence, no procedures for the destruction or decontamination if released to air, soil or (drinking) water have been developed.

Upon accidental release: Prevent further leakage or spillage if safe to do so. Ensure adequate ventilation. Prevent product from entering drains. Dam up. Soak up with inert absorbent material.

**PROCEDURES FOR WASTE MANAGEMENT OF THE BIOCIDAL PRODUCT AND ITS PACKAGING**

The ready to use preparations are not classified as hazardous for the environment according to Regulation EC 1272/2008. The active substance iodine is quickly neutralised by reaction with organic matter. Furthermore, iodine is a natural oligo-element and is an essential micronutrient. Therefore, preliminary treatment of waste is not necessary. Waste from residues, unused product and its packaging should be disposed of in accordance with local regulations. The empty containers may not be recycled or re-used.

**PROCEDURES FOR CLEANING APPLICATION EQUIPMENT WHERE RELEVANT**

The applicator should be rinsed with water after each use.

**SPECIFY ANY REPELLENTS OR POISON CONTROL MEASURES INCLUDED IN THE PRODUCT**

Not applicable, products do not contain any repellents or poison control measures.

### Assessment of a combination of biocidal products

For biocidal products that are intended to be authorised for the use with other biocidal products. Not applicable.

# Annexes

## List of studies for the biocidal product (family)

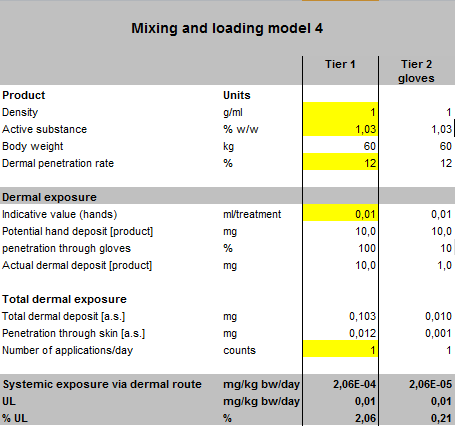
See enclosed **Appendix 1** for list of studies.

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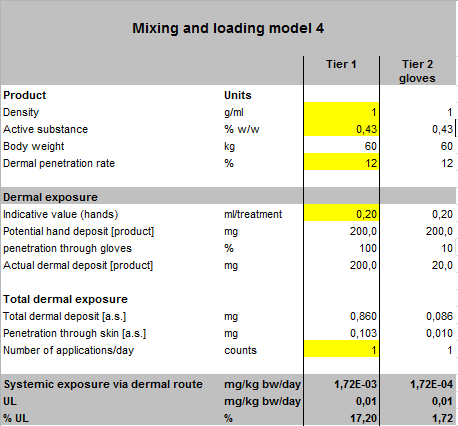
## Output tables from exposure assessment tools

**Toxicology**

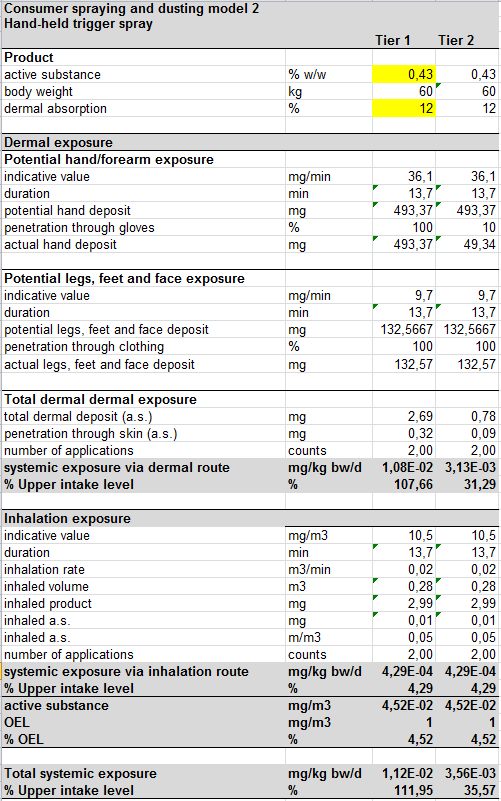
Scenario 1: M&L concentrate



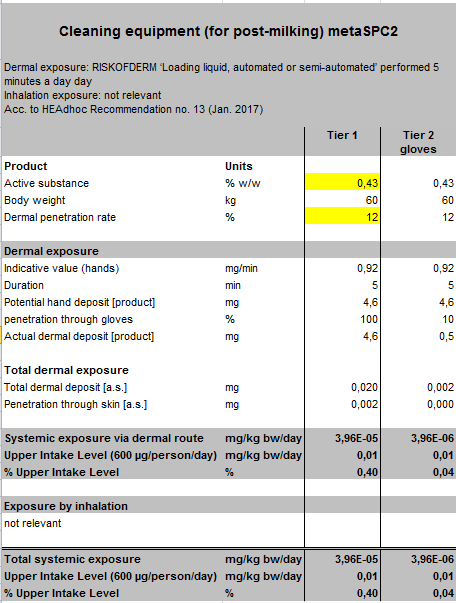
Scenario 1: M&L RTU



Scenario 3: Application by manual spraying



Scenario 5: Cleaning of equipment





**Environment**



## New information on the active substance

Not applicable, no new information on the active substance is provided.

## Residue behaviour

Not applicable, no new information on the active substance is provided.

## Summaries of the efficacy studies (B.5.10.1-xx)

Summaries are provided in 2.2.5.5 and in IUCLID.

## Confidential annex

See separate document

## Other

Not applicable

1. Additional table provided by applicant (DeLaval NV) [↑](#footnote-ref-1)
2. 0.790 kg iodine is release to the manure intended for grassland or arable land (ESD outcome). Cows produce 7185 kg nitrogen annually (ESD default) which requires 21.0 ha agricultural land considering a nitrogen emission standards of 170 kg/ha for both arable land and grassland. [↑](#footnote-ref-2)
3. Johanson, K.J. Iodine in soils, Technical Report TR-00-21, Svensk Kärnbränslehantering AB, Stockholm, Sweden. [↑](#footnote-ref-3)