

## **Biocidal Products Committee (BPC)**

### **Opinion on the Union authorisation of HYPRED's iodine based products**

ECHA/BPC/178/2017

Adopted

12 December 2017



## Opinion of the Biocidal Products Committee

### on the Union authorisation of HYPRED's iodine based products

In accordance with Article 44(3) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products, the Biocidal Products Committee (BPC) has adopted this opinion on the application for Union authorisation of:

**Name of the biocidal product family:** HYPRED's iodine based products

**Authorisation holder:** Hypred SAS

**Active substance common name:** Iodine, including polyvinylpyrrolidone iodine

**Product type:** 3

This document presents the opinion adopted by the BPC, having regard to the conclusions of the evaluating Competent Authority (eCA).

### Process for the adoption of BPC opinions

Following the submission of an application on 16 July 2015, recorded in R4BP3 under case number BC-LC018584-49, the evaluating Competent Authority (The Netherlands) submitted a draft product assessment report (PAR) containing the conclusions of its evaluation and the draft Summary of Product Characteristics (SPC) to ECHA on 6 June 2017. In order to review the draft PAR, the conclusions of the eCA and the draft SPC, the Agency organised consultations via the BPC (BPC-23) and its Working Groups ([WGIV-2017]). Revisions agreed upon were presented and the draft PAR and the draft SPC were finalised accordingly.

## **Adoption of the BPC opinion**

### **Rapporteur: The Netherlands**

The BPC opinion on the Union authorisation of the biocidal product/biocidal product family was adopted on 12 December 2017.

The BPC opinion was adopted by consensus. The opinion is published on the ECHA website.

## Detailed BPC opinion and background

### 1. Overall conclusion

The biocidal product family is eligible for Union authorisation in accordance with Article 42(1) of Regulation (EU) No 528/2012 and falls within the scope of the Regulation (EU) No 528/2012 as defined in Article 3(s).

The biocidal product family may be expected to fulfil the conditions laid down in Article 19(6) of Regulation (EU) No 528/2012 and therefore may be authorised. The detailed grounds for the overall conclusion are described in the PAR.

The BPC agreed on the draft SPC of HYPRED's iodine based products referred to in Article 22(2) of Regulation (EU) No 528/2012 (Annex I to this BPC opinion).

### 2. BPC Opinion

#### 2.1 BPC Conclusions of the evaluation

##### a) Summary of the evaluation and conclusions of the risk assessment

The sections below are a concise summary of the evaluation and conclusions of the assessment of the biocidal product family.

#### General

The biocidal product family 'HYPRED's iodine based products' consists of products containing 0.25% to 2.5% of the active substance iodine for disinfection of teats of milk producing animals. The biocidal product family consists of 5 meta SPCs, each containing 1 or 2 products. The structuring of the BPF into meta SPCs was based on:

- The hazard and precautionary statements (H319 and H412 for ready-to-use products (RTU), H318, H373, H411 for the concentrated product)
- Application method (manual or automated dipping, spraying, foaming)
- Target organism (algae, bacteria, yeast, viruses)

The following uses have been assessed:

meta SPC 1 : Dipping products – RTU

- Use 1.1: Manual or automated dipping after milking

meta SPC 2 : Dipping, spraying, foaming products – RTU

- Use 2.1: Manual or automated dipping, foaming or spraying before milking
- Use 2.2: Manual or automated dipping, foaming or spraying after milking

meta SPC 3 : Dipping, spraying, foaming concentrated products

- Use 3.1: Manual or automated dipping, foaming or spraying before milking
- Use 3.2: Manual or automated dipping, foaming or spraying after milking –virucidal activity

meta SPC 4 : Dipping products reaching virucidal activity – RTU

- Use 4.1: Manual or automated dipping after milking

meta SPC 5 : Dipping, foaming, spraying products 5500 ppm – RTU

- Use 5.1: Manual or automated dipping, foaming or spraying before milking
- Use 5.2: PT3 - Manual or automated dipping, foaming or spraying after milking- virucidal activity

## Physico-chemical properties

Products included in HYPRED's iodine based product family are brown liquids with characteristic or iodine odour. The pH of products within the family varies from 3.3-5.5. All products are stable according to accelerated storage test (at 30°C +/-2°C for 18 weeks), long term storage test at ambient temperature and low temperature stability test. The shelf life of all products is 2 years in HDPE packaging. The level of foam generated of concentrated product (meta SPC 3) at in use concentration is too high to use CIPAC MT 47.2. As this product is intended to produce foam, the persistent foaming test was waived. Dilution of the concentrated product (meta SPC 3) is stable at the maximum in use concentration. All relevant phys-chem properties have been determined for 5 out of 7 products. The provided data are considered to cover the complete family including non-existing theoretical products.

## Efficacy

For the 5 meta SPC's in this family efficacy test data have been submitted. Depending on the intended use, pre- or post-milking disinfection of teats, efficacy tests under different conditions (3g/L Bovine albumin or skimmed milk 1% resp.) have been submitted.

The tests demonstrated the following:

- All pre-milking products in the family have bactericidal and yeasticidal effect at minimal contact time of 1 minute (meta SPC 2, 3, 5).
- All post-milking products in the family have bactericidal, yeasticidal, and algacidal effect at minimal contact time of 5 minute (meta SPC 1, 2, 3, 4, 5). Efficacy at a contact time of 1 minute with milk soiling was not fully demonstrated since a simulated-use test at 30 seconds did not pass the 4 log reduction criterion (lg red=3.24). Only the test with 5 min contact time did, 1 min was not tested.
- Post-milking products with 0.5% iodine and more (meta SPC 3, 4, 5) also have virucidal activity at minimal contact time of 5 minutes.

## Human health

For the purpose of the human health risk assessment, exposure to iodine arising from professional use of iodine products and via the diet was compared with the relevant upper limit (UL) values for iodine for adults (600 µg/day) and infants (200 µg/day). Acceptable risks were identified if exposure was below the iodine UL.

The professional user is exposed during mixing and loading, application, and cleaning of the teats and the equipment. In addition, exposure from the biocidal use of these products can arise via the diet. The general public are also exposed via the diet through consumption of milk from treated cows following biocidal use. The human health exposure assessments are based on model calculations using models and default values from the HEAdhoc Recommendation no. 13 (Jan. 2017). Either pre- or post-treatment per milking event for the product family is assessed, since products included in the product family can only be used for pre- or post-application. This is also reflected in the instruction included in the section for general risk mitigation measures (RMM) of the SPC for meta SPC 2, 3 and 5 (as these are the only meta SPCs that include uses for pre- as well as post-application).

However, at the BPC Human Health Working Group IV 2017, it was decided that the consumer risk assessment should not only consider the iodine exposure resulting from teat treatment with iodine-containing disinfectants, but also exposure to iodine from other sources. According to the European Food Safety Authority, milk and other dairy products are by far the main source of iodine in the human diet. However, it is noted that the level of iodine in milk varies greatly across Europe and is only partly due to teat treatment with iodine-containing disinfectants. The main non-biocidal factors influencing the level of iodine

in milk are the dairy cattle diet (i.e. drinking water and grass), the use of iodine feed supplements, farming practices, seasonal variations and milk processing technologies. Other non-biocidal sources of iodine in the human diet include eggs, grain products, fish and iodized salt.

In order to undertake the consumer risk assessment, the Human Health Working Group, agreed harmonised values for background levels of iodine in milk and other dietary sources, as well as the approach to be taken for the consumer exposure assessment. The agreed background levels of iodine were 200 µg/L iodine from milk (EFSA monitoring data<sup>1</sup> and the O'Brien study, 2013<sup>2</sup>) and from sources other than milk, 185 µg/day for adults and 96 µg/day for children (UK retail survey of iodine in UK produced dairy foods<sup>3</sup>).

It should be noted that the regulation of iodine exposure pathways that are not a consequence of biocidal use are outside the remit of the BPC. Where unacceptable risks are identified as a result of consideration of total dietary intake of iodine in addition to exposure arising from biocidal use, a risk management decision cannot be taken in isolation with respect to the biocides use only. It would be advisable that this issue is addressed at European level in order to ensure that all relevant regulatory bodies can be involved in agreeing a way forward.

## **Professional user risk assessment**

### Professional use, pre-milking application

The risk assessment covers professional exposure to a concentrate (3.44 % total iodine concentration; in-use concentration 0.344 % total iodine (meta SPC 3)) and a ready to use (RTU) product (0.7489 % total iodine (meta SPC 2/5)).

### ***Exposure to the concentrate products***

When only exposures arising from the biocidal use are considered, acceptable risks are identified for pre-milking disinfection by manual dipping/foaming and automated spraying/automated dipping/foaming without PPE and for pre-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

When exposure arising from biocidal use and total dietary intake are considered, acceptable risks are identified for pre-milking disinfection by manual dipping/foaming and automated spraying/automated dipping/foaming without PPE and for pre-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

### ***Exposure to RTU products***

When only exposures arising from the biocidal use are considered, acceptable risks are identified for pre-milking disinfection by manual dipping/foaming and automated spraying/automated dipping/foaming without PPE and for pre-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

When exposure arising from biocidal use and total dietary intake are considered, acceptable risks are identified for pre-milking disinfection by automated spraying/automated dipping/foaming without PPE and for pre-milking disinfection by manual dipping/foaming and manual spraying using a trigger or electronic sprayer when appropriate PPE is worn

<sup>1</sup> EFSA Journal 2013;11(2):3101

<sup>2</sup> O'Brien et al. Iodine concentrations in milk. Irish Journal of Agricultural and Food Research 52: 209–216, 2013

<sup>3</sup> FSIS 02/08, 16 June 2008

(chemical resistant gloves and/or coveralls).

#### Professional use, post-milking application

The risk assessment covers professional exposure to a concentrate (3.44 % total iodine concentration; in-use concentration 0.689 % total iodine) (meta SPC 3) and ready to use (RTU) products (0.9058% total iodine (meta SPC 1/4); 0.7489 % total iodine (meta SPC 2/5)).

#### ***Exposure to the concentrate products***

When only exposures arising from the biocidal use are considered, acceptable risks are identified for post-milking disinfection by manual dipping/foaming and automated spraying/automated dipping/foaming without PPE and for post-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

When exposure arising from biocidal use and total dietary intake are considered, acceptable risks are identified for post-milking disinfection by manual dipping/foaming and automated spraying/automated dipping/foaming without PPE and for post-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

#### ***Exposure to RTU products***

When only exposures arising from the biocidal use are considered, acceptable risks are identified for post-milking disinfection by manual dipping/foaming and automated spraying/automated dipping/foaming without PPE and for post-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

When exposure arising from biocidal use and total dietary intake are considered, acceptable risks are identified for post-milking disinfection by automated spraying/automated dipping/foaming without PPE, for post-milking disinfection by manual dipping/foaming if PPE is worn as appropriate (chemical resistant gloves as necessary) and for post-milking disinfection by manual spraying using a trigger or electronic sprayer when appropriate PPE is worn (chemical resistant gloves/coveralls).

#### **Consumer risk assessment**

Dietary risk via iodine residues in milk and other dietary sources has been assessed for both adults and children. Exposure to residues is based on the worst-case exposure scenario for the worst case meta SPC 5.

When only exposures arising from the biocidal use are considered, acceptable risks are identified for both adults and toddlers following both pre-milking and post-milking application.

However, when exposure arising from the biocidal use and total dietary intake are considered, an acceptable risk is identified for adults but an unacceptable risk is identified for toddlers following both pre-milking and post-milking application. As a result the assessment was also performed at all other meta SPC levels included in the application and the same conclusions were found.

It should be noted that the unacceptable risk identified for toddlers is mainly due to



exposure to iodine from sources other than the biocidal use, accounting for 94% of the iodine UL.

A more elaborate discussion and proposal for decision is included in the overall conclusions of this draft BPC opinion (see below).

## **Environment**

Teat disinfectants are released to the environment due to spillage during application, cleaning of the applied equipment, and dripping from animal's teats and udders. As most dairy farms are not connected to the public sewer, residues are predominantly discharged to the manure storage and eventually to soils when manure is applied as a fertiliser. Iodine is not volatile and is persistent as it does not degrade biologically or abiologically. Depending on the redox conditions and acidity, iodine will be transformed into iodide or iodate. Both species exist in water, but iodate is the dominant species in soils.

When residues are released to the sewer, no unacceptable risks are expected for micro-organisms in the municipal 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). Although the iodine concentrations in soils after distribution of sewage sludge on land does result in an exceeding of the PNEC, no unacceptable risks are expected as soils are aerobic and therefore iodine is transformed into iodate for which the PEC is well below the PNEC. However, emission to individual waste water treatment systems may result in malfunctioning of the installation as such systems are vulnerable for high loads of biocides due to their size. Diluted residues and waste water must be discharged to the sewer where legally allowed or to the manure storage.

Release via manure results in unacceptable risks for surface water adjacent agricultural soils (PEC:PNEC ratios up to 8.05) due to runoff and concentrations in groundwater (42-69 µg iodine/L) that are well above the 0.1 µg/L threshold and acceptable human intake limits. However, the calculated concentrations are within the natural background range (0.5-70 µg/L). Because iodine is a natural occurring compound and many uncertainties exist in the applied methodology as appropriate models for runoff to surface water and leaching to groundwater are not available for inorganic substances like iodine, background concentration has been accepted as standard. From an environmental perspective the application of iodine-based teat disinfectants is therefore acceptable. No risk mitigation measures are necessary.

## **Overall conclusion**

Overall, when exposure arising from biocides use is considered in isolation, no unacceptable risks are identified for professional users if PPE is worn as appropriate or for the general public as a result of the consumer risk assessment.

Once exposure from biocides use is considered in conjunction with total dietary exposure of iodine, acceptable risks are still identified for professional users if appropriate risk mitigation measures are in place and for adults following exposure to iodine in the diet. However, an unacceptable risk is identified for toddlers which is mainly due to exposure from non-biocidal sources of iodine accounting for 94% of the UL for toddlers.

The regulation of iodine exposure pathways that are not a consequence of biocidal use are outside the remit of the BPC. Unacceptable risks have been identified as a result of consideration of total dietary intake of iodine in addition to exposure arising from biocidal use. Thus it is not considered appropriate to take risk management decisions in isolation with respect to the biocides use to address concerns that arise from the risk assessment. It

would be advisable that this issue is addressed at European level in order to ensure that all relevant regulatory bodies can be involved in agreeing a way forward.

It is noted that the impact of taking into account total dietary exposure of iodine is not a new issue. In an EFSA scientific opinion intakes were reported to exceed the UL 2-fold for adults and 4-fold for toddlers with the current authorised maximum contents of total iodine in complete feed of 5 mg/kg. As a result of these exceedances, the FEEDAP Panel of EFSA recommended a reduction for iodine in feed of 2 mg/kg. However, even this reduced value would lead to exceedance of the iodine UL of the high consuming toddler (168% of the UL).

The following elements were taken into consideration for a decision on the authorisation of iodine teat disinfection products:

- The reference values for iodine of 600 µg/d for adults and 200 µg/d for children are not toxicological reference values but upper intake levels. These values have been derived with the aim of setting recommendations for intake and do not represent toxicological cut-off values for risk assessment. For trace elements like iodine, generally no toxicologically cut-off values are set. Therefore, it was agreed at Human Health Working Group II-2017 to use the upper intake levels as reference values. Furthermore, it is noted that effects that were taken into account for the derivation of the limit values were considered marginal and not associated with clinical effects. Moreover, the assessment factor taken into account is relatively high for a nutrient. It is further noted that WHO derived a value of 1000 µg/d for people in general, but not for children specifically. Therefore, the limit values used in this assessment are considered conservative.

- The estimated intakes are based on theoretical worst case levels of iodine in milk and were calculated based on a chronic exposure, which was considered to be the most appropriate based on how the UL was derived. Furthermore, it is noted that the SCF (from which the UL for adult and toddler are included in the CAR for iodine) also reports adapted UL values for older children. As the estimated residue levels of iodine in milk are based on a worst case assessment and the data are based on short term consumption studies, then the intakes seen in reality may not be of concern if the lifelong exposures from varying sources of food were considered.

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

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

To summarise, taking all information into consideration and noting that:

- the assessment is based on worst case theoretical levels of iodine in milk, using a conservative limit value and using worst case short term exposure studies for long term exposure;
- 94% of UL for toddlers in the dietary assessment is due to used background in milk and other dietary sources;
- exceedance of the UL is reported based on dietary intake (without teat disinfection) and the biocidal use itself is not responsible for the exceedance of the UL for toddlers;
- the major contributor of iodine in milk is feed, due to natural sources and/or supplements;
- the authorized maximum iodine of 5 mg/kg content in feed lead to 400% of the UL for toddlers;
- within Europe iodine deficiency is considered a major public health problem and iodine supplementation programs are ongoing;

the BPC considers that using the products belonging to this biocidal product family according to the conditions as stated in the SPC, the products will be efficacious and will not by themselves present an unacceptable risk to human and animal health nor the environment.

#### **b) Presentation of the biocidal product family including classification and labelling**

The description of the biocidal product and of the structure of the family is available in the SPC.

The hazard and precautionary statements of the biocidal product (family) according to the Regulation (EC) 1272/2008 are available in the SPC.

#### **c) Description of uses proposed to be authorised**

The uses claimed in the application and their assessment are described in the PAR. The description of the uses proposed to be authorised are available in the SPC.

#### **d) Comparative assessment**

The active substance iodine contained in the biocidal product family does not meet the conditions laid down in Article 10(1) of Regulation (EU) No 528/2012 and is not considered a candidate for substitution. Therefore, a comparative assessment of the biocidal product family in accordance with Article 23 of the BPR is not required.

#### **e) Overall conclusion of the evaluation of the uses proposed to be authorised**

The physico-chemical properties, the safety for human and animal health and for the environment and the efficacy of the intended use(s) of the biocidal product/biocidal product family have been evaluated.

The chemical identity, quantity and technical equivalence requirements for the active substance in the biocidal product family are met.

The physico-chemical properties of the biocidal product/biocidal product family are deemed acceptable for the appropriate use, storage and transportation of the individual biocidal products.

For the proposed authorised use(s), according to Article 19(1)(b) of the BPR, it has been concluded that:

1. the biocidal product family is sufficiently effective;
2. the biocidal product family has no unacceptable effects on the target organisms, in particular unacceptable resistance or cross-resistance;
3. the biocidal product family has no immediate or delayed unacceptable effects itself, or as a result of its residues, on the health of humans, including that of vulnerable groups, or animals, directly or through drinking water, food, feed, air, or through other indirect effects;
4. the biocidal product family has no unacceptable effects itself, or as a result of its residues, on the environment, having particular regard to the following considerations:
  - the fate and distribution of the biocidal product family in the environment,
  - contamination of surface waters (including estuarial and seawater), groundwater and drinking water, air and soil, taking into account locations distant from its use following long-range environmental transportation,
  - the impact of the biocidal product family on non-target organisms,
  - the impact of the biocidal product family on biodiversity and the ecosystem.

The outcome of the evaluation, as reflected in the PAR, is that the use(s) described in the SPC may be authorised.

## **2.2 BPC opinion on the Union authorisation of the biocidal product/biocidal product family**

It is proposed that the biocidal product family HYPRED's iodine based products shall be authorised, for the uses described under section 2.1 of this opinion, subject to compliance with the proposed SPC.

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## **Annex I: draft Summary of Product Characteristics**