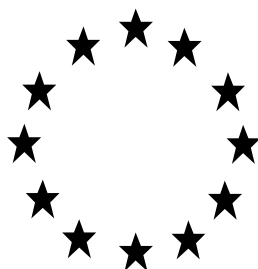


Regulation (EU) No 528/2012 concerning the
making available on the market and use of
biocidal products

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

(submitted by the evaluating Competent Authority)



MAMICAMP SELLADOR

Product type(s) 3

PVP iodine as included in the Union list of approved
active substances

Case Number in R4BP: BC-AE019732-60

Evaluating Competent Authority: Spain

October 2023

1 Table of Contents

1	CONCLUSION.....	4
2	ASSESSMENT REPORT	7
2.1	SUMMARY OF THE PRODUCT ASSESSMENT	7
2.1.1	<i>Administrative information.....</i>	7
2.1.1.1	Identifier of the product	7
2.1.1.2	Authorisation holder.....	7
2.1.1.3	Manufacturer(s) of the product.....	7
2.1.1.4	Manufacturer(s) of the active substance(s).....	7
2.1.2	<i>Product composition and formulation.....</i>	8
2.1.2.1	Identity of the active substance.....	8
2.1.2.2	Candidate(s) for substitution	8
2.1.2.3	Qualitative and quantitative information on the composition of the biocidal product.....	9
2.1.2.4	Information on technical equivalence	9
2.1.2.5	Information on the substance(s) of concern.....	9
2.1.2.6	Type of formulation	9
2.1.3	<i>Hazard and precautionary statements.....</i>	10
2.1.4	<i>Authorised use(s).....</i>	10
2.1.4.1	Use description	10
2.1.4.1.1	Use-specific instructions for use	11
2.1.4.1.2	Use-specific risk mitigation measures.....	11
2.1.4.1.3	Where specific to the use, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment	11
2.1.4.1.4	Where specific to the use, the instructions for safe disposal of the product and its packaging.....	11
2.1.4.1.5	Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage	11
2.1.5	<i>General directions for use.....</i>	11
2.1.5.1	Instructions for use.....	11
2.1.5.2	Risk mitigation measures.....	12
2.1.5.3	Particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment.....	12
2.1.5.4	Instructions for safe disposal of the product and its packaging.....	12
2.1.5.5	Conditions of storage and shelf-life of the product under normal conditions of storage.....	13
2.1.6	<i>Other information.....</i>	13
2.1.7	<i>Packaging of the biocidal product.....</i>	13
2.1.8	<i>Documentation.....</i>	14
2.1.8.1	Data submitted in relation to product application	14
2.1.8.2	Access to documentation.....	14
2.2	ASSESSMENT OF THE BIOCIDAL PRODUCT.....	14
2.2.1	<i>Intended use(s) as applied for by the applicant.....</i>	14
2.2.2	<i>Physical, chemical and technical properties.....</i>	15
2.2.3	<i>Physical hazards and respective characteristics.....</i>	19
2.2.4	<i>Methods for detection and identification.....</i>	22
2.2.5	<i>Efficacy against target organisms.....</i>	24
2.2.5.1	Function and field of use.....	24
2.2.5.2	Organisms to be controlled and products, organisms or objects to be protected	24
2.2.5.3	Effects on target organisms, including unacceptable suffering	24
2.2.5.4	Mode of action, including time delay	24
2.2.5.5	Efficacy data.....	26
2.2.5.6	Occurrence of resistance and resistance management	30
2.2.5.7	Known limitations	30
2.2.5.8	Evaluation of the label claims	30
2.2.5.9	Relevant information if the product is intended to be authorised for use with other biocidal product(s)...	30
2.2.6	<i>Risk assessment for human health.....</i>	30
2.2.6.1	Assessment of effects on Human Health	31

2.2.6.2 Exposure assessment 37

2.2.6.3 Risk characterisation for human health 54

2.2.7 *Risk assessment for animal health*..... 62

2.2.8 *Risk assessment for the environment* 62

2.2.8.1 Effects assessment on the environment 64

2.2.8.2 Exposure assessment 72

2.2.8.3 Risk characterisation..... 89

2.2.9 *Measures to protect man, animals and the environment* 96

2.2.10 *Assessment of a combination of biocidal products*..... 96

2.2.11 *Comparative assessment* 96

3 ANNEXES..... 101

3.1 LIST OF STUDIES FOR THE BIOCIDAL PRODUCT..... 101

3.2 OUTPUT TABLES FROM EXPOSURE ASSESSMENT TOOLS 104

3.3 NEW INFORMATION ON THE ACTIVE SUBSTANCE 107

3.4 RESIDUE BEHAVIOUR 107

3.5 SUMMARIES OF THE EFFICACY STUDIES (B.5.10.1-xx) 107

3.6 CONFIDENTIAL ANNEX..... 107

3.7 OTHER..... 107

1 CONCLUSION

Physical-chemical properties

MAMICAMP SELLADOR is a GW (Water soluble gel, RTU) product. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable. Its technical characteristics are acceptable for an GW formulation. The stability data indicate a shelf life of at least 2 years at ambient temperature.

The biocidal product is not classified from the physico-chemical aspect.

The analytical methods provided are fully validated for the determination of the active substance, PVP Iodine. Methods for the determination of the residues are available in the CAR of the active substances.

Efficacy

The product supports a sufficient efficacy for teat disinfection at 10% (v/v) dilution in water with a contact time of 5 minutes for post-milking teat disinfection, at soiling conditions of 10 g/l of skimmed milk. Therefore, it is considered that it will be effective at RTU. (See point 2.2.5 Efficacy against target organisms for details)

Human health

MamicampOrdeño contains Iodine (CAS 7553-56-2) that is used in biocidal products for the disinfection of animals' teats/udder and animal houses. In the products type 3, iodine is complexed with Polyvinylpyrrolidone (iodophor type 2).

In accordance with Article 15(2) 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 review of approval of the active substance iodine and polyvinylpyrrolidone iodine. These substances are identified as having endocrine-disrupting properties.

Therefore, the active substance iodine (including PVP-iodine) does meet the exclusion criteria according to Article 5(1 d) BPR, the following exclusion criteria met; has endocrine disrupting properties. According to article 23 BPR, the evaluating competent authority (ES), will perform a comparative assessment as part of the evaluation of an application for authorisation of a biocidal product.

Exposure assessment

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 exposure arising from the biocidal use is considered, acceptable systemic exposure is identified for manual dipping without PPE. However, from the local effects

assessment, due to the classification of the product as H319 (Causes serious eye irritation), it is mandatory to wear eye protection when handling it.

When exposure arising from biocidal use and total dietary intake are considered, acceptable risks are identified for two post-milking disinfection per day by manual dipping or three post-milking disinfection by automated dipping.

Note: 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 (conclusion reached at Secure Webex meeting 3-10-2017 for exposure to residues from iodine based union authorisation applications).

From the risk assessment approach, the safe use of the product does not require the use of gloves at any time, however, according to the CAR, for hygienic reasons it is standard practice to use at least gloves (in order to reduce the risk of possible cross contamination) and protective clothing.

Consumer risk assessment

Based on the risk assessment of consumers, taking into account only the effect from the use of the product, safe use is identified (adult 12.82% UL and toddler 39.31% 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 exceeded (i.e. 133.31% UL). In any case, the iodine intake that can be attributed to the use of the product 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.

Considering the above, we consider the exceedance of the UL for toddlers (i.e. 133.31%) taking into account teat disinfection and dietary intake acceptable.

Note: a more detailed argument has been developed in the section "Risk for consumers via residues in food", through the ES CA decision.

Environmental risk

Based on the available information related to the use of the product MAMICAMP SELLADOR, the environmental assessment is acceptable.

Explanatory note (only for Spain authorisation):

According to national legislation, in Spain there are three user categories:

Trained professional users (TP): pest control operators, having received specific training in biocidal product uses according to the national legislation in force.

Professional users (P): professionals that use the biocidal products in the context of their profession, that is not pest control operator, and that are unlikely to have received any specific training in biocidal product use according to the national legislation in force. It can be expected that they have some knowledge and skills handling chemicals (if they must use it in their job) and they are able to use correctly some kind of PPE if necessary.

Non-professional users (NP): users who are not professionals and that apply the biocidal product in the context of their private life. (Note: this user has not been claimed by the applicant for this product).

The conclusions reached in this PAR, which affect the intermediate category of "Professional", will only be applicable at the Spanish level.

2 ASSESSMENT REPORT

2.1 Summary of the product assessment

2.1.1 Administrative information

2.1.1.1 Identifier of the product

Identifier	Country (if relevant)
MAMICAMP SELLADOR	Spain

2.1.1.2 Authorisation holder

Name and address of the authorisation holder	Name	PRODUCTOS QP S.A.
	Address	Ctra. Logroño km 10.2 50180 Utebo Zaragoza SPAIN
Authorisation number	ES/APP(NA)-2023-03-00901	
Date of the authorisation	30/10/2023	
Expiry date of the authorisation	30/10/2028	

2.1.1.3 Manufacturer(s) of the product

Name of manufacturer	PRODUCTOS QP S.A.
Address of manufacturer	Ctra.Logroño, km 10.2 50180 Utebo Zaragoza Spain
Location of manufacturing sites	Ctra.Logroño, km 10.2 50180 Utebo Zaragoza Spain

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

Active substance	Polyvinylpyrrolidone Iodine (PVP Iodine)
Name of manufacturer	Laboratorios Montplet, SLU
Address of manufacturer	Via Trajana, 53-55 08020 Barcelona Spain
Location of manufacturing sites	ISP CHEMICALS LLC AFFILIATE OF ASHLAND 455 N.Main St (HWY 95) Calvert City KY 42029 USA
	BASF Corporation

8404 River Road
Geismar, LA 70734
USA

NB: the sources of Iodine, active substance included in Polyvinylpyrrolidone (iodophor type 2) has been provided in the confidential annex.

2.1.2 Product composition and formulation

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

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

Yes

No

2.1.2.1 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	995 g/kg
Structural formula	I-I
Iodine is formulated as PVP-Iodine in the product.	
IUPAC Name	Polyvinylpyrrolidone iodine (common name PVP-iodine)
EC number	607-771-8
CAS number	25655-41-8
Minimum purity / content	For polyvinylpyrrolidone iodine: the iodine content shall have a purity of 995 g/kg
Structural formula	

2.1.2.2 Candidate(s) for substitution

In accordance with Article 15(2) 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 review of approval of the active substance iodine and polyvinylpyrrolidone iodine. These substances are identified as having endocrine-disrupting properties.

Hence, the active substance iodine (including PVP-iodine) does meet the exclusion criteria according to Article 5(1 d) BPR. And therefore, does meet the conditions laid down in Article 10 BPR, and is consequently a candidate for substitution.

According to article 23 BPR, the evaluating competent authority (ES), will perform a comparative assessment as part of the evaluation of an application for authorisation of a biocidal product.

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

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
PVP Iodine	Polyvinylpyrrolidone Iodine	Active substance	25655-41-8	607-771-8	2.5% as PVP Iodine
Iodine available					(0.19-0.34% as av. Iodine)

Details of the product composition and information on the co-formulants are confidential and are presented in the confidential part of the dossier.

When "PVP-Iodine" or "Active substance (AS)" is written in this dossier, it refers to "Polyvinylpyrrolidone Iodine". The active element is the available iodine (I₂) released from Polyvinylpyrrolidone Iodine when is in water dissolution, and so all data are referred to available iodine (I₂) too.

2.1.2.4 Information on technical equivalence

Productos QP, S.A. has submitted a Declaration of SCC, secretary of "IRG" (BPR Iodine Registration Group) indicating that Laboratorios Montplet S.L.U. is a member of this Group which submitted complete dossiers for the approval of the biocidal active substance Iodine (including polyvinylpyrrolidone (PVP) iodine) under the review programme of Directive 98/8/EC.

So, the sources of iodine (including PVP-iodine) are the same as evaluated for inclusion in the Union list of approved substances.

Hence, no assessment of technical equivalence is needed.

2.1.2.5 Information on the substance(s) of concern

According to PART II of Guidance on the Biocidal Products Regulation Volume IV Environment - Assessment & Evaluation (Parts B+C) (Version 2.0 October 2017), the biocidal product contains no substances of concern.


Please see the confidential annex for further details.

2.1.2.6 Type of formulation

GW – Water soluble gel, RTU

2.1.3 Hazard and precautionary statements

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

Classification	
Hazard category	Eye Irrit.2; Aquatic chronic 3
Hazard statement	H319, H412
Labelling	
Signal words	Warning
Pictograms	 GHS07
Hazard statements	H319: Causes serious eye irritation H412: Harmful to aquatic life with long lasting effects
Precautionary statements	P264: Wash hands thoroughly after use P273: Avoid release to the environment P280: Wear protective gloves and eye 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. P501: Dispose of contents/container as hazardous waste to a registered establishment or undertaking, in accordance with current regulations.

*ES CA will apply article 37 according to BPR in the authorisation of this product including in this section the P statements that are recommended and highly recommended according to the result of the risk assessment of the product and considering the Guidance on labelling and packaging in accordance with Regulation (EC) No 1272/2008 (Version 4.2 March 2021).

2.1.4 Authorised use(s)

2.1.4.1 Use description

Table 1. Use # 1 – Post-milking teat disinfection by dipping

Product Type	PT03 – Veterinary hygiene (Disinfectants)
Where relevant, an exact description of the authorised use	Teat disinfection (non-medical) after milking
Target organism (including development stage)	Bacteria and yeasts
Field of use	Indoor
Application method(s)	Manual or automatic dipping cups treatment

Application rate(s) and frequency	<p>Application rate: RTU after milking -daily cows: 4 ml/cow/event -sheep and goats: 2 ml/animal/event</p> <p>Contact time: 5 minutes after milking</p> <p>The frequency of application is: 2 events/day for manual milking or 3 events/day for milking systems for dairy cows, and 1 application per day for ewes or goats.</p>
Category(ies) of users	Trained professional and Professional users
Pack sizes and packaging material	Please see the relevant section.

2.1.4.1.1 Use-specific instructions for use

See section 2.1.5.1.

2.1.4.1.2 Use-specific risk mitigation measures

See section 2.1.5.2.

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

See section 2.1.5.3.

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

See section 2.1.5.4.

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

See section 2.1.5.5.

2.1.5 General directions for use

2.1.5.1 Instructions for use

For hygienic reasons it is standard practice to use gloves and protective clothing.

Please read the label or leaflet before use and follow all the instructions provided. This biocidal product is specially formulated to be applied for disinfection of the udder/teat hole after milking. It is indicated for dairy cows, sheeps, goats and other lactating females.

Apply by dipping cups manually or automatically on animal's teats on the full length of the teat after milking.
Respect the conditions of use of the product (concentration, contact time, temperature, pH, etc.).
After milking, remove all organic debris from teats before applying post-milking teat dipping with a paper or cloth towel.

Post-milking Teat Dipping: Cover the entire teat with dip cup containing 10-20 ml of pure BP (one cup with 20 ml is used for approximately 5-6 cows or 10-12 sheep and goats). Once the teats are dipped, the operator slightly moves the teats to allow the formation of a droplet on the sphincter at the basis of the teat. This is the crucial place to be protected since it is the entry point of the contaminants. Keep the cows in the milking parlour and let the product dry on the udder, making sure that the animal does not lie down until the product has dried, at least 5 min (contact time).

Inform the registration holder if the treatment is ineffective.

The frequency of application is: 2 events/day for manual milking or 3 events/day for milking systems for dairy cows, and 1 application per day for ewes or goats.

2.1.5.2 Risk mitigation measures

Wear eye protection when handling the product.
Avoid contact with eyes and skin.

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

IF INHALED: If symptoms occur call a POISON CENTRE or a doctor
IF SWALLOWED: Rinse mouth. Give something to drink, if exposed person is able to swallow. DO NOT induce vomiting. Call a POISON CENTRE or a doctor.
IF ON SKIN: Wash skin with water. If symptoms occur call a POISON CENTRE or a doctor
IF IN EYES: Rinse with water. Remove contact lenses, if present and easy to do. Continue rinsing for 5 minutes. Call a POISON CENTRE or a doctor

IF MEDICAL ADVICE IS NEEDED, HAVE THE PRODUCT CONTAINER OR LABEL AT HAND AND CONTACT THE POISON CONTROL CENTER

Environmental precautions:
Absorb the spillage using sand or inert absorbent and move it to a safe place. Do not absorb in sawdust or other combustible absorbents.
Avoid spillage into an aqueous medium as it contains substances potentially dangerous for this. Contain the product absorbed in hermetically sealed containers.
In the case of serious spillage into an aqueous medium notify the relevant authorities.

2.1.5.4 Instructions for safe disposal of the product and its packaging

In Spain:
Empty containers, unused product, washing water, containers and other waste generated during the treatment are considered hazardous waste. Deliver those

wastes to a registered establishment or undertaking, in accordance with current regulations.

Code the waste according to Decision 2014/955 / EU.

Do not release to soil, ground, surface water or any kind of sewer.

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

Store it protected from direct sunlight
Shelf-life: 2 years

2.1.6 Other information

Definitions:

Professional: User applying biocidal products in the workplace. This user has some knowledge and skills in the handling of chemicals, and is able to correctly use personal protective equipment (PPE) if necessary.

Trained professional: pest control operators, having received specific training in biocides according to the national legislation in force.

2.1.7 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)
Jerry can	5L, 10L, 20L and 25L	Plastic: HDPE	Plastic: HDPE	Professional & Trained professional	yes
Drum	60L, 200L	Plastic: HDPE	Plastic: HDPE (with tap)	Professional & Trained professional	yes
IBC / (intermediate bulk container)	1000L	Plastic: HDPE	Plastic: HDPE (with tap)	Professional & Trained professional	yes

Description and safety of the packaging: opaque HDPE that does not let pass light, homologated for ADR/IMDG/IATA transport.

2.1.8 Documentation

2.1.8.1 Data submitted in relation to product application

The reference list (including updates) for the studies submitted have been included in Annex 3.1 whilst the reference list for the studies considered confidential has been included in the PAR confidential.

2.1.8.2 Access to documentation

Productos QP, S.A. has submitted a Letter of access from Laboratorios Montplet S.L.U. (formerly Alcoholes Montplet S.L.U.) to iodine (including PVP Iodine) data, as participant for iodine, under the review programme of Directive 98/8/EC.

The sources of Iodine used and included in PVP-Iodine for the production of biocidal product MAMICAMP SELLADOR has been declared by Alcoholes Montplet S.L.U.

2.2 Assessment of the biocidal product

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

Table 2. Intended use # 1 - name of the use¹

Product Type(s)	PT03 - Veterinary hygiene (Disinfectants)
Where relevant, an exact description of the authorised use	BP for external topic use for disinfecting and sealing of the udder/teat hole after milking, providing a protective barrier against the entry of germs into the udder through the teat hole, protecting and softening the skin and mucous membranes. Indicated for topical use in dairy cows, ewes, goats and other lactating females.
Target organism (including development stage)	Bacteria aerobic gram-positive and gram-negative, and yeasts
Field of use	Indoor
Application method(s)	Manual disinfecting treatment with dipping cups after milking
Application rate(s) and frequency	1 ml pure BP per teat (4 ml per cow), 2 times per cow and day, every day
Category(ies) of user(s)	Professional
Pack sizes and packaging material	Please see the relevant section.

¹ Copy this section as many times as necessary (one table per use).

2.2.2 Physical, chemical and technical properties

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
Physical state at 20 °C and 101.3 kPa	Visual	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Viscous Liquid	-
Colour at 20 °C and 101.3 kPa	Visual	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Brown	-
Odour at 20 °C and 101.3 kPa	Olfactory	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Characteristic iodine odour, very weak	-
pH Acidity / alkalinity	CIPAC MT 75.3 CIPAC MT 191	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	4.69 at 20 ±2°C (undiluted product) 4.84 at 20 ±2°C (1%) 0.317% as H ₂ SO ₄	Report n° 15-4885-01 (2015)
Relative density / bulk density	CIPAC MT.3 (OECD 109 - pycnometer)	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	1.0261 g/mL at 20 °C	Report n° 15-4885-01 (2015)
Storage stability test – accelerated storage	CIPAC MT.46	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Temperature 54°C ± 2°C (14 days) <u>PVP Iodine (% w/w)</u> [C] ₀ =0.2904% [C] _f =0.2128% Δ[C]=-26.72% No change in product appearance.	Report n° 15-4885-01 (2015)
Storage stability test – long term storage at ambient temperature	GIFAP monograph 17	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	[C] ₀ = 0.292% [C] _{3M} = 0.265% Δ[C] = -9.25% < 10% [C] ₀ = 0.292% [C] _{6M} = 0.235%	Report n° 16-4885-02 (2016)

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
			$\Delta[C] = -19.52 > 10\%$ $[C]_0 = 0.292\%$ $[C]_{12M} = 0.212\%$ $\Delta[C] = -27.40 > 10\%$ $[C]_0 = 0.292\%$ $[C]_{18M} = 0.187\%$ $\Delta[C] = -35.96 > 10\%$ $[C]_0 = 0.292\%$ $[C]_{24M} = 0.173\%$ $\Delta[C] = -40.75 > 10\%$	
Storage stability test – low temperature stability test for liquids	CIPAC MT 39.3	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	<p>The test item was physically stable after 7 days at 0 ± 2°C.</p> <p>The sample is homogeneous. There is not phase separation or crystallized material.</p>	Report n° 15-4885-01 (2015)
Effects on content of the active substance and technical characteristics of the biocidal product - light	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	<p>The PVP Iodine is a complex which stabilizes the iodo, therefore it is considered more stable to the effect of light. On the other hand, according to the Assesment report of Iodo/PVP Iodine, in water solution coexist, I₂, I⁻ and IO₃⁻, being able to form photolitically I₂ from I⁻ and IO₃⁻ so it can be considered that the effect of light could be positive.</p> <p>However, as a precaution, it is going to be included in the label the sentence "Store it</p>	-

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
			protected from direct sunlight".	
Effects on content of the active substance and technical characteristics of the biocidal product - temperature and humidity	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Stability at elevated and decreased temperatures confirmed by the respective storage stability test. Humidity does not affect the properties of the product as the product is water based.	-
Effects on content of the active substance and technical characteristics of the biocidal product - reactivity towards container material	GIFAP monograph 17	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	No changes were observed in the HDPE original container after storing it for 24 months at 25°C	Report n° 16-4885-02 (2016)
Wettability	-	-	Not applicable	-
Suspensibility, spontaneity and dispersion stability	-	-	Not applicable	-
Wet sieve analysis and dry sieve test	-	-	Not applicable	-
Emulsifiability, re-emulsifiability and emulsion stability	-	-	Not applicable	-
Disintegration time	-	-	Not applicable	-
Particle size distribution, content of dust/fines, attrition, friability	-	-	Not applicable	-
Persistent foaming	CIPAC MT 47.2	PVP-Iodine: 2.5%	(Water D)	Report n° 15-4885-01 (2015)

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
		(0.19-0.34% as I ₂)	The level of foam generated is >60 mL after 1 minute it is applied directly on the udders by dipping. The product won't be stirred or sprayed so the possibility of forming foam that could cause risk to the operator or animal is very low.	
Flowability/Pourability/Dustability	-	-	Not applicable	-
Burning rate — smoke generators	-	-	Not applicable	-
Burning completeness — smoke generators	-	-	Not applicable	-
Composition of smoke — smoke generators	-	-	Not applicable	-
Spraying pattern — aerosols	-	-	Not applicable	-
Physical compatibility	-	-	Not applicable	-
Chemical compatibility	-	-	Incompatible with reducing agents and alkaline metals.	(ATQ expert declaration)
Degree of dissolution and dilution stability	CIPAC MT.41	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	No sediment, clear solution (3%). There is not separated material. The result was recorded after 18 hours.	Report n° 15-4885-01 (2015)
Surface tension	EEC A5	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	28.4 ± 0.079 mN/m at 20 °C	Report n° 15-4885-01 (2015)

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
Viscosity	OCDE 114	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Dynamic viscosity: 13337 mPa·s at 20°C (at 0.03 rpm) 12252 mPa·s at 20°C (at 0.04 rpm) 10594 mPa·s at 20°C (at 0.05 rpm)	Report n° 15-4885-01 (2015)

Conclusion on the physical, chemical and technical properties of the product

The product "MAMICAMP SELLADOR" is a WG (Water soluble gel, RTU) product. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable. The appearance of the product is a brown viscous liquid with a very weak characteristic odour. It has a pH of 4.5-6.5.

According to the efficacy tests presented in phase 2/1 and phase 2/2 (see section 2.2.5.5. Efficacy data), it is concluded that the product diluted to 10% is active against the bacteria and yeast tested under the conditions established for post-milking teat disinfectants of animals, for therefore, the aged product, which presents a loss of 41% of available iodine after 2 years of storage at room temperature, will continue to be effective for such use.

Therefore, an expiration date of at least 2 years is established.

All other technical characteristics are acceptable for an WG formulation.

2.2.3 Physical hazards and respective characteristics

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
Explosives	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	None of the components of the product are explosive. Therefore, it is safe to assume the product itself will not be explosive.	(ATQ expert declaration)
Flammable gases	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	The product is water based; therefore, it is not	(ATQ expert)

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
			expected to release flammable gas	declaration)
Flammable aerosols	-	-	Not applicable	-
Oxidising gases	-	-	Not applicable	-
Gases under pressure	-	-	Not applicable	-
Flammable liquids	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	None of the components of the product are classified as flammable. Therefore, it is safe to assume the product itself will not be flammable.	(ATQ expert declaration)
Flammable solids	-	-	Not applicable	-
Self-reactive substances and mixtures	-	-	Not applicable	-
Pyrophoric liquids	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	The product is water based, therefore it is not expected to have pyrophoric properties.	(ATQ expert declaration)
Pyrophoric solids	-	-	Not applicable	-
Self-heating substances and mixtures	-	-	Not applicable	-
Substances and mixtures which in contact with water emit flammable gases	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	The product is water based, therefore it is not expected that in contact with water, release flammable gas.	(ATQ expert declaration)
Oxidising liquids	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	None of the components of the product are oxidising. Therefore, it is safe to assume the product itself will not be oxidising.	(ATQ expert declaration)
Oxidising solids	-	-	Not applicable	-
Organic peroxides	-	-	Not applicable	-

Property	Guideline and Method	Purity of the test substance (% (w/w))	Results	Reference
Corrosive to metals	UN-Test C.1	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	Not corrosive to steel (max weight loss 4.0% in 7 days) nor aluminium (max weight loss 0.5% in 7 days).	Report n° S30160 11253R 1 (2022)
Auto-ignition temperatures of products (liquids and gases)	-	PVP-Iodine: 2.5% (0.19-0.34% as I ₂)	None of the components of the product is self-igniting. Therefore, it safe to assume the product itself will not be self igniting.	(ATQ expert declaration)
Relative self-ignition temperature for solids	-	-	Not applicable	-
Dust explosion hazard	-	-	Not applicable	-

Conclusion on the physical hazards and respective characteristics of the product

MAMICAMP SELLADOR product (WG) has no oxidizing, no corrosive, no organic peroxides and explosive properties. Hence, the product does not require classification under Regulation (EC) No 1272/2008 for physical hazards.

2.2.4 Methods for detection and identification

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		
Active Substance (as available iodine)	volumetric thiosulphate method (European Pharmacopeia 5.0)	30-200% (6 measurements)	$y = 0.0441 + 0.9693 x$ ($R^2 = 0.9999$)	Not specific for I ₂	98-102%	100%	1%	n.d.	Report n° 16-4885-02 (2016)
Iodide	Pharmacopiea USP (*)	5-15 ml (6 measurements)	$y = 0.385x - 0.1083$ ($R^2 = 0.9997$)	Specific for Iodine/iodide	102-107%	105%	2%	n.d.	Report n° 21-4885-01 (2021)

n.d. = no data available

(*) U.S. Pharmacopeia National Formulary (USP XXII, L 27065, 1990), pg. 703.

Principle of method and LOQ:

El PVP-Iodine content is not directly determined but calculated from total available Iodine (I₂). Total available iodine content can be determined by various well-known methods such as volumetric thiosulphate method (European Pharmacopeia, 5th Edition). Samples are diluted with water and hydrochloric acid, and the available iodine obtained is volumetrically determined with sodium thiosulfate 0.1N. This method was validated according to SANCO/3030/99 rev.4

On the other hand, the available iodide is determined by the sequential titration method in which the free iodine is determined in the first part (titration with 0.1 N sodium arsenite) and then the free iodide is determined (0.05M potassium iodate titration), and all from the same initial aliquot of test product, according to Pharmacopeia USP. This method was validated according to SANCO/3030/99 rev.4 too.

Analytical methods for monitoring									
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
					Recovery	Mean	Standard Deviation		
Active Substance (as available iodine)	volumetric thiosulphate method (European Pharmacopeia 5.0)	30-200% (6 measurements)	$y = 0.0441x + 0,9693$ ($R^2 = 0.9999$)	Not specific for I_2	98-102%	100%	1%	n.d.	Report nº 16-4885-02 (24 months report)
Iodide	Pharmacopiea USP (*)	5-15 ml (6 measurements)	$y = 0.385x - 0.1083$ ($R^2 = 0.9997$)	Specific for Iodide	10-107%	105%	2%	n.d.	Report nº 21-4885-01

n.d. = no data available

(*) U.S. Pharmacopeia National Formulary (USP XXII, L 27065, 1990), pg. 703.

Conclusion on the methods for detection and identification of the product

According to guideline SANCO/3030/99 the analytical methods provided are fully validated for the determination of the active substance: PVP Iodine.

Concretely, adequate methodology exists for the determination of the active substance, as available Iodine (I_2) and iodide (I^-), in the biocidal product: The volumetric thiosulfate method for the determination of available iodine and the Pharmacopiea USP method for determination de iodide, in the biocidal product are validated.

Also, adequate methodologies exist for the determination of residues of the active substance (I_2) in air, soil, waters, human body fluids and tissues, and food and feeding stuff.

2.2.5 Efficacy against target organisms

2.2.5.1 Function and field of use

It is declared that the biocidal product contains PVP-Iodine to have available iodine in the range of 0.19-0.34%.

Field of use:

MG01: Disinfectants. PT3: Veterinary hygiene - Teat disinfection of milk producing animals

Indoor use

This product is used by professional users for disinfecting and sealing of the udder/teat hole after milking, providing a protective barrier against the entry of germs (bacteria and yeasts) into the udder through the teat hole.

Indicated for topical use in dairy cows, sheeps, goats and other lactating females.

The BP can be applied by dipping (manually or automatically) with an 10% v/v BP dilution in post-milking.

For manual dipping special dip cups are used.

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

The product is used to control bacteria, such as *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus uberis*, and yeast as *Candida albicans* in the post-milking process of lactating animals.

2.2.5.3 Effects on target organisms, including unacceptable suffering

The product is intended to produce a reduction in the number of viable bacterial cells (bactericidal activity) and of yeast cells (yeasticidal activity) of relevant test organisms under defined conditions according to the EN 1656 and EN 1657 (phase 2 step 1).

Since there is still no established a specific standard for teat disinfection in phase 2, step 2, the quantitative bactericidal and yeasticidal carrier test with artificial skin has been carried out according to the PR NF EN 17422:2019 pre-standard. The test method described by the draft standard PR NF EN 17422:2019 is based on the standard EN 16437, but takes into account the practical conditions of application of teat disinfectants.

The unacceptable suffering has not been possible to assess.

2.2.5.4 Mode of action, including time delay

Available iodine is the active form. It has a high germicidal power, even at low concentrations. The action of iodine is rapid and lasts several hours. It is combined with carbohydrates and bacterial lipids and oxidizes them (binds to C = C bonds of fatty acids). Also precipitates bacterial proteins and nucleic acids, thus killing the

microorganism. In proteins binds to N-H, S-H bonds and phenols, being the oxidation of S-H bonds very fast and irreversible.

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

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

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

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

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

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

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

2.2.5.5 Efficacy data

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test system / concentrations applied / exposure time	Test results: effects	Reference
Bactericide	Teat disinfection post-milking (PT3) Indoor	MAMICAMP SELLADOR (2.55% PVP Iodine)	Bacteria: <i>Escherichia coli</i> CECT 405 <i>Streptococcus uberis</i> CECT 994 <i>Staphylococcus aureus</i> CECT 239	EN 1656:2010	Phase 2 step 1 (suspension test) Concentrations tested: 80%; 10% and 6% (v/v) Temperature: 30°C Contact time: 5 minutes Soiling conditions: 10 g/l skimmed milk Criteria: at least a 5 log reduction	Bactericidal activity demonstrated at 10% (v/v)	2.2.5/ N° 150095861
Bactericide	Teat disinfection post-milking (PT3) Indoor	MAMICAMP SELLADOR (2.5% PVP Iodine = 0.28% Iodine)	Bacteria: <i>Escherichia coli</i> CECT 405 <i>Streptococcus uberis</i> CECT 994 <i>Staphylococcus aureus</i> CECT 239	PR NF-EN 17422: 2019	Phase 2 step 2 (carrier test) Concentrations tested: 50%, 10% and 0.01% (v/v) Temperature: 30°C Contact time: 5 minutes Soiling conditions: 10 g/l skimmed milk	Bactericidal activity demonstrated at 10% (v/v)	2.2.5/ D/21/B0494

					Test surface: VitroSkin® (human synthetic skin) Criteria: at least a 4 log reduction		
Yeasticide	Teat disinfection post-milking (PT3) Indoor	MAMICAMP SELLADOR (0.28% Iodine)	Yeast: <i>Candida albicans</i> CECT 1394	EN 1657:2016	Phase 2 step 1 (suspension test) Concentrations tested: 50%, 10% and 4% (v/v) Temperature: 30°C Contact time: 5 minutes Soiling conditions: 10 g/l skimmed milk Criteria: at least a 4 log reduction	Yeasticidal activity demonstrated at 10% (v/v)	2.2.5/ N° 210076620
Yeasticide	Teat disinfection post-milking (PT3) Indoor	MAMICAMP SELLADOR (2.5% PVP Iodine = 0.28% Iodine)	Yeast: <i>Candida albicans</i> CECT 1394	PR NF-EN 17422: 2019	Phase 2 step 2 (carrier test) Concentrations tested: 25%, 5% and 0.01% (v/v) Temperature: 30°C Contact time: 5 minutes Soiling conditions: 10 g/l skimmed milk Test surface: VitroSkin®	Yeasticidal activity demonstrated at 5% (v/v)	2.2.5/ D/21/B0495

					(human synthetic skin) Criteria: at least a 3 log reduction		
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Conclusion on the efficacy of the product

According to the Guidance on the Biocidal Products Regulation – Volume II Efficacy – Assessment and Evaluation (Parts B+C), veterinary biocidal products to disinfect teats should be at least sufficiently effective against bacteria and yeasts. Efficacy tests with these organisms should always be provided.

The biocidal product has a bactericidal and yeasticidal activity, that has been demonstrated according to the international European Standards EN 1656 and EN 1657 (phase 2, step 1), under specific test conditions for post-milking teat disinfectants.

Since there is still no established a specific standard for teat disinfection in phase 2, step 2, the quantitative bactericidal and yeasticidal carrier test with artificial skin has been carried out according to the PR NF-EN 17422:2019 pre-standard (Chemical disinfectants and antiseptics - Quantitative surface test for the evaluation of teat disinfectants used in the veterinary area - Test method and requirements (phase 2 step 2) under conditions suitable for post-milking disinfection, and similar to those used for the EN 1656 and EN 1657 standards, as agreed with the eCA.

The test method described by the draft standard PR NF EN 17422:2019 is based on the standard EN 16437 (Chemical disinfectants and antiseptics. Quantitative surface test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics used in veterinary area on porous surfaces without mechanical action. Test method and requirements (phase 2, step 2)), but takes into account the practical conditions of application of teat disinfectants, adapting the test conditions that may influence their activity in practical application, including the test surface, contact time and temperature.

The recommended post-milking modes of application are by dipping (without mechanical action).

MAMICAMP SELLADOR has been shown to be effective diluted at a 10% against bacteria *Escherichia coli* CECT 405, *Streptococcus uberis* CECT 994 and *Staphylococcus aureus* CECT 239, in the assay conditions established in the UNE-EN 1656:2010 (phase 2, step1), for post-milking teat disinfectants (30°C, 5 minutes of contact time and 10 g/l of skimmed milk as interfering substance), and also when is carried out the quantitative carrier tests according to PR NF-EN 14722:2019 (phase 2, step 2) with artificial skin, in the same conditions (at 30°C, 5 minutes of contact time and with 10 g/l skimmed milk as interfering substance).

In addition, this BP has been shown to be effective at a 10% dilution against the yeast *Candida albicans* CECT 1394 in the assay conditions established in the UNE-EN 1657:2016 (phase 2, step1), for post-milking teat disinfectants (30°C, 5 minutes of contact time and 10 g/l of skimmed milk as interfering substance), and at 5% dilution when is carried out the quantitative carrier tests according to PR NF-EN 14722:2019 (phase 2, step 2) with artificial skin, in the same conditions (at 30°C, 5 min. of contact time and with 10 g/l skimmed milk as interfering substance).

Concluding, the biocidal product MAMICAMP SELLADOR is considered to be effective as post-milking teat disinfectant from a 10% (v/v) dilution.

It is considered that using the product according to the conditions as stated in the SPC, the product will be effective.

2.2.5.6 Occurrence of resistance and resistance management

Taking into account the mode of action of iodine which is non-selective, development of resistance against iodine is unlikely. Iodine / iodophors have been used for over 170 years as disinfectants for a variety of applications. Such applications include disinfection of skin in the human hygiene and medical area but also skin of animals using teat dips as well as surfaces such as milk tanks. No reduction in efficacy was reported to the producers of iodine/iodophorbased products for such applications indicating that no development of resistant microorganisms or viruses has occurred

2.2.5.7 Known limitations

Not available.

2.2.5.8 Evaluation of the label claims

MAMICAMP SELLADOR is a post-milking teat disinfectant of dairy animals intended to apply by dipping cups without mechanical action.

The assessment of the disinfectant activity of the product demonstrated that it has a good level of efficacy at the dilution rate of 10% (v/v) as bactericide against *Escherichia coli*, *Streptococcus uberis* and *Staphylococcus aureus* and as yeasticide against *Candida albicans*.

(Please see efficacy tests summarized in point 6.7. of the IUCLID6 dossier).

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

MAMICAMP SELLADOR biocidal product is not intended to be use with other biocidal products.

2.2.6 Risk assessment for human health

Data of the active substance (a.s.) iodine were evaluated by the Rapporteur Member State (RMS) Sweden (RMS SE, 2013). No new data have been required. The following data on active substance issued from Iodine Assessment Report, Sweden, December 2013 (Iodine CAR) will be used for human health risk assessment:

Endpoint	Values
AEL	0.01 mg/kg bw/d
AEC inhalation	1 mg/m ³ (0.1 ppm)
Vapour Pressure (Pa) at 25°C	40.7 Pa at 25°C
Molecular weight (g/mol)	253.81 g/mol

Mamicamp Ordeño contains Iodine (CAS 7553-56-2) that is used in biocidal products for the disinfection of animals’ teats/udder and animal houses. In some products type 3, iodine is complexed with Polyvinylpyrrolidone (iodophor type 2).

An iodophor is a preparation containing iodine complexed with a carrier and/or a solubilizing agent, such as polycarbonic acids, surfactants or polymers as povidone (PVP,

Polyvinylpyrrolidone). In this way, a controlled release of iodine is accomplished. Iodine is an essential dietary trace element for mammals. It is required for the synthesis of the thyroid hormones, which control metabolism and play an important role in reproduction, growth and development.

2.2.6.1 Assessment of effects on Human Health

Not acute toxicity studies (oral, dermal, inhalation toxicity, skin and eye irritation/corrosion and skin sensitisation) have been performed for the biocidal product.

The classification of the product has been carried out according the classification of the components and the Regulation (CE) 1272/2012 on classification, labelling and packaging of substances and mixtures (CLP)

Skin corrosion and irritation

Data waiving	
Information requirement	Skin corrosion and irritation
Justification	The BP does not contain any component classified as skin corrosive, and contains 2.2% of PVP-Iodine, the only substance classified as Skin Irritant 2, with not specific concentration limit and, according the CLP Regulation criteria for classification of mixtures with the addition method, this BP is not classified as skin irritant because contains less than the generic concentration limit (10%). No classification is triggered for skin irritation.

Eye irritation

Data waiving					
Information requirement	Eye irritation				
Justification	The BP is classified according the CLP Regulation criteria, from components data, applying the additivity approach. The mixture has 2 components classified by their eye effects: <table border="0"> <tr> <td>Polyvinylpyrrolidone Iodine Eye Dam. 1</td> <td>2.5%</td> </tr> <tr> <td>Alcohol ethoxylate (C9-C11) Eye Dam. 1</td> <td>0.394%</td> </tr> </table> and is classified as Eye Dam.1 according to the formula: Σ Eye Effects Category 1 + Σ Skin Corrosive Category 1 \geq 3% $2.5\% + 0.394\% + 0 = 2.894 < 3\%$ Therefore, the BP is classified it as Eye Irrit. 2. (H319)	Polyvinylpyrrolidone Iodine Eye Dam. 1	2.5%	Alcohol ethoxylate (C9-C11) Eye Dam. 1	0.394%
Polyvinylpyrrolidone Iodine Eye Dam. 1	2.5%				
Alcohol ethoxylate (C9-C11) Eye Dam. 1	0.394%				

Respiratory tract irritation

Data waiving	
Information	Respiratory tract irritation

requirement	
Justification	Regarding the content of a.s and co-formulants, and according to the classification rules laid down in the CLP regulation, no classification is required for respiratory tract irritation.

Skin sensitization

Data waiving	
Information requirement	Skin sensitization
Justification	Regarding the content of a.s and co-formulants, and according to the classification rules laid down in the CLP regulation, no classification is required for skin sensitization.

Respiratory sensitization (ADS)

Data waiving	
Information requirement	Respiratory sensitization
Justification	No animal or human data have been provided to assess the potential for respiratory sensitization. Regarding the content of a.s and co-formulants, and according to the classification rules laid down in the CLP regulation, no classification is required for respiratory sensitization.

Acute toxicity

Value used in the Risk Assessment – Acute oral toxicity	
Value	DL ₅₀ >2000mg/kg bw
Justification for the selected value	<p>The BP is classified according the CLP Regulation criteria, from components data: Iodine is not classified for acute oral toxicity. Alcohol ethoxylate (C9-C11) (DL50 oral: 1400 mg/kg), at 0.394%</p> <p>The Acute Toxicity Estimation for the mixture (ATE_{mix}) is calculated according to the formula:</p> $\frac{100}{ATE_{mix}} = \sum_{i=1}^n \frac{C_i}{ATE_i}$ <p style="text-align: right;"> $\frac{100}{ATE_{mix}} = \frac{0.394}{1400}$ $ATE_{mix} = 14000$ </p> <p>Were: C_i = concentration of component i (% w/w o % v/v) i = individual component, varying i from 1 to n (number of components in mixture) ATE_i = Acute Toxicity Estimation of component i. ATE_{mix} = Acute Toxicity Estimation of the mixture.</p>

	And Result: $ATE_{mix} = 355329.9 > 2000 \rightarrow$ the BP is NOT classified for oral acute toxicity
Classification of the product according to CLP and DSD	MAMICAMP SELLADOR is not classified following criteria of the Regulation (EC) N° 1272/2008 (CLP Regulation).

Data waiving	
Information requirement	Oral acute toxicity
Justification	Not necessary. The BP is not classified as Oral Acute Toxic, according the addition method of CLP Regulatory for mixtures, from components data, because the $ATE_{mix} > 2000$.

Acute toxicity by inhalation

Value used in the Risk Assessment – Acute inhalation toxicity	
Value	CL ₅₀ : >5mg/l
Justification for the selected value	<p>Acute toxicity by inhalation studies with the biocidal product. have not been conducted. Iodine is subject to harmonised classification and labelling. According to annex VI of CLP Regulation, iodine is classified for acute inhalation toxicity as Acute tox 4*; H332. The co-formulants are not classified for acute toxicity by inhalation.</p> <p>The Acute Toxicity Estimation for the mixture (ATE_{mix}) is calculated according to the formula:</p> $\frac{ATE_{mix}}{100} = \frac{\sum C_i ATE_i}{\sum ATE_i}$ <p style="text-align: center;"> $\frac{ATE_{mix}}{100} = \frac{1.5}{100} = 0.015$ </p> <p style="text-align: right;">0.34 %</p>
Classification of the product according to CLP and DSD	MAMICAMP SELLADOR is not classified following criteria of the Regulation (EC) N° 1272/2008 (CLP Regulation).

Data waiving

Information requirement	Inhalation acute toxicity
Justification	Regarding the content of a.s and co-formulants, and according to the classification rules laid down in the CLP regulation, no classification is required for inhalation acute toxicity

Acute toxicity by dermal route

Value used in the Risk Assessment – Acute dermal toxicity	
Value	DL ₅₀ : >2000mg/kg bw
Justification for the selected value	<p>Acute dermal toxicity studies with the biocidal product. have not been conducted.</p> <p>Iodine is subject to harmonised classification and labelling. According to annex VI of CLP Regulation, iodine is classified for acute dermal toxicity as Acute tox 4*; H312. The co-formulants are not classified for acute dermal toxicity.</p> <p>The Acute Toxicity Estimation for the mixture (ATE_{mix}) is calculated according to the formula:</p> $\frac{ATE_{mix}}{100} = \frac{\sum_{i=1}^n C_i \cdot ATE_i}{100}$ <p style="text-align: center;"> ATE_{mix} ATE_{mix} ATE_{mix} ATE_{mix} </p> <p style="text-align: center;"> 0 110 0 0.34 % </p> <p>Were: C_i = concentration of component i (% w/w o % v/v) i = individual component, varying i from 1 to n (number of components in mixture) ATE_i = Acute Toxicity Estimation of component i. ATE_{mix} = Acute Toxicity Estimation of the mixture.</p> <p>And Result: ATE_{mix} = 323530 > 2000 mg/kg bw → the BP is NOT classified for dermal acute toxicity</p> <p>The concentration of iodine in the biocidal product is 0.19% and 0.34% w/w in the form of 2.55% PVP-I, using the criteria for classifying mixtures under CLP Regulation, the calculation of ATE_{mix} for dermal toxicity results in >2000mg/kg bw and no classification is triggered.</p>
Classification of the product according to CLP	MAMICAMP SELLADOR is not classified following criteria of the Regulation (EC) N° 1272/2008 (CLP Regulation).

Data waiving	
Information requirement	Dermal acute toxicity

Justification	Regarding the content of a.s and co-formulants, and according to the classification rules laid down in the CLP regulation, no classification is required for dermal acute toxicity.
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Information on dermal absorption

An in vitro skin penetration study, in order to obtain the percutaneous absorption rate of total iodine from two biocide formulations, Biocide 1006 (a concentrate PB of 2.63% Iodine to dilute 4 times until 0.66% of Iodine concentration) and PE 305-1 (a ready-to-use solution containing PVP-iodine, with a 0.26% total iodine content, similar to MAMICAMP SELLADOR), through human (split-thickness) skin membranes was presented by the Iodine Registration Group for the approval of this AS

This study concludes that the mean total absorption was 11.3%-12% total iodine of the dose applied for the biocidal formulations tested considering the amounts of iodine found in the receptor fluid, the receptor compartment wash, the skin membranes, and levels 3-15 of the tape strips.

Based on these results, a dermal penetration rate of 12% could be used for the human health exposure assessment and the subsequent risk characterisation, and it is considered unnecessary to perform the dermal absorption assay with the BP.

Value used in the Risk Assessment – Dermal absorption	
Substances	Iodine
Value	12%
Justification for the selected value	According to the Swedish CAR for the active substance Iodine (including PVP-I), using the data obtained in the dermal absorption studies, the dermal absorption was estimated to 12%.

Data waiving	
Information requirement	Dermal absorption assay
Justification	No study on dermal absorption has been provided for MAMICAMP SELLADOR. The active substance dossier on iodine (incl. PVP-iodine) (Sweden 2013), includes a human skin <i>in-vitro</i> dermal absorption study (De Ligt, 2009), in which two iodine-based biocidal products have been investigated. Both products are different from the compositional point of view and contain a different iodine concentration. The results of the two dermal absorption studies demonstrated that regardless of iodophor type (i.e. alcohol ethoxylate-complexed iodine or PVP-iodine) and type and concentration of co-formulants, the dermal absorption of total iodine was ca. 12%. On the other hand, although the formulation contains one co-formulant that is irritating or corrosive to the skin, it is below its specific classification limit, so MAMICAMP SELLADOR is not classified with regards to skin irritation properties. Therefore, no impact on the skin integrity and on the dermal absorption of iodine from the biocidal product is expected. In addition, only alcohol etoxylate is

	classified for eye damaging effect which causes the classification of MAMICAMP SELLADOR as H319, however, it is present at lower level compared to the tested formulation in the CAR. For these reasons, a dermal absorption of 12% will be used for the calculation of human health exposure.
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Endocrine Disruption

In accordance with Article 15(2) 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 review of approval of the active substance iodine and polyvinylpyrrolidone iodine.

According to the Commission Delegated Regulation (EU) No 2017/2100, a substance is identified as having endocrine-disrupting properties with respect to humans if it meets the following three criteria

it shows an adverse effect in an intact organism or its progeny;
it has an endocrine mode of action, i.e., it alters the function(s) of the endocrine

system; and

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

Iodine, in excess of physiological needs, meets all the above three criteria – it shows adverse effects (thyroid disorders) in humans; it has an endocrine mode of action (disruption of thyroid hormones metabolism and hypothalamic-pituitary-thyroid axis); and the adverse effects are a consequence of the endocrine mode of action. Therefore, the biocidal active substances, iodine and PVP-iodine, are identified as having endocrine-disrupting properties with respect to humans.

Assessment of the ED properties of non-active substances (co-formulants):

After reviewing the potential ED properties of co-formulants (please refer to the Confidential Annex), none of them are subject to an on-going evaluation or a decision regarding their ED properties. Based on the available information, ES CA considers that there is no concern regarding the ED properties of these co-formulants.

According to the document agreed at the CG-49 meeting on Criteria – significant indications of ED properties for non-active substances at present, non-active substances contained in the biocidal product MAMICAMP SELLADOR should not be considered as having significant indication of ED properties.

Overall conclusion on the biocidal product regarding ED properties:

The biocidal product contains an active substance with endocrine disrupting properties.

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

Not relevant

Available toxicological data relating to a mixture

Not relevant

Other

Specific target organ toxicity, repeated exposure (STOT RE)

Value used in the Risk Assessment – STOT RE	
Justification	For Iodine a concern for specific target organ toxicity was identified. According to database of registered substances under REACH in ECHA website, the Iodine REACH consortium has proposed a classification for Iodine with STOT RE (thyroid gland), category 1 (H372). In line with other biocides dossier evaluations, this classification and the generic concentration limit for mixture classification (if the concentration is $\geq 1\%$ →STOT RE 2; H373
Classification of the product according to CLP	Regarding the content of Iodine, and according to the classification rules laid down in the CLP regulation, no classification is required for Specific target organ toxicity, repeated exposure (STOT RE).

2.2.6.2 Exposure assessment

MAMICAMP SELLADOR is a ready to use water soluble gel, containing 2.5% w/w PVP-Iodine, equivalent to 0.19-0.34% w/w of available Iodine. This product is intended to be used by professionals workers to disinfect teats of cows, ewes and goats, manually or automatically, as follows:

Post-milking with the RTU product in dipping cups, and an application dose of 1 ml/teat/event, in 2 events/day for manual milking or 3 events/day for automated milking systems.

After milking, remove all organic debris from teats with a disposable paper or towel before do **post-milking teat dipping disinfection**: Cover the entire teat with dip cup containing 10-20 ml of pure BP (one cup with 20 ml is needed to approximately 5-6 cows). Once the teats are dipped, the operator slightly moves the teats to allow the formation of a droplet on the sphincter at the basis of the teat. This is the crucial place to be protected since it is the entry point of the contaminants. It is needed keep the cows in the milking parlour and let the product dry on the udder, making sure that the animal does not lie down until the product has dried, at least 5 min (contact time), or more if possible. This PB has been designed to be viscous in order to avoid dripping and possible splashing after its application.

The frequency of application is: 2 applications per day (manually) or 3 applications per day (automatically) for dairy cows, and 1 application per day for ewes or goats. We will consider the worst-case scenario for the Exposure Assessment: 2 events for manual application and 3 events for automated applications.

The container of the cup is filled with 500 ml of BP, the cap or cup is screwed and the cup is filled with 10-20 ml of BP by manual pressure, as the cup is emptied.

See below photos of the tasks of disinfection post-milking



We will consider the worst-case scenario for the Exposure Assessment: a concentration of AS in BP of 0.34% as I₂ (w/w), 1 ml/teat x 4 teats/cow (4 ml BP/cow) and 2 times/day (manually) or 3 times/day (automatically).

Introductory note on the transferability of the following exposure assessment to buffaloes, sheep and goats

The following exposure assessment is performed for the use in dairy cows. The teat disinfection of dairy cows is an important use of the product, but not limited to this use. The products can also be used for the disinfection of the teats of buffaloes, sheep and goats.

The following exposure assessment for cows also covers the use in buffaloes, sheep and goats because:

Buffaloes: equal to dairy cows, buffaloes have four teats. The application rates per animal and milking are equal to dairy cows. Buffaloes are only milked two times a day. Consequently, the exposure of the milker to iodine teat disinfectants per day is equal or even lower in the case of buffaloes than for cows (assuming a herd with the same number of animals and the same milking techniques).

Sheep and goats: these animals have only two teats per animal and they are only milked 1-2 times per day.

It is therefore concluded that the exposure of a milker of dairy cows covers the exposure of a milker of buffaloes, sheep and goats.

General considerations:

The exposure assessment has been performed considering 0.34% of available iodine.

The exposure assessments are based on model calculations using models and default values from the HEAdhoc Recommendation no. 13 (Jan. 2017) – “Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3)”.

As a first step, exposure assessments are performed for all individual scenarios (work tasks: loading of the product, application by dipping cups or robot, and cleaning) which are relevant for teat disinfection (see table “list of scenarios” below). In a second step, the exposure calculated for the individual work tasks are combined.

In line with HEAdhoc Recommendation no. 13 (Jan. 2017), it is considered that the default value for a dairy cow herd size is 100 animals (ESD for PT3, Jan. 2012) and that

dairy cows are regularly milked twice per day. Taking into account the lactation period for dairy cows (i.e. 270-300 days), 82 milk producing cows from a herd size of 100 dairy cows are milked per day (100 cows x 300/365 = 82 cows). **For higher animal numbers or more milkings per day, an additional milker is needed.**

Farmers are likely to apply the product themselves and are considered to be professional users for this type of product i.e. they are used to handling these product types regularly, they have access to relevant safety information and they can be expected to wear personal protective equipment (PPE) when handling the products. The protection factors for personal protective equipment (PPE) used for the exposure assessments are defaults from the HEEG opinion 9, agreed in TM I 2010 "Default protection factors for protective clothing and gloves".

Explanatory note:

According to national legislation, in Spain there are three user categories:
 Trained professional users (TP): pest control operators, having received specific training in biocidal product uses according to the national legislation in force.
 Professional users (P): professionals that use the biocidal products in the context of his profession, that is not pest control operator, and that are unlikely to have received any specific training in biocidal product use according to the national legislation in force. It can be expected that they have some knowledge and skills handling chemicals (if they must use it in their job) and they are able to use correctly some kind of PPE if necessary.
 Non-professional users (NP): users who are not professionals and that apply the biocidal product is in his private life. (Note: this user has not been claimed by the applicant for this product).

The conclusions reached in this PAR, which affect the intermediate category of "Professional", will only be applicable at the Spanish level.

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.	No	n.a	n.a.	No	No	No
Dermal	n.a.	Yes	n.a	n.a.	No	No	No
Oral	n.a.	No	n.a	n.a.	No	No	Yes

"n.a." (not applicable)

Inhalation exposure is not assessed, since due to the application method aerosol formation is not expected. In addition, according to the agreed in HH-WG IV-2017, as the active substance is complex-bound, evaporation is not considered relevant. Primary oral exposure is ruled out for professional users.

List of scenarios

Summary table: scenarios for post-milking disinfection by dipping			
Scenario number	Scenario	Primary or secondary exposure Description of scenario	Exposed group
1.1	Manual mixing and loading of RTU product for dip cup	Primary exposure: the product (RTU) is filled undiluted into the reservoir of a dip cup. By squeezing the reservoir, the disinfectant is pumped into the dip cup above the reservoir which is then ready for dipping.	Trained professional & professional
1.2.	Mixing and loading of RTU product for automated dipping-system	Primary exposure: a can containing the RTU product is opened and a suction tube of the automated dipping-system is inserted. Empty cans are replaced by new ones.	
2.1	Application of teat disinfectant by manual dipping	Primary exposure: after milking, the dip cup prepared as described in scenario 1.1 is put over each teat from below making sure that the full length of each teat is immersed into the disinfectant.	
2.2	Application of teat disinfectant by automated dipping-system	Primary exposure: after milking, the vacuum is shut off and the teat dip is injected into a manifold on the clawpiece. The teats are coated with dip.	
3.1	Cleaning of manual equipment (dip cups) after use	After disinfection, the reservoir is emptied and the entire dip equipment is cleaned with water. Only a small amount of diluted product remains in the application equipment, however, this will be highly diluted by the wash-water.	
3.2	Cleaning of automated dipping-system	Rinsing of automated dipping-system after disinfection	
4.	Cleaning of teats: removal of dried residues from post-milking treatment	Cleaning of teats by wiping with a dry cloth before milking is only relevant if the cows have received a post-milking treatment. The disinfectant is expected to have completely dried up and either fallen off or rubbed off during the time span between treatment and cleaning. Therefore, any exposure to remains of the disinfectant on the teats is considered to be negligible.	

Industrial exposure

No industrial use is foreseen for the product MAMICAMP SELLADOR. Therefore, the assessment of industrial exposure is not relevant.

Professional exposure

Scenario [1.1]: mixing and loading of RTU for dip cup

Description of Scenario [1.1] – Mixing and loading of RTU for dip cup		
<p>The product (RTU) is filled undiluted into the reservoir of a dip cup. By squeezing the reservoir, the disinfectant is pumped into the dip cup above the reservoir which is then ready for dipping.</p> <p>In line with HEAdhoc Recommendation no. 13 (Jan. 2017) – “Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3)” - for mixing and loading of RTU products M/L model 4 is recommended for repeated loading of small quantities. This guidance document states that the indicative value should be used based on the total amount of required solution/day.</p> <p>For the dermal exposure, the total amount of the required solution that is needed per day is of importance, and according to this amount, the model provides indicative hand exposure values of 0.01 ml/treatment for handling 1 l, 0.2 ml/treatment for handling 5 l and 0.5 ml/treatment for handling 10 L and 20 L.</p> <p>The applicant has given a maximum application rate of 4 ml of in-use solution/cow/treatment. Cows are milked 2x per day per farmer when considering manual application. As the product can be applied only post-milking to a herd size of 82 cows, the total amount of the RTU product per day can be calculated as 4 ml x 82 cows x 2 times/day = 0.656 l.</p> <p>Thus, for dermal (hand) exposure, handling of volumes of up to 1 l of the RTU product is considered worst-case, resulting in an indicative value of 0.01 ml/treatment.</p> <p>Inhalation exposure is not assessed, since aerosol formation is not expected. In addition, as the active substance is complex-bound, evaporation is not considered relevant.</p> <p>The model covers all relevant mixing and loading tasks performed by a worker on an 8-h working day. Thus, re-filling of the equipment with the RTU product is covered within the mixing and loading step and does not need to be assessed separately.</p>		
	Parameters	Value
Tier 1	Total iodine (active substance in the BP)	0.34%
	Dermal penetration	12%
	Body weight	60 kg
	Indicative value for hand exposure (for handling of product volumes up to 1 l)	0.01 ml/treatment
	No PPE	0% protection
	Density of the product	1.0261 g/ml
Tier 2	Gloves	90% protection

Calculations for Scenario [1.1]

In the following, the results of the calculations are provided for scenario 1.1

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 [1.1]	Tier 1/ No PPE	-	6.98E-5	-	6.98E-5
Scenario [1.1]	Tier 2/ Gloves	-	6.98E-6	-	6.98E-6

The calculation sheets are provided in Anexo 3.2.

Further information and considerations on scenario [1.1]

As we will see, the quantitative risk for this scenario is acceptable without PPE.

Combined scenarios

This scenario 1.1 combines with the scenarios 2.1-3.1 & 4, although exposure in scenarios 2.1 and 4 is irrelevant.

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)
Scen [1.1]/ No PPE	-	6.98E-5	-	6.98E-5
Scen [1.1]/ Gloves	-	6.98E-6	-	6.98E-6
Scen [2.1]	-	-	-	-
Scen [3.1]/ No PPE	-	6.26E-5	-	6.26E-5
Scen [3.1]/ Gloves	-	6.26E-6	-	6.26E-6
Scen [4]	-	-	-	-
Scen / No PPE 1.1+2.1+3.1+4	-	1.32E-4	-	1.32E-4
Scen / Gloves 1.1+2.1+3.1+4	-	1.32E-5	-	1.32E-5

Scenario [1.2]: Mixing and loading for automated dipping-system in robotic milking device

Description of Scenario [1.2]. Mixing and loading for automated dipping-system		
<p>If robotic milking device is used, a can containing the RTU product is opened and a suction tube of the automated dipping-system is inserted. The exposure duration of 1 min per operation. It is expected that this operation will be carried out only once a day, but as a worst case we have assumed that it is carried out by the same operator in each milking event, setting a maximum of 3 milkings per day for an automated device.</p> <p>According to the HEAdhoc Recommendation no. 13 (Jan. 2017), the RISKOFDERM toolkit for connecting lines is recommended for automated mixing and loading with an indicative value of 0.92 mg/min for dermal exposure.</p> <p>Inhalation exposure is not assessed, since aerosol formation is not expected. In addition, as the active substance is complex-bound, evaporation is not considered relevant.</p>		
	Parameters	Value
Tier 1	Total iodine (active substance in the BP)	0.34%
	Dermal penetration	12%
	Body weight	60 kg
	Indicative value for dermal exposure	0.92 mg/min

	Exposure duration per event	1 min/event
	Events per day (automated milking)	3 events/d
	No PPE (Penetration)	100%
Tier 2	PPE (Gloves penetration)	10%

Calculations for Scenario [1.2]

In the following, the results of the calculations are provided for scenario 1.2

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 [1.2]	Tier 1/ No	-	1.88E-5	-	1.88E-5
Scenario [1.2]	Tier 2/ Gloves	-	1.88E-6	-	1.88E-6

The calculation sheets are provided in Annexo 3.2.

Further information and considerations on scenario [1.2]

As we will see, the quantitative risk for this scenario is acceptable without PPE.

Combined scenarios

This scenario 1.2 combines with the scenarios 2.2-3.2 & 4, but exposure in each of them is irrelevant.

Scenario [2.1]. Application of teat disinfectant by manual dipping

Description of Scenario [2.1] – Application by manual dipping
<p>After milking, the dip cup prepared as described in scenario 1.1 is put over each teat from below making sure that the full length of each teat is immersed into the disinfectant.</p> <p>Dermal exposure during use of the cup is not expected based on the design of the dipping cup. This kind of cup has an upper compartment for application of the dip cup and a lower compartment as a reservoir for the dipping solution. During the application, the worker holds the cup at the lower compartment. Thus, direct hand exposure to the product or treated teat is avoided. Based on the HEAdhoc Recommendation no. 13 (Jan. 2017), any possible spillage is considered covered by the dermal exposure as calculated by the scenario of mixing and loading. As such, no further consideration of cow teat disinfection through dipping is required.</p>

Calculations for Scenario [2.1]

No exposure is expected in this scenario.

Scenario [2.2]. Application of teat disinfectant by automated dipping

Description of Scenario [2.2] – Application by automated dipping
<p>This scenario was not considered in the CAR, but according to HEAdhoc Recommendation no. 13 (Jan. 2017), no exposure estimate required for automated applications (by robot). Therefore, no exposure of professionals occurs.</p>

Calculations for Scenario [2.2]

No exposure is expected in this scenario.

Scenario [3.1]. Cleaning of manual equipment (dip cups) after use

Description of Scenario [3.1] – Cleaning of manual equipment after use		
<p>After disinfection, the reservoir is emptied and the entire dip is cleaned with water. A small amount of product will remain in the application equipment; however this will be highly diluted by the wash-water. Therefore it is concluded that exposure during cleaning of application equipment is lower in comparison to the exposure during mixing and loading and application operations.</p> <p>Due to the lack of appropriate exposure model for the scenario “cleaning of equipment”, the model RISKOFDERM toolkit, Connecting lines is used as a surrogate model according to the HEAdhoc Recommendation no. 13 (Jan. 2017) using indicative model value for hand exposure of 0.92 mg/min.</p> <p>Inhalation exposure is not assessed, since aerosol formation is not expected. In addition, as the active substance is complex-bound, evaporation is not considered relevant.</p> <p>The duration of this task is considered to be 5 min.</p> <p>It is expected that this operation will be carried out only once a day but, as a worse case, it is assumed that the cleaning step is performed after each milking event (twice per day).</p>		
	Parameters	Value
Tier 1	Parameters	Value
	Total iodine (active substance in the BP)	0.34%
	Dermal penetration	12%
	Body weight	60 kg
	Indicative value for dermal exposure	0.92 mg/min
	Exposure duration per event	5 min/event
	Events per day (automated milking)	2 events/d

	No PPE (Penetration)	100%
Tier 2	PPE (Gloves penetration)	10%

Calculations for Scenario [3.1]

Summary table: estimated exposure from professional uses					
Exposure scenario	Tier/PP E	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 [3.1]	Tier 1/ No PPE	-	6.26E-5	-	6.26E-5
Scenario [3.1]	Tier 2 / Gloves	-	6.26E-6	-	6.26E-6

The calculation sheets are provided in Annexo 3.2.

Further information and considerations on scenario [3.1]

As we will see, the quantitative risk for this scenario is acceptable without PPE.

Combined scenarios

Please, see combined scenarios in scenario 1.1

Scenario [3.2]. Rinsing of automated dipping-system

Description of Scenario [3.2] – Rinsing of automated dipping-system

This scenario was not considered in the CAR
Every liner of the automated dipping-system is thoroughly rinsed with water and blown out with compressed air. Afterwards, the milking system is ready for the next milking event. The whole process is automated and, therefore, there is no human exposure.

Calculations for Scenario [3.2]

No exposure is expected in this scenario.

Scenario [4]. Removal of dried disinfectant residues from post-milking treatment

Description of Scenario [4] - Removal of dried residues from treatment

This work step was not considered in the CAR.
According to the HEAdhoc Recommendation no 13, after a post-milking treatment, the disinfectant is expected to have completely dried up and either fallen off or rubbed off during the time span between treatment and cleaning. Therefore, any exposure to remains of the disinfectant on the teats is considered to be negligible.

Calculations for Scenario [4]

No exposure is expected in this scenario.

Non-professional exposure

The product is intended for professional use only, and no non-professional exposure is foreseen. Therefore, the assessment of non-professional exposure is not relevant.

Exposure of the general public

The general public does not have access to the milking parlour. Therefore, no general public primary or secondary exposure is foreseen.

Monitoring data

There is no monitoring data available for this product.

Dietary exposure

Iodine is essential for life and it can be consumed from many different sources. 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. For this reason the mean exposure to iodine from the rest of the diet has also been presented.

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. According to the European Scientific Committee on Food, the most important sources of iodine in industrialised countries are dairy products. More recently, calculations by EFSA confirm that for both adults and toddlers, milk is by far the main source of iodine, but the total iodine level in milk vary greatly between different regions in Europe.

Dietary exposure is discussed in various human health working group meetings and WebEx meetings for evaluating various iodine based union authorisations application. For the exposure to residues, the O'Brien study can be used. The assumptions that could be considered for the exposure to residues via milk were that needs to be considered are included below:

Exposure in accordance to intended use (WGIII 2017).

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".

Take into account a density of 1.03 kg/L for whole milk (Ullmanns's Food and Feed, 3 Volume set. (Elvers, B. (2017). 1st ed. Weinheim, Germany: Wiley-VCH, page 344).

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 the calculations, information from the O'Brien study was used. The O'Brien study assessed the effect of a teat disinfection product is used, based on 0.5% available iodine on the total iodine content in milk. Therefore, the measured residues in milk are from the O'Brien study need to be corrected for our case (0.34% available iodine), which is included below.

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." (See WG V 2017).

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. (See WG V 2017).

Consumers are exposed to residues of iodine due to various sources. 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.

Based on the details above the following three theoretical intakes will be calculated and evaluated:

Iodine intakes resulting from only the proposed teat treatment.

Iodine intakes from milk (sum of; the proposed teat treatment + background levels in milk (200 µg/L)).

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

The estimated dietary intakes of iodine have been compared to the relevant UL for adults (600 µg/day) and infants (200 µg/day)

List of scenarios for dietary exposure

Summary table of main representative dietary exposure scenarios		
Scenario number	Description of scenario	Subject of exposure
5.	Residual exposure from teat treatment	Adults Toddlers
6.	Exposure from total milk intake	Adults Toddlers
7.	Exposure from total dietary intake	Adults Toddlers

Scenario 5. Residual exposure from teat treatment

The residual level of iodine due to teat disinfection was investigated by O'Brien study et al (2013). The effect of milk iodine concentrations of a teat disinfectant containing 0.5 % iodine and applied post- or pre- and post-milking were investigated in this survey. Another objective of this study was to quantify combined effects of teat disinfection and dietary supplementation of iodine. Feed fortification levels tested were 30 mg and 70 mg per cow per day. In this evaluation, only the results of the teat disinfection without considering the influence of iodine supplementation by feed are presented. The results of the study have been presented in following Table:

Study	Iodine (%)	Applications	Mean treated residue (µg/kg)	Mean control residue (µg/kg)	Difference (additional iodine residues in milk) (µg/kg)
O'Brien 2013*	0.5	2x post milking	461	217	244

O'Brien, B., Gleeson, D. and Jordan, K. (2013): Iodine concentrations in milk. Irish Journal of Agricultural and Food Research 52

For the control group, in which cows were treated with non-iodine teat disinfectant and 0 mg iodine/day feed supplementation, a 'baseline' of 217 µg/kg iodine in milk was established. This is equivalent to 224 µg/L based on the density of whole milk (1030 g/L).

Therefore, from data of O'Brien, 244 µg/kg is the theoretical additional residues after post-milking teat disinfection; this value has been calculated by subtracting the iodine level of the control group (217 µg/kg) from the residue level after post-milking treatment (461 µg/kg). The value 244 µg/kg is used as a starting point for extrapolation to the product concentration of 0.34%:

Additional iodine residues in milk due to treatment with Mamicamp Sellador:

$$244 \mu\text{g/Kg} \times (0.34/0.5) = 165.9 \mu\text{g I/Kg milk}$$

Based on the density of whole milk (1.03 Kg/L):

$$165.9 \mu\text{g/Kg} \times 1.03 \text{ Kg/L} = 170.9 \mu\text{g I/L milk}$$

The daily milk consumption is 0.45 L/day for adults and 0.46 L/day for infant/toddlers. Therefore, the iodine intakes resulting from only the proposed teat treatment are:

Adults: $170.9 \mu\text{g I/L} \times 0.45 \text{ L/d} = \mathbf{76.9 \mu\text{g I/d}}$

Toddlers: $170.9 \mu\text{g I/L} \times 0.46 \text{ L/d} = \mathbf{78.6 \mu\text{g I/d}}$

Considering the Upper Intake Level (UL): 600 µg/d for adults and 200 µg/d for toddlers:
Percentage UL = (76.9/600) x 100 = 12.82% adult
Percentage UL = (78.6/200) x 100 = 39.31% toddler

Scenario 6. Exposure from total milk intake

The value of 200 µg/L iodine in milk is the background milk:
 Adult: 200 µg/L x 0.45 L/d = 90 µg I/d
 Toddler: 200 µg/L x 0.46 L/d = 92 µg I/d

Total iodine intakes from milk is the sum of the residual exposure from teat treatment + background levels in milk. Therefore:

Adults: 76.9 µg I/d + 90 µg I/d = **166.9 µg I/d**
Toddlers: 78.6 µg I/d + 92 µg I/d = **170.61 µg I/d**

Considering the Upper Intake Level (UL): 600 µg/d for adults and 200 µg/d for toddlers:
Percentage UL = (166.9/600) x 100 = 27.82% adult
Percentage UL = (170.61/200) x 100 = 85.31% toddler

Scenario 7. Exposure from total dairy intake

Iodine dietary intake from other sources than milk was set:
 185 µg/day for adults
 96 µg/day for toddler.

Total iodine intakes from all dietary sources is the sum of the proposed teat treatment + background levels in milk (200 µg/L) + mean intake associated with other dietary sources:

Adults: 76.9 µg I/d + 90 µg I/d + 185 µg I/d = **351.9 µg I/d**
Toddlers: 78.6 µg I/d + 92 µg I/d + 96 µg I/d = **266.61 µg I/d**

Considering the Upper Intake Level (UL): 600 µg/d for adults and 200 µg/d for toddlers:
Percentage UL = (351.9/600) x 100 = 58.65% adult
Percentage UL = (266.61/200) x 100 = 133.31% toddler

As we can see, the total daily intake for toddlers exceeds the upper limit value, representing 133.31%.

Summary table of other (non-biocidal) uses			
	Sector of use	Intended use	Reference value(s)
1.	Veterinary use	Veterinary medicine as antiseptics and sanitisers (reduction of mastitis,	"No MRL required" for all target tissues according to Commission Regulation (EU) No 37/2010. (EMA) ¹

		prevention of infections in wounded, etc)	
2.	Food additives	Fortification of food (iodised salt)	The amount of iodine added varies from 10-75 mg/kg salt with a majority of values in the range of 15-30 mg/kg, according to EFSA NDA Panel, 2014, Scientific Opinion on Dietary Reference Values for iodine, EFSA Journal 2014; 12(5);3660 (doi:10.2903/j.efsa.2014.3660)
3.	Feed additives	Supplementation of animal feed	Dairy cows: 5 mg I/kg of complete feeding stuff according to Commission Regulation (EC) No 1459/2005 of 8 Sept. 2005 2 mg I/kg recommended according to EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Scientific opinion on the safety and efficacy of iodine compounds (E2) as feed additives for all animal species [...], EFSA Journal 2013; 11(2):3099 (doi:10.2903/j.efsa.2013.3099)

Information of non-biocidal use of the active substance

¹ European Agency for the Evaluation of Medical Products (EMA). Iodine report from Committee for Veterinary Medical Products

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

A direct exposure of animals is determined for Mamicamp Sellador, since it is a topical product applied to the teats.

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. Calculations on residues in milk presented in the dietary assessment are therefore covering potential residues in meat and considered as sufficient for the product.

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

Mamicamp Sellador is not used in a manner which may cause direct contact with food. Calculations for estimating dietary exposure via residues in milk have been provided above.

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

Not required since Mamicamp Sellador is not intended to be used by non-professionals.

Exposure associated with production, formulation and disposal of the biocidal product

Exposure during production and formulation of a biocidal product is not assessed under the requirements of the BPR (Regulation No. 528/2012).

Aggregated exposure

Although iodine is released from multiple sources, aggregated exposure is not assessed since a respective methodology is not available yet.

Summary of exposure assessment

Scenarios and values to be used in risk assessment			
Scenario number	Exposed group	Tier/PP E	Estimated total uptake (mg/kg bw/d)
1.1 - Manual mixing and loading of RTU product for dip cup	Trained professional & Professional	1 / No PPE	6.98E-5
		2 / Gloves	6.98E-6

1.2 - Mixing and loading of RTU product for automated dipping-system	Trained professional & Professional	1 / No PPE	1.88E-5
		2 / Gloves	1.88E-6
2.1 - Application of teat disinfectant by manual dipping	Exposure is covered by scenario 1.1		-
2.2 - Application of teat disinfectant by automated dipping-system	Exposure is considered irrelevant		-
3.1 - Cleaning of manual equipment (dip cups) after use	Trained professional & Professional	1 / No PPE	6.26E-5
		2 / Gloves	6.26E-6
3.2 - Cleaning of automated dipping-system	Exposure is considered irrelevant		-
4 - Cleaning of teats: removal of dried residues from post-milking treatment	Exposure is considered irrelevant		-
Combined: 1.1 + 3.1	Trained professional & Professional	1 / No PPE	1.32E-4
		2 / Gloves	1.32E-5

2.2.6.3 Risk characterisation for human health

Reference values to be used in Risk Characterisation

Reference	Study	NOAEL (LOAEL)	A F	Correction for oral absorption	Value
AEL _{short-term}	Not derived in the CAR and not relevant for HHRA				
AEL _{medium-term}	Not derived in the CAR and not relevant for HHRA				
AEL _{long-term} = Upper Intake Level (UL)	EU Scientific Committee on Food (SCF, 2002) ¹ Human data				600 µg/day (0.01 mg/kg bw/d) for adults and 200 µg/day for toddlers
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				ppm / 1 mg/m ³

The SCF (2002) established an Upper Intake Level (UL) of 600 µg/day for adults and 200-450 µg/day for children and school pupils. The UL is equal to the AEL. These values are as given in the AR for iodine.

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.

Maximum residue limits or equivalent

No MRL required for all target tissues according to Commission Regulation (EU) No 37/2010 of 22 Dec. 2009.

Risk for industrial users

Industrial exposure is not relevant.

Risk for professional users

Systemic effects

The total uptakes for adult users (professionals), as indicated in the corresponding scenarios have been summarized in the following table:

Task/ Scenario	Tier	Upper intake Level (UL) mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ UL (%)	Acceptable (yes/no)
Scenario 1.1	1(No PPE)	0.01	6.98E-05	0.7	Yes
	2(Gloves)	0.01	6.98E-06	0*	Yes
Scenario 1.2	1(No PPE)	0.01	1.88E-05	0.19	Yes

	2 (gloves)	0.01	1.88E-06	0*	Yes
Scenario 2.1	1(No PPE)	0.01	Exposure is covered by scenario 1.1		
Scenario 2.2	1(No PPE)	0.01	Exposure is considered irrelevant		
Scenario 3.1	1(No PPE)	0.01	6.26E-5	0.63	Yes
	2(Gloves)	0.01	6.26E-6	0*	Yes
Scenario 3.2	1(No PPE)	0.01	Exposure is considered irrelevant		
Scenario 4	1(No PPE)	0.01	Exposure is considered irrelevant		
Combined task					
(1.1)+(3.1)	1(No PPE)	0.01	1.32E-4	1.3	Yes
	2 (gloves)	0.01	1.32E-5	0.1	Yes
Dietary exposure					
		Upper intake level (UL) µg/d	Estimated uptake µg/d		
Scenario 5	-	600	76.9	12.82	Yes
Scenario 6	-	600	166.9	27.82	Yes
Scenario 7	-	600	351.9	58.65	Yes

As a worst-case, the estimated daily iodine intakes by dietary exposure have been added to the individual worker exposure tasks/scenarios.

Task/ Scenario	Tier / PPE	Estimated total systemic 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
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Manual mixing and loading / [1.1]	1/ none	6.98E-05	0.7	13.52	28.52	59.35
	2/ gloves	6.98E-06	0*	12.89	27.89	58.72
Automated mixing and loading / [1.2]	1/ none	1.88E-05	0.19	13.01	28.01	58.84
	2/ gloves	1.88E-06	0*	12.84	27.84	58.67
Application by manual dipping / [2.1]	Exposure is considered covered by the mixing and loading scenario 1.1					
Automated dipping application / [2.2]	1/ none	-	0	12.82	27.82	58.65
Cleaning of manual equipment / [3.1]	1/ none	6.26E-5	0.63	13.44	28.44	59.28
	2/ gloves	6.26E-6	0*	12.88	27.88	58.71
Cleaning of automated dipping-system / [3.2]	1/ none	-	0	12.82	27.82	58.65
Removal of dried residues post-milking /4	1/ none	-	0	12.82	27.82	58.65
Combined: 1.1 + 3.1	1/ none	1.32E-4	1.32	14.14	29.14	59.97
	2/ gloves	1.32E-5	0.13	12.95	27.95	58.78

*Negligible exposure (e.g. 0.07)

As can be seen in the table above, from a systemic approach, all scenarios present an acceptable risk without using PPE.

Local effects

The biocidal product MAMICAMP SELLADOR is classified for eye irritation (H319: Causes serious eye irritation). This is categorised as hazard cat. "low" for local effects according to the Guidance for human health risk assessment:

Summary table: estimated local exposure from professional uses							
Hazard category	Effects in terms of C&L	Who is exposed	Tasks, uses, processes	Potential exposure route	Frequency and duration of potential exposure	Relevant RMMM & PPE	Conclusion on risk
Low	Eye Irr. H319	Professional	Loading the product in dipping cups, application by dipping the product, cleaning of dipping cups	Skin Eye (splashes, hand to eye transfer)	Minutes during mixing and loading, and cleaning of equipment For application, an hour per day	P280 Wear eye protection Avoid contact with eyes or skin	Acceptable

During the mixing and loading process, it is necessary to handle the concentrated product, which can cause serious eye irritation (it is H319). Therefore, the use of protective goggles is mandatory.

During application by manual dipping, the worker holds the cup at the lower compartment, so direct hand exposure to the biocide product or a treated teat is avoided. The cup has an upper compartment for application of the dip and a lower compartment as reservoir for the dipping solution. The correct quantity of liquid to cover a teat is pushed in the top of the dip by pressure on the flexible reserve flask containing MAMICAMP SELLADOR. In addition, given the design of the cup, splashes and spills can be avoided.

No exposure of professionals occurs during automated dipping. Even so, at least wear chemical goggles will be recommended, due to local effects.

Conclusion

It is mandatory to wear eye protection when handling the product. From the risk assessment approach, the safe use of the product does not require the use of gloves at any time, however, according to the CAR, for hygienic reasons it is standard

practice to use at least gloves (in order to reduce the risk of possible cross contamination) and protective clothing.

Risk for non-professional users

Non-professional exposure is not relevant.

Risk for the general public

Direct exposure of the general public is not relevant.

Risk for consumers via residues in food

The risk for consumers via residues in food concerns both professionals and general public (secondary exposure).

Some scenarios are theoretically envisageable but not relevant because not realistic or covered by the main scenario of residues in milk following teat disinfection. Indeed the exposure to residues in meat following use of teat disinfectants is covered by the exposure to residues in milk following the same use according to the CAR of iodine.

Dietary risk via iodine residues in milk has been assessed for both adults and children. For more details please refer to the exposure section "Dietary exposure" above.

Based on a worst case assumption of two manual milking's per day, the estimated daily iodine intakes and % UL for adults and toddler are presented in the following table:

	Adults (0.45 L/day)	Toddler (0.46 L/day)
	Estimated daily intake (µg/day) [% of UL]	Estimated daily intake (µg/day) [% of UL]
Post-milking teat-disinfection, RTU product (0.34% available iodine)		
Intake from milk due to teat treatment	76.9 (12.82%)	78.61 (39.31%)
Total milk intake	166.9 (27.82%)	170.61 (85.31%)
Total dietary intake	351.9 (58.65%)	266.61 (133.31%)

For adults, the estimated daily iodine residue in milk resulting from use of the product is in maximum 12.82% of the UL. When adding background values for iodine in milk, daily iodine intake is in maximum 27.82% of the UL. Finally, the total dietary intake of iodine resulting from milk consumption and from other dietary sources is in maximum 58.65% of the UL.

For toddler, the estimated daily iodine residue in milk resulting from the use of the product is at maximum 36.31% of the UL. When adding background values for iodine in milk, daily iodine intake is at maximum 85.31% of the UL. Finally, the total dietary intake of iodine resulting from milk consumption and from other dietary sources at in maximum 133.31% of the UL.

ES CA decision:

Human health risk is acceptable for all milking applications based on estimated intakes, except for toddlers, where total daily intake considerably exceeds (133.31%) the UL. Iodine from toddler dietary intake, arising from every other source except from iodine

containing teat disinfection product residues, takes up almost the whole fraction of the UL if current EU data is used.

Considering the above, the following elements have been taken into account to make the decision to authorize the product Mamicamp Sellador:

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.

In the specific case of Spain, the study by Serra et al (2003)¹ shows that children in Spain have lower milk consumption than the Dutch children population, used as a default value for the risk assessment. The study was done by a representative sample of the Spanish population (n = 3.534 individuals, 1.905 female and 1.629 male). Both a 24-hours recall and a general questionnaire with socio-economic, demographic and lifestyle items were administered. The results show that the daily intake of milk is 0.37 L/day for boys and 0.35 L/day for girls (aged 2-5 years). A median of 0.36 L/day can be used to re-assess the calculations.

The daily products consumption is also lower than in The Netherlands: according to Serra et al study, is 514 g for boys and 496 g/day for girls. The iodine content in daily products is estimated as 35 µg/100 g (Public Health England, 2015); therefore, the intake by other foods would be estimated as 48 µg/day, far from the assumed 96 µg/day for the calculations above.

A recent study (Vila et al, 2020)² reviews the iodine nutrition in Spain and concludes that "Although iodine nutrition in Spain has improved in recent years, the problem is not completely resolved. It is necessary that health institutions establish measures to ensure an adequate iodine nutrition of the population, especially among the highest risk groups (children and adolescents, women of childbearing age, pregnant women and nursing mothers)."

It can be inferred that the iodine intake in Spain may be of concern due to the low levels rather than excessive levels. Therefore, the contribution of milk intake to iodine nutrition is welcomed and does not represent a risk.

References:

- L. Serra Majem, L. Ribas Barba, C. Pérez Rodrigo, B. Roman Viñas, J. Aranceta Bartrina Dietary habits and food consumption in Spanish children and adolescents (1998–2000): socioeconomic and demographic factor *Med Clin (Barc)*, 121 (2003), pp. 126-131
- Public Health England, 2015. McCance and Widdowson's composition of foods integrated dataset. Available from: <https://www.gov.uk/government/publications/composition-of-foodsintegrated-dataset-cofid>. (Accessed 13 November 2015).
- Lluís Vila, Anna Lucas, Sergio Donnay, Antonio de la Vieja, Silvia Wengrovicz, Piedad Santiago, Orosia Bandrés, Inés Velasco, Eduardo Garcia-Fuentes, Susana Ares, José Carlos Moreno Navarro, Mercedes Espada, Antonio Muñoz, Juan Carlos Galofré, Manel Puig-Domingo La nutrición de yodo en España. Necesidades para el futuro. *Endocrinología, Diabetes y Nutrición*, Volume 67, Issue 1, January 2020, Pages 61-69

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

Not relevant, since neither additional active substances nor substances of concern are contained in the teat disinfection product.

2.2.7 Risk assessment for animal health

In line with similar UA for iodine, eCA ES will refer to previous justification and decision taken.

With reference 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. In addition, iodine-based teat-disinfection products have a long history as safe veterinary hygiene and medicinal products.

The product MAMICAMP SELLADOR is classified by its local effects as H319 (causes serious eye irritation), but no adverse effects are expected because it is directly applied on the teats of dairy animals and exposure of the animal's eyes is not expected.

2.2.8 Risk assessment for the environment

ES CA:
The risk assessment for the environment is reported as submitted by the Applicant. The ES CA assessment is presented in separate boxes on a green background.

Authorisation is requested for the product MAMICAMP SELLADOR® containing Iodine as active substance. The biocidal product is a disinfectant for application in product types PT3 [Veterinary hygiene biocidal products]. The product is for professional use to disinfect teats of cows, ewes and goats (PT3) in **Post-milking** with the RTU product in dipping cups.

The intended uses and the dosages of the products are described in table below.

Product name	Type of application	Conc a.s. in PB (% w/w)	Dosage a.s. (g Iodine/treatment/cow) ¹
Disinfection of cow teats after milking (PT3)			
MAMICAMP SELLADOR®	Applied by dipping	2.5% as PVP-Iodine (0.34% as Iodine*)	10 ml/treatment/cow x 0.35% as Iodine* (0.035 g Iodine/treatment/cow) *
¹ The actual dose of the product (4 ml/treatment/cow) is not used for the environmental risk assessment, but the mandatory dose according to the ESD PT3.; *Worst-case dose which is used in the environmental risk assessment.			

ES CA:
The above values were accepted after the following explanation from the applicant:

“The range of the available iodine (0.19-0.34%) has been calculated taking into account, in addition to the concentration range of the raw material, a possible admissible error in manufacturing ($\pm 10\%$) like this: $2.5\% \text{ PVP-iodine} \pm 10\% = 2.25\% - 2.75\% \text{ PVP-iodine}$, and applying the range of iodine concentration available from the raw material (9-12% I2) a wider range of iodine comes out (0.19-0.34% I2), and this maximum value (0.34% I2) has been used as the worst-case scenario for HH and ENV risk assessments.”

There is no difference between de MAMICAMP a.s. composition and those BP included in the Iodine (and PVP-iodine) Assessment Report submitted by Sweden on 13th December 2013 (Iodine CAR) for its approval under Regulation No 528/2012 for PT1-3-4-22.

There are not new studies concerning the active ingredient (Iodine and PVP-Iodine) since the product applied for authorisation is similar to the representative products in the CAR and the intended use (the application rate as well summed up) and the exposure to the environment is identical a very short summary of the environmental risk assessment can be presented here which could be copied from the assessment report or from the CAR

The risk for the environment was assessed using the AEAT report ED48587/R1 (2007), TGD (2002), the ECHA’s Guidance on the Biocidal Products Regulation (Volume IV Environment - Assessment and Evaluation, version 2.0, october 2017), ESD PT3 (2011) and the agreement reach in the WG-I-2018 (Technical Agreements for Biocides, TAB 2018-ENV 64), with their mandatory items:

- 10 ml/treatment/cow for treatment with dipping cups
- 2 events/day for manual milking or 3 events/day for milking systems
- emission to slurry (milking in the stable) and emission to waste wather (in a milking parlour outside the stabel)

A short abstract of Iodine Assessment Report/CAR is showed in the next sections.

ES CA:

MAMICAMP SELLADOR is a biocidal product for external topic use against bacteria aerobic gram-positive and gram-negative and yeasts for use by professional and trained professional users for cleaning, disinfecting and sealing of the udder/teat hole after milking in dairy cows, ewes, goats and other lactating females. The application method is both manual and automatic cleaning after milking.

MAMICAMP SELLADOR is a gel RTU formulation containing Polyvinylpyrrolidone Iodine as active substance (a.s.) (2.5% as PVP Iodine, 0.19-0.34% Iodine). This a.s. is classified as Aquatic Acute 1 M=1, Aquatic Chronic 1 M=1 according to their entry in Annex VI of Regulation (EC) No. 1272/2008.

MAMICAMP SELLADOR has other co-formulants in the formulation. ES CA analysed the information available on the co-formulants (i.e. Safety Data Sheets, C&L Inventory, REACH Registration dossiers, REACH Evaluation Reports and CARs of approved biocidal

active substances). Some of the co-formulants are not classified for environmental hazards and therefore do not contribute to the classification or possible risks of the mixture. But one co-formulant carries environmental hazard classification. However, it is below the concentration limits specified in Regulation (EC) No. 1272/2008 leading the product to be regarded as hazardous. Therefore, it doesn't contribute to the classification of the biocidal product for environmental hazards.

Therefore, the biocidal product MAMICAMP SELLADOR does not contain Substances of Concern for the environment. Consequently, all the information concerning the environmental risk assessment for this product is based on data of the actives substances as included in the Assessment Reports of PT3 uses (final CAR of December 2013).

The assessment of MAMICAMP SELLADOR has been made by considering that the application on the udder/teat hole is by dipping cup with 10 ml of pure product (dose rate of 0.035 g Iodine/treatment/cow) at post-milking treatment (taking into account a maximum of 12% of iodine in the PVP-Iodine complex and a density of 1.02 kg/L).

2.2.8.1 Effects assessment on the environment

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

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. Test conducted with Iodine, Iodate and Iodide: EC₅₀ are expressed as p.p.m. (mg/L or mg/kg wwt).

Summary table of further ecotoxicological studies: Iodine (I ₂), Iodide (I ⁻) and Iodate (IO ₃ ⁻)									
Method, Guideline, GLP status, Reliability	Species/ Inoculum	End point	Exposure		Results			Remarks	Reference ¹
			Design	Duration	EC ₅₀ (mg/L)	EC ₁₀₀ (mg/L)			
OECD 203	<i>Oncorhynchus mykiss</i>	dead	acute	96h		Iodine: 1.67 Iodate: 220 Iodide: 3780		Fish test	2.2.8 *

OECD 202	<i>Daphnia magna</i>	Immobilisation	acute	48h		Iodine: 0.59 Iodate: 58.5 Iodide: 0.83		Daphnia test	2.2.8*
OECD 201	<i>Desmodesmus subspicatus</i>	Inhibition growth		72h		Iodine: 1.3 Iodate: N.A. Iodide: N.A.		Algae test	2.2.8*

From the Assessment Report of Iodine (including PVP-iodine) for Product types 1, 3, 4, 22. Approved on 13th December 2013 submitted by Sweden.

Based on these data and the chronic for Iodine, PB is not classified as Hazardous to the environment

Further Ecotoxicological studies

Summary table - Further ecotoxicological studies

Test conducted with Iodine: EC50 are expressed as mg/L of Iodine (I₂), Iodide (I⁻) or Iodate (IO₃⁻)

Summary table of further ecotoxicological studies for Iodine (I ₂), Iodide (I ⁻) and Iodate (IO ₃ ⁻)									
Method, Guideline, GLP status, Reliability	Species/Inoculum	End point	Exposure		Results			Remarks	Reference ¹
			Doses	Duration	EC ₅₀ (mg/L)	EC ₁₀₀ (mg/L)	EC ₁₀ (mg/L)		
OECD 219	Sewage activated sludge micro-organisms			3h		Iodine: 290 Iodate: N.A. Iodide: N.A.			2.2.8*

From the Assessment Report of Iodine (including PVP-iodine) for Product types 1, 3, 4, 22. Approved on 13th December 2013 submitted by Sweden.

N.A. Not Available data in the CAR

Data waiving	
Information requirement	Not necessary
Justification	There are not new studies concerning the active ingredient (Iodine and PVP-Iodine) since the product applied for authorisation is similar to the representative products in the

	CAR and the intended use (the application rate as well summed up) and the exposure to the environment is identical to the approved under Regulation No 528/2012 for PT1-3-4-22
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Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk (ADS)

Summary table of effects on specific, non-target organisms believed to be at risk									
Method, Guideline, GLP status, Reliability	Species/Inoculum	End point	Exposure		Results			Remarks	Reference ¹
			Design	Duration	EC ₀ (mg/L)	EC ₅₀ (mg/L)	EC ₁₀ (mg/L)		
OECD 207	<i>Eisenia foetida</i>	Dead	Acute	14 d		Iodine: >1000 Iodate: N.A. Iodide: N.A			2.2.8*
OECD 208	<i>Avena sativa</i>	Seeding emergence and growth	Chronic	21 d		Iodine: 11.8 Iodate: 30.4 Iodide: 4.3	mg/kg gwwt		2.2.8*
OECD 217	<i>Soil microorganisms</i>	Respiration inhibition		28 d		Iodine: 148.7 Iodate: N.A. Iodide: N.A			2.2.8*
OECD 216	<i>Soil microorganisms</i>	Nitratification		28 d		Iodine: 82.6 Iodate: N.A. Iodide: N.A			2.2.8*

From the Assessment Report of Iodine (including PVP-iodine) for Product types 1, 3, 4, 22. Approved on 13th December 2013 submitted by Sweden.

N.A. Not Available data in the CAR

Background levels

Iodine and iodine compounds are ubiquitously distributed and there is a natural cycle of iodine species in the environment. Background levels should be taken into account in the environmental risk assessment. There are show in the next table:

Summary table of background levels	
Compartment	Background level (as iodine)

Soil	Typically 0.5- 20 mg/kg wt but with extremes up to 98 mg/kg wt Global mean value of 5 mg/kg wt
Groundwater	Mean concentration: 1 µg/L Range: < 1 - 70 µg/L with extremes up to 400 µg/L
Freshwater (river & lake)	0.5 - 20 µg/L
Marine water	45 - 60 µg/L
Rainwater	0.1 - 15 µg/L
Freshwater sediment	Typically: 6 mg/kg
Marine sediment	Typically: 3 - 400 mg/kg
Air	Atmosphere: 10 - 20 ng/m ³ Atmospheric concentration: over land 2 - 14 ng/m ³ ; over ocean 17 - 52 ng/m ³ Marine air contains: 100 µg/L (may refer to local inhalable air)

PNEC Derivation

The RGB requires that the environmental risk is assessed on basis of Predicted No Effect Concentrations (PNEC), which is determined in line with the Technical Guidance document (version 2003 chapter 3). PNEC values for the different compartments are derived from ecotoxicity data and applying assessment factors. Depending on the type of data (acute or chronic) and number of data a certain assessment factor is selected.

PNEC derivation for different compartments for Iodine (I ₂), Iodate (IO ₃ ⁻) and Iodide (I ⁻)		
Compartment	PNEC values	Remarks
Freshwater (µg/L) (PNEC _{surface water})	Iodine= 0.59 Iodate=58.5 Iodide=0.83	The lowest EC50 of 0.59 mg/L for iodine was determined in the study on acute toxicity to <i>Daphnia magna</i> . Therefore, PNEC _{aquatic} values for the relevant iodine species using an assessment factor 1000.
Freshwater sediment (mg/kg) (PNEC _{sediment})	Iodine= 0.029 Iodate= 2.84 Iodide= 0.043	The PNEC _{sediment} values were calculated on the basis of the PNEC _{aquatic} values, using the equilibrium partitioning method according to the TGD.
Soil (mg/kg wwt) (PNEC _{soil})	Iodine= 0.01182 Iodate= 0.304 Iodide= 0.0043	The lowest EC50 of 13.4 mg/kg dwt (= 11.82 mg/kg wwt) for iodine was determined in the study on non-target plants (<i>Avena sativa</i> – shoot fresh weight). Therefore, the PNEC _{terrestrial_EC50} value for Iodine was derived on the basis of the EC50 value using an assessment factor 1000. It should be noted that iodine is not a xenobiotic substance but is present in soil at natural background concentrations of 0.5 to 20 mg/kg soil. Therefore, the application of an assessment factor of 1000 must be considered as unrealistic worst case in the case of iodine.
STP (µg/L) (PNEC _{STP})	Iodine= 2900 Iodate= -* Iodide= -*	The estimated of EC50 value for respiration inhibition based on the water solubility of iodine is 290 mg/L. The assessment factor normally applied to this type of endpoint is 100 (TGD II, 2003). Thus, the PNEC _{STP} microorganisms is derived as.

Air	Not relevant	
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no PNEC derived in the Iodine CAR (2013)

	Values for Iodine		Values for Iodide	Values for Iodate
Via manure/slurry application (10 years applications)	Background	PNEC	PNEC	PNEC
Surface Water-grass (µg/L)	0.5 <-> 20	0,5900	0,8300	58,5000
Surface Water-arable (µg/L)		0,5900	0,8300	58,5000
Soil arable (mg/Kg wwt)	0.565 <-> 22.6 extremes up to 110.74	0,0118	0,0043	0,3040
Soil grassland (mg/Kg wwt)		0,0118	0,0043	0,3040
Groundwater-grass (µg/L)	1<->70	>0,1	>0,1	>0,1
Groundwater-arable (µg/L)		>0,1	>0,1	>0,1
Via STP				
STP (mg/L)	-	2,9000	not relevant	not relevant
Surface Water (µg/L)	0.5 <-> 20	0,5900	0,8300	58,5000
Soil (mg/Kgwwt)	0.565 <-> 22.6 extremes up to 110.74	0,0118	0,0043	0,3040
Groundwater (µg/L)	1<->70	>0,1	<0,1	>0,1

ES CA:

Just a note, PECs for sediments has not been calculated as no predicted no effect concentrations (PNECs) are available. As it is stated on the iodine AR (December 2013), no further risk assessment has been performed as both the PEC and PNEC values for sediment would have been calculated using the equilibrium partitioning method, and consequently the resulting risk quotient would be the same as described for surface water.

ES CA:

Endocrine disruption activity of non-active substances

The Commission Delegated Regulation (EU) 2017/2100 specifying the scientific criteria for the determination of endocrine-disrupting properties (ED criteria) under Regulation (EU) No 528/2012 (BPR) establishes that the ED criteria become applicable by 7 June 2018 for biocides.

No further ecotoxicological studies are available for MAMICAMP SELLADOR. The product was not tested for potential endocrine disruption properties. MAMICAMP SELLADOR contains the active substance iodine and various co-formulants (see confidential PAR).

For the active substance, no ED assessment is required because for active substances which have been approved, the EU assessment should be followed. As discussed in the Assessment Report for iodine (December 2013), Iodine is an essential element and has a physiological function in thyroid hormone synthesis (i.e. intentionally interacts with the endocrine system). This means that both iodine deficiency as well as iodine excess can impair thyroid homeostasis/thyroid hormone levels. This is to be considered as an endocrine effect. However, it would not be justified to conclude from this that iodine should be considered to be an endocrine disruptor. In contrast to typical xenobiotic substances, which are not needed at all for the functioning of the human body, and which normally only have negative effects on man, Iodine is a physiologically essential element.

Consequently, the concept of endocrine disruption is not meaningful for essential elements such as iodine since it neglects that they are needed for maintaining hormone homeostasis. Furthermore, neither iodine nor iodide are included in the lists of the EU on substances suspected of interfering with the hormone systems of humans and wild-life.

For the co-formulants a screening was performed by consulting: ECHA data for identification of ED and PBT, under REACH, BPR or CLP Identified as ED by United States EPA (<https://comptox.epa.gov/dashboard/>) Identified as ED by the United Nations Environment (July 2017) Programme (http://wedocs.unep.org/bitstream/handle/20.500.11822/25634/edc_report2.pdf?sequence=1&isAllowed=y and https://wedocs.unep.org/bitstream/handle/20.500.11822/25635/edc_report2_factsheet.pdf?sequence=1&isAllowed=y)

During screening performance none of the co-formulant triggered an alert for ED property thus, ES CA considered that there is no concern regarding the ED properties of this co-formulants.

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

Not relevant for the foreseen use of this BP.

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

Data waiving	
Information requirement	Not necessary
Justification	Not applicable for the foreseen use of this BP

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

Not relevant for the foreseen use of this BP.

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

Exposure to the environment is described in the ESC for PT3. The route of exposure of iodine to the environment is either via application of manure/slurry to agricultural land or by release from the facility drain to an STP and subsequent compartments. Relevant receiving compartments are soil, groundwater and surface water. Release to seawater may occur in the case of teat dip use and disinfection of milking equipment through runoff after sewage sludge application, but the calculated PEC's are negligible compared to the natural background levels in seawater of 40-65 µg/L and are thus not explicitly summarised here.

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

Data waiving	
Information requirement	Not necessary

Justification	The BP are for indoor use (in animal houses) only. Any exposure to the environment is indirect via liquid manure and via STP, leading to a separation of the components before reaching the environment.
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ES CA:

New environmental fate and behaviour on the a.s. or product specific data are not available as they are not considered necessary. All agreed endpoints have been taken from the CAR of the a.s. in PT 3. The co-formulants are not considered Substances of Concern.

Leaching behaviour (ADS)

The products are for indoor use (in animal houses) only. Any exposure to the environment is indirect via liquid manure and via STP, leading to a separation of the components before reaching the environment. The leaching process to the ground water is taken into account in the PEC_{gw} calculations in the risk evaluation process.

ES CA:

Additional data on leaching behaviour of the a.s. or the biocidal product are not necessary. New data are not available.

Testing for distribution and dissipation in soil (ADS)

The Iodine K_{oc} 165.8 cm³/g was calculated from the OECD 106 test. The solids-water adsorption coefficients to be used in the environmental exposure calculations are K_{psoil} = 5.8 cm³/g and K_{psusp} = 2.2 x 10² cm³/g. (CAR, 2013).

Mineralization (aerobic)	Not applicable due to the fact that iodine is an element
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT _{50lab} (20°C, aerobic): Not applicable
	DT _{90lab} (20°C, aerobic): Not applicable
	DT _{50lab} (10°C, aerobic): Not applicable
	DT _{50lab} (20°C, anaerobic): Not applicable
	degradation in the saturated zone: Not applicable
Field studies (state location, range or median with number of measurements)	DT _{50f} : No data available and no data required
	DT _{90f} : No data available and no data required
Anaerobic degradation	Not applicable
Soil photolysis	No data available and no data required
Non-extractable residues	No data available and no data required
Relevant metabolites - name and/or code, % of	Not applicable due to the fact that iodine is an element

ES CA:

Additional data on distribution and dissipation in soil of the a.s. or the biocidal product are not necessary. New data are not available.

Testing for distribution and dissipation in STP, water and sediment (ADS)

STP distribution

Iodide is not highly adsorbed to sludge under typical conditions and iodate can form complexes with calcium which easily adsorb to negatively charged particle surfaces, the majority of the iodine that passes an STP will most probably not be retained in sludge and a sludge retention factor of 20% is chosen for the risk assessment (i.e. 80% of the iodine discharged to the STP remains in the effluent) (CAR, 2013).

Water and Sediment Distribution

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

Ka
 Ka_{oc}
 pH dependence (yes / no) (if yes type of dependence)

<u>Lab-data</u>	
	1.22 to 124 cm ³ /g (five soils); 5.8 cm ³ /g (geometrical mean)
	51.3 to 3650 cm ³ /g (five soils)
	No pH dependency
<u>Data from open literature</u>	
	K _{p_susp} = 220 cm ³ /g (geometrical mean)
	K _{p_soil} = 0.01- 580 cm ³ /g; 6.9 cm ³ /g (geometrical mean)

ES CA:

Additional data on distribution and dissipation in water and sediment of the a.s. or the biocidal product are not necessary. New data are not available.

Testing for distribution and dissipation in air (ADS)

According to the CAR of the Iodine:

Direct photolysis in air	Rapid photolysis of I ₂ takes place in the lower atmosphere due to its strong absorption of light in the visible wavelengths (400 < λ < 700 nm). Lifetime = 5-10 s for an overhead sun
Quantum yield of direct photolysis	No data available
Photo-oxidative degradation in air	Methyl iodide and molecular iodine are the predominant iodine species in air. Both iodine and methyl iodide undergo photochemical reactions to form iodine radicals, which can then go on to form a number of other iodine species through a complex series of reaction pathways.
Volatilization	Iodine is volatilised in several forms with methyl iodide (CH ₃ I) probably being the most important one.

However, the Iodine in the BP is in the form of complexing-bounded with Polyvinylpyrrolidone, and then is not expected to be volatile.

ES CA:

Additional data on distribution and dissipation in air of the a.s. or the biocidal product are not necessary. New data are not available.

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

Not relevant for the foreseen use of this BP, since the product is used indoor for disinfection and only can reach the environment mixed with manure/slurry or wastewater.

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

Not relevant for the foreseen use of this BP, since the product is used indoor for disinfection and only can reach the environment mixed with manure/slurry or wastewater.

2.2.8.2 Exposure assessment

General information

Assessed PT	PT3. Animal disinfectant
Assessed scenarios	Scenario 1: Post-milking with ready to use product applied by dipping
ESD(s) used	PT3a: Manual non-medical teat disinfection and udder washes. PT3b: Automatic teat disinfection (covered by PT3a).
Approach	Average consumption
Distribution in the environment	Calculated based on ECHA- Guidance on the biocidal Products Regulation - Volume IV Environment - Part B Risk Assessment (active substances) Version 1.0; April 2015
Groundwater simulation	Not relevant
Confidential Annexes	Yes (see Excel spreadsheet with ESD PT3 calculations in 3.6 CONFIDENTIAL Annex)
Life cycle steps assessed	Scenario 1: Production: No Formulation: No Use: Yes Service life: No

Remarks	<p>Emission Scenario Document for Product Type 3 (ESD PT3) Veterinary hygiene biocidal products</p> <p>Drafted by Scientific Consulting Company (SCC) GmbH Revised by the Biocides Technical Meeting Endorsed by the Biocides Competent Authorities Meeting Edited by B. Raffael and E. van de Plassche</p> <p>EUR25116EN-2011 European Commission. Joint Research Centre Institute for Health and Consumer Protection</p> <p>Since Euses 2.1.2 does not implement the "PT3-Disinfection for veterinary hygiene: non-medical teat dips" scenario, the calculations were implemented in a Excel® sheet following the equations and intermediate outputs posed in the ESD PT3 document.</p>
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ES CA:	
Assessed PTA1:B12	PT3. Animal disinfectant
Assessed scenarios	<p>Scenario 1: Dairy cows. Post-milking with ready to use product applied by dipping</p> <ul style="list-style-type: none"> - Scenario 1a: Manual teat disinfection. - Scenario 1b: Automatic teat disinfection.
ESD(s) used	<p>* Emission Scenario Document for Product Type 3 (ESD PT3): Veterinary hygiene biocidal products, 2011</p> <p>* Technical Agreements for Biocides Environment (ENV), July 2021</p>
Approach	Average consumption
Distribution in the environment	Calculated based on ECHA- Guidance on the biocidal Products Regulation - Volume IV Environment - Part B Risk Assessment (active substances) Version 2.0; October, 2017
Groundwater simulation	Not relevant
Confidential Annexes	No
Life cycle steps assessed	<p>Production: No</p> <p>Formulation: No</p> <p>Use: Yes</p> <p>Service life: No</p>
Remarks	<p>Since Euses 2.1.2 does not implement the "PT3-Disinfection for veterinary hygiene: non-medical teat dips" scenario, the calculations were implemented in a Excel® sheet following the equations and intermediate outputs posed in the ESD PT3 document.</p>

Iodine is used in veterinary hygiene biocidal products (PT3) for the purpose of manual and automatic non-medical teat disinfection. Application methods are spraying and dipping of teats, with dipping being most commonly used. In this last case, the teats are immersed before and/or after milking using a cuplike container that holds the disinfectant. At least the lower third of the teats should be immersed. Dip solution remaining in the cuplike container should be discharged. After application through spraying or dipping, the applied teat disinfectant is left to dry on the teat surface and remains there as a protective film, otherwise the worker wipes the treated teats after application.

Two emission pathways are possible: emission to waste water or to the slurry. This depends on whether the cows are milked in the stable (emission to slurry) or in a milking parlour outside the stable (emission to waste water). When the product is discharged in manure, indirect emission will occur to agricultural soil through fertilization with manure. The amount of manure to be used for fertilization is controlled by nitrogen and phosphorus emission standards. When the product is discharged to waste water, indirect emission to surface water and agricultural soil occurs (fertilization with sewage sludge).

Air exposure route

Concerning emissions to air, iodine has a low vapour pressure (40.7 Pa at 25°C) and in view of the high background values of iodine in air, emission to air resulting from application of iodine as disinfectant is not considered to be relevant. This approach is in line with the one taken in the CAR (2013).

STP exposure route

The PEC and PNEC values were calculated based on the assumption that 100% iodine (I₂) is transferred either to two iodide (I⁻) or iodate (IO₃⁻) ions. The molecular weight of two iodide ions corresponds to the molecular weight of iodine, consequently the PECs for iodide are the same as for iodine. The molecular weight of two iodate ions is a factor of 1.382 higher than the molecular weight of iodine, therefore the PECs for iodate were calculated by multiplying the PECs of iodine by this factor. No degradation is considered for any of the PEC values. The concept of degradation is not applicable as iodine is an element.

Manure/slurry exposure route

Manure and slurry applications were considered on 10 years applications following the WGIC-2017 discussions. The equations of the Addendum to the OECD SERIES ON EMISSION SCENARIO DOCUMENTS, Number 14: Emission Scenario Document for Insecticides for Stables and Manure Storage Systems were applied following the WG-I-2018 recommendations (and its available spread sheets in the document), it has been taking into account the dissipation via leaching process in soil with a DT₅₀ of 643 days for grassland and 2571 days for arable land as agreed at the European level.

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. Therefore, only the predicted environmental concentrations (PECs) based on the nitrogen emission standards are presented in the current PAR.

Soil exposure route

The PEC_{soil} values have been calculated according to the legal standards for phosphate and nitrogen loading in the appendix. In the case of dairy cows, the nitrogen emission standard limits the emission to the environment. Only the results regarding to nitrogen is presented in this ERA.

Emission estimation

ES CA:

MAMICAMP SELLADOR is a biocidal product for cleaning, disinfecting and sealing of the udder/teat hole in dairy cows, ewes, goats and other lactating females. The ESD for PT 3 does not provide default values for relevant parameters for e.g. buffaloes, sheep and goats. Cows are considered worst-case with reference to teat disinfection, as herds are larger than herds of buffaloes, ewes and goats. In addition, cows have a higher number of teats compared to other dairy species like sheep and goats, resulting in a lower consumption per treatment. So, the current scenario in this PAR cover also ewes, goats and other lactating females, the other target species of this product.

The product MAMICAMP SELLADOR is applied manually two times a day, but three times in milking robots so the scenario 1b: "Automatic teat disinfection" is therefore the worst-case and consequently applied in the environmental risk assessment.

Scenario 1:

Post-milking, treatment of teats by dipping using the product. This is considered the worst scenario

Content of active ingredient (F_{bioc})

The MAMICAMP SELLADOR® contains 2.4% PVP-iodine at their maximum range. As proposed in the assessment report, the risk assessment is conducted on pure iodine concentration and not PVP-Iodine content. Thus, the max. iodine content of the evaluated formulations is 3.5 g Iodine/L (worst case).

Input parameters for calculating the local emission			
Input	Value	Unit	Remarks
Scenario 1: PT3a: Manual non-medical teat disinfection and udder washes. PT3b: Automatic teat disinfection (covered by PT3a).			
Application rate of biocidal product (<i>V_{prod}</i>)	10*	mL/cow (4 teats)	The standard values proposed in ESD PT3 for Dipping application were used (Appendix I, Table 1)
Concentration of active substance (Iodine) in the product (<i>V_{prod i1,i2,i3,i4}</i>)	3.5*	g/L	Worst case, provided by the applicant
Times of application	Post-milking		

Concentration of active substance in treatment (Fbioc)	RTU (ready to use) product		
Frequency (milking events per day)	3	day	2 events for manual milking 3 events milking systems*
Resulting product volume per day	30	mL/cow/day	The standard values proposed in ESD PT3 (Appendix I, Table 1) were used

as the worst case (2.5 times the actual dose recommended : 1 ml/teat/cow/event = 4 ml/cow/event)

F_{bioc}: Content of active ingredient (iodine) in formulation (product)

V_{prod i1,i2,i3,i4}: Amount of product prescribed to be used for one treatment (dipping of the four teats) of one animal

F_{dil}: Dilution factor (for preparation of the working solution from the formulation (product))

Calculations for Scenario 1. PEC Calculations

Predicted Environmental Concentrations (PEC) to soil and pore water were calculated using the revised draft ESD (Supplement to the methodology for risk evaluation of biocides, Emission Scenario Document for Product Type 3: Veterinary hygiene biocidal products) for PT3 scenarios in Excel.

Resulting local emission to relevant environmental compartments		
Compartment	Local emission (E _{local,compartment}) [kg/d]	Remarks
STP (Qai-STP)	0.004315 kg/d	Daily emission to the sewer system. See results in Annex 3.2
Soil _{grassland} (Qai-grass _{i1,i2,i3,i4})	0.278 kg/d	Amount of active ingredient in manure after the relevant number of biocide applications for the manure application to grassland
Soil _{arableland} (Qai-arab _{i1,i2,i3,i4})	1.113 kg/d	Amount of active ingredient in manure after the relevant number of biocide applications for the manure application to arable land

ES CA:

We agree with the exposure assessment proposed by the applicant, but methodological changes from recommendation of the BPC Ad hoc Working Group on Environmental Exposure (agreed at the Environment Working Group V on November 26, 2015) and the proposal for revision of AHEE Recom WG V 2015 (agreed at the WG-I-2018 on January, 2018), included in the Technical Agreements for Biocides Environment (ENV), July 2021, must be taken into account in the risk assessment update.

According to label instructions, the MAMICAMP SELLADOR application rate is 1 ml per teat (4 teats/cow; 4 ml/cow, i.e. resulting product volume per day of 12 ml/cow/day). On the other hand, the standard values proposed in Guidance on the Biocidal Products Regulation Volume III Human Health - Assessment & Evaluation (Parts B+C), Version 4.0, December 2017 (Section 6.5.4.1, Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products) has been used (for dipping 10ml/cow/milking), taking into account what was stated by the applicant in his emission estimation and that this is the worst case.

The tables below present the input parameters for the calculation of emissions to manure or STP in accordance with the characteristic of the product and the ESD for PT03.

Input parameters for emission calculations for the worst case Scenario 1b: "Automatic teat disinfection"				
Parameters	Nomenclature	Value	Unit	Origin
Type of housing/manure storage (for application of the notification)	Cat-Subcat (i1)	1 - Dairy Cows	[-]	S (ESD Appendix 1: Table 7)
Type of biocide	bioctype (i2)	1 - Disinfectant	[-]	S (ESD Appendix 1: Table 7)
Type of application	appway (i3)	2 (dipping)	[-]	S (ESD Appendix 1: Table 7)
Relevant emission stream	stream (i4)	1 and 3 (STP and slurry/manure)	[-]	P (ESD Appendix 1: Table 7)
Content of active ingredient in formulation (product)	F_{bioc}	3,06	[g.l ⁻¹]	S
Amount of product prescribed to be used for one treatment (dipping of the four teats) of one animal	$V_{prod_{i1,i2,i3}}$	0,01	[l]	S
Dilution factor (for preparation of the working solution from the formulation (product))	F_{dil}	1	[-]	S
Fraction of active ingredient released	$F_{stp} = F_{ww} (1 - F_{teat})$	0,5	[-]	D
Fraction of active ingredient released	$F_{slurry/manurry} (1 - F_{teat})$	0,5	[-]	D
Fraction of active ingredient released	F_{air}	0	[-]	D
Fraction of active ingredient released	F_{teat}	0,5	[-]	D
Number of teat dipping events for one animal and one day (dipping of the four teats of one animal = one disinfectant application)	$N_{app-teat}$	3	[-]	D
Number of days of lactation period (corresponds to number of emission days)	$N_{day-lact} (= T_{emission})$	300	[-]	D
Number of disinfectant applications in one year (equals number of disinfectant applications in one lactation period)	$N_{app-bioc}$	900	[-]	D (TAB ENV 64)
Interval between two disinfectant applications (dipping events)	$T_{bioc-int}$	0,33	[d]	D (TAB ENV 64)
Number of manure applications for grassland	$N_{lapp-grass}$	4	[-]	D
Number of manure applications for arable land	$N_{lapp-arab}$	1	[-]	D
Manure application time interval for grassland	T_{gr-int}	53	[d]	D/S (ESD PT3, 2011; Appendix1: Table 12)
Manure application time interval for arable land	$T_{ar-int} (T_{manure-int}_{arab})$	212	[d]	D/S (ESD PT3, 2011; Appendix1: Table 12)
Number of animals in housing for category/subcategory	$N_{animal_{i1}}$	100	[-]	D/S (ESD PT3, 2011; Appendix1: Table 8)
Number of milk producing animals per day	N_{mp_animal}	82	[-]	D/S (TAB ENV 63)
Amount of nitrogen per animal for category/subcategory	$Q_{nitrog_{i1}}$	0,3389	[kg.d ⁻¹]	D(ESD PT3, 2011; Appendix1: Table 11)

<i>If nitrogen immission standards are applied:</i>				
Nitrogen immission standard for one year on grassland	$Q_{N,grassland}$	170	[kg.ha ⁻¹]	D(ESD PT3, 2011; Appendix1: Table 13)
Nitrogen immission standard for one year on arable land	$Q_{N,arable_land}$	170	[kg.ha ⁻¹]	D(ESD PT3, 2011; Appendix1: Table 13)
Mixing depth with soil, grassland	$DEPTH_{grassland}$	0,05	[m]	D
Mixing depth with soil, arable land	$DEPTH_{arable_land}$	0,2	[m]	D
Density of wet bulk soil	$RHO_{soil_{wet}}$	1700	[kg.m ⁻³]	D

Intermediate Calculations	Nomenclature	Value	Unit	Origin
Number of biocide applications during storage period for application on grassland	Napp-manure_{gr}	159 [-]		O (TAB ENV 212)
Number of biocide applications during storage period for application on arable land	Napp-manure_{ar} (=Napp-biomanure_ar2)	636 [-]		O (TAB ENV 212)
	Qai-prescr=10⁻³*Fbioc*Vprod*Fdil (ESD PT3)			
Amount of active ingredient to be used for one application (one treatment of one animal)	Qai-prescr_{i1,i2,i3}	3,06E-05 [kg]		O
	Qai-manure = Fslurry/manure*Qai-prescr*Nmp_animal (ESD PT3)			
Amount of active ingredient in relevant stream i4 after one application for all animals	Qai_{i1,i2,i3,i4}	1,25E-03 [kg]		O (TAB ENV 63)
	Qai-grass = Qai*Napp-manuregr (ESD PT3)			
Amount of active ingredient in manure or slurry after the relevant number of biocide applications for the manure application to grassland	Qai-grass_{i1,i2,i3,i4}	1,99E-01 [kg]		O
	Qai-arab = Qai*Napp-manurearable (ESD PT3)			
Amount of active ingredient in manure or slurry after the relevant number of biocide applications for the manure application to arable land	Qai-arab_{i1,i2,i3,i4}	7,98E-01 [kg]		O
	Qnitrog-grass = Nanimal*Qnitrog*Tgr-int (ESD PT3)			
Amount of nitrogen produced during the relevant period for every relevant (sub)category of animal/housing i1 and application to grassland	Qnitrog-grass_{i1,i4}	1796,2 [kg]		O
	Qnitrog-arable = Nanimal*Qnitrog*Tar-int (TAB ENV62)			
Amount of nitrogen produced during the relevant period for every relevant (sub)category of animal/housing i1 and application to arable land	Qnitrog-arab_{i1,i4}	7184,7 [kg]		O

*D: default from ESD, S: set based on product, O:output

¹ For arable land:

If Tbioc-int ≥ a) Tmanure-intar2, then Napp-biomanure_ar2 = 1.

If Tbioc-int < Tmanure-intar2, then Napp-biomanure_ar2 = ROUND (z,[n])b (Tmanure-intar2/Tbioc-int), with n=1.

If Napp-biomanure_ar2 > Napp-bioc. then Napp-biomanure_ar2 = Napp-bioc

² For grass land:

If Tbioc-int ≥ a) Tgr-intb, then

Napp-manuregr = 1

If Tbioc-int < Tgr-int, then

Napp-manuregr = ROUND (z,[n])c (Tgr-int/Tbioc-int), with n=1.

If Napp-manuregr > Napp-prescr, then

Napp-manuregr = Napp-prescr

Fate and distribution in exposed environmental compartments

Identification of relevant receiving compartments based on the exposure pathway									
Scenario	Fresh-water*	Freshwater sediment	Sea-water*	Seawater sediment	STP	Air	Soil	Ground-water	Birds / mammals
Scenario 1 (via STP)	yes	yes	no	no	yes	Not relevant	yes	yes	Not relevant
Scenario 1 (via slurry/manure)-10 year application	yes	yes	no	no	yes	Not relevant	Yes	yes	Not relevant

ES CA:

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

- Release to the wastewater treatment plant, or
- Release into the manure.

Both emission pathways are considered in the environmental risk assessment.

The exposed compartments 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	n.r.	n.r.	yes	n.r.	yes	yes	no
Via slurry/manure	yes	yes	n.r.	n.r.	n.r.	n.r.	yes	yes	no

Input parameters (only set values) for calculating the fate and distribution in the environment

Input	Value	Unit	Remarks
Molecular weight	253.81	g/mol	AR, 2013
Melting point	113.5-113.7	°C	AR, 2013
Boiling point	184.24-184.5	°C	AR, 2013
Vapour pressure (at 0°C) Vapour pressure (at 25°C) Vapour pressure (at 50°C)	4 40.7 287	Pa	AR, 2013
Water solubility (at 0°C) Water solubility (at 25°C) Water solubility (at 50°C)	0.29 0.3-0.35 0.78	mg/l	AR, 2013
Log Octanol/water partition coefficient	Not relevant to a purely inorganic substance like iodine	Log 10	AR, 2013
Organic carbon/water partition coefficient (K _{oc})	51.3 to 3650	l/kg	AR, 2013
Henry's Law Constant (at X C) <i>[if measured data available]</i>	34.43	Pa/m ³ /mol	AR, 2013
Biodegradability	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.		AR, 2013
Rate constant for STP <i>[if measured data available]</i>		h ⁻¹	
DT ₅₀ for biodegradation in surface water	Not applicable because Iodine is an element		AR, 2013
DT ₅₀ for hydrolysis in surface water	Hydrolysis reaction of iodine occurs to a very small extent because iodine is sparingly soluble. Hydrolysis of I ₂ as the reactant is a pH-dependent dynamic equilibrium reaction with iodide (I ⁻) and iodate (IO ₃ ⁻) as products. At pH values between 4 and 9, iodide is the predominant species. In alkaline and well oxidized waters iodate is the predominant species.	d or hr (at 12°C)	AR, 2013
DT ₅₀ for photolysis in surface water	In water, iodide and iodate are the predominant species. In addition a natural background level of methyl iodide might also be found in water. Photolytic dissociation of these compounds can result in the formation of elemental iodine and inorganic iodine species.	d or hr (at 12°C /pH)	AR, 2013

DT ₅₀ for degradation in soil	Not applicable due to the fact that iodine is an element	d or hr	AR,20 13
DT ₅₀ for degradation in air	Rapid photolysis of I2 takes place in the lower atmosphere due to its strong absorption of light in the visible wavelengths (400 < λ < 700 nm). Lifetime = 5-10 s for an overhead sun	d or hr (at 12°C)	AR,20 13

Calculated fate and distribution in the STP [if STP are a relevant compartment]			
Compartment	Percentage [%]		Remarks
	Scenario 1	Scenario n	
Air	N.R	n.a.	Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products. Evaluation of active substances. AR, 2013.
Water	80	n.a.	
Sludge	20	n.a.	
Degraded in STP	0	n.a.	

N.R.: Not Relevant

n.a. not applicable

ES CA:
Input parameters

Input parameters for calculating the fate and distribution in the environment for Iodine, Iodide and Iodate			
Parameters for iodine	Value	Unit	Remarks
Molecular weight	235.81	g.mol ⁻¹	CAR (2013)
Vapour pressure (at 25°C)	40.7	Pa	CAR (2013)
Water solubility (at 20°C)	290	mg/l	CAR (2013)
Log OctaNoI/water partition coefficient	-	-	Inorganic substance
Organic carbon/water partition coefficient (K _{oc})	Not relevant	L/kg	Inorganic substance
Henry's Law Constant (at 25°C)	34.43	Pa/m ³ /mol	
Biodegradability	Not biodegradable	-	Inorganic substance
DT50 for degradation in soil	1.0E+06	D	Inorganic substance
Solids-water partition coefficient in suspended matter (K _{p, susp})	220	L/kg	CAR (2013)
Solids-water partition coefficient in soil (K _{p, soil})	5.8	L/kg	CAR (2013)
Solids-water partition coefficient in soil (K _{soil-water})	8.90	m ³ .m ⁻³	Calculated
Susp-water partition coefficient (K _{susp-water})	55.9	m ³ .m ⁻³	Calculated
Parameters for iodide	Value	Unit	Remarks
Transformation rate in surface water iodine to iodide (%)	100	%	
Transformation rate in soil iodine to iodide via the STP (%)	14	%	
Transformation rate in soil iodine to iodide via manure (%)	100	%	
Molecular equivalent iodide/iodine	1		
Parameters for iodate	Value	Unit	Remarks
Transformation rate in surface water iodine to iodide (%)	100	%	
Transformation rate in soil iodine to iodide via the STP (%)	100	%	
Transformation rate in soil iodine to iodide via manure (%)	100	%	
Molecular equivalent iodate/iodine	1.382		

Calculated PEC values

Summary table on calculated PEC values								
	PEC _{STP}	PEC _{water}	PEC _{sed}	PEC _{sea water}	PEC _{sed}	PEC _{soil}	PEC _{GW1}	PEC _{air}
	[mg/l]	[µg/l]	[mg/kg _{wwt}]	[mg/l]	[mg/kg _{wwt}]	[mg/kg]	[µg/l]	[mg/m ³]
Scenario 1	I ₂ :0.0017	I ₂ :0.0002	N.A.	N.A.	N.A.	I ₂ :0.0017	I ₂ :0.3231	N.A.
Via STP	I ⁻ :0.0017	I ⁻ :0.0002				I ⁻ :0.0002	I ⁻ :0.0452	

	IO ₃ ⁻ :0.00 24	IO ₃ ⁻ :0.00 02				IO ₃ ⁻ :0.00 23	IO ₃ ⁻ :0.446 5	
Scenario 2 Via manure-10 years application (grassland)	N.A.	I ₂ :1.7905 I ⁻ :1.7905 IO ₃ ⁻ :2.4745	N.A.	N.A.	N.A.	I ₂ :0.0515 I ⁻ :0.0511 IO ₃ ⁻ :0.0711	I ₂ :17.9051 I ⁻ :17.9051 IO ₃ ⁻ :24.7448	N.A.
Scenario 2 Via manure (arable)-10 years application	N.A.	I ₂ :0.9824 I ⁻ :0.9824 IO ₃ ⁻ :1.3577	N.A.	N.A.	N.A.	I ₂ :0.0938 I ⁻ :0.0938 IO ₃ ⁻ :0.1296	I ₂ :9.8242 I ⁻ :9.8242 IO ₃ ⁻ :13.5771	N.A.

¹ If the PEC_{GW} was calculated by using a simulation tool (e.g. one of the FOCUS models), please provide the results for the different simulated scenarios in a separate table.

N.A. Not applicable

ES CA:

It should be noted that the nitrogen standard is the most relevant in Europe, notably in Spain. Therefore, regarding emission via manure application, PEC values were calculated for application to grassland and arable land on the nitrogen standard.

According to the Technical Agreements on Biocides 2021, (version 2.0, entry ENV-63):

In the emission to STP, the value for the number of milk producing cows is refined to 82.
In the emission to slurry, the value for the number of milk producing cows is 100.

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. Only for PECs in soil were recalculated taking into account the following: for spreading of sewage sludge on arable land it is assumed that 100% of iodine is transformed into iodate and 14% into iodide (according to CAR). 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 calculated with ESD PT3 represents the concentration after manure application on arable land and grassland (PIEC). Since fertilizers are applied repeatedly, iodine would accumulate in the soil after consecutive manure applications. This accumulation is counteracted by the effect of degradation and leaching. Concentrations in soil after ten years are therefore calculated according to the Addendums for PT18 (WGV2015 and WGI2018). The emission to soil from the application of slurry/manure has been determined taking degradation and leaching to deeper soil layer into account for a period of 10 years (agreed at BPC WGIV2017).

Based on the biodegradation data of iodine in soil and leaching, the experimentally derived water-solids distribution coefficient for soils is 5.8 L/kg, iodine is practically eliminated from the soil by leaching, maintaining half-lives for topsoil leaching of 2571 days in arable land (20 cm) and 643 days in grassland (5 cm). Due to the value for leach is derived from the soil depth, this value is different for arable and grassland. These two values have been validated in WG for Union Authorisations containing iodine.

Input parameters for the $PEC_{soil,10years}$ calculations considering degradation and leaching of iodine to deeper soil layers are listed in the table below:

Parameters	Symbol	Value	Unit	S/D/O/R
Fraction of rain water that infiltrates into soil	Finf_soil	0.25	-	Guidance on BPR:Vol IV Environment (ECHA, 2017) Equation (55)
Rate of wet precipitation (700 mm/year)	RAINrate	1.92E-03	m/d	Guidance on BPR:Vol IV Environment (ECHA, 2017) Equation (55)
Half-life for biodegradation in bulk soil	DT50biosoil	1.00E+6	d	CAR
First-order rate constant for leaching from soil layer (grassland)	kleach_gr	1.08E-03	d ⁻¹	Guidance on BPR:Vol IV Environment (ECHA, 2017) Equation (55)
Half-life for leaching from soils (grassland)	DT50soil_gr	642.71	d	BPC WGIV2017
First-order rate constant for leaching from soil layer (arable land)	kleach_ar	2.70E-04	d ⁻¹	Guidance on BPR:Vol IV Environment (ECHA, 2017) Equation (55)
Half-life for leaching from soils (arable land)	DT50soil_ar	2570.82	d	BPC WGIV2017
First-order rate constant for removal from top soil layer (grassland)	ktot_gr	1.08E-03	d ⁻¹	Guidance on BPR:Vol IV Environment (ECHA, 2017) Equation (56)
First-order rate constant for removal from top soil layer (arable land)	ktot_ar	2.70E-04	d ⁻¹	Guidance on BPR:Vol IV Environment (ECHA, 2017) Equation (56)

Finally, according to the CAR, all considered compartment with PEC/PNEC ratio above 1 will be assessed by a comparison between PEC values for iodine and background level determined for each compartment.

Summary table on calculated PEC and background levels (as iodine)				
	Values for Iodine		Values for Iodide	Values for Iodate
	Background	PEC	PEC	PEC
Via manure application (10 years applications)				
Surface water grassland (µg.L ⁻¹)	0.5-20	1,17E+00	1,17E+00	1,62E+00
Surface water arable (µg.L ⁻¹)		7,07E-01	7,07E-01	9,77E-01
Soil grassland (mg.kg _{wwt})	0.565-22.6 extremes up to 110.74	6,16E-02	6,16E-02	8,51E-02
Soil arable (mg.kg _{wwt})		3,71E-02	3,71E-02	5,12E-02
Groundwater grassland (µg.L ⁻¹)	1-70	1,18E+01	1,18E+01	1,62E+01
Groundwater arable (µg.L ⁻¹)		7,08E+00	7,08E+00	9,78E+00
Via STP				
Elocal (kg/d)	3,77E-03			
STP (mg/L)	-	1,51E-03	1,51E-03	2,09E-03
Surface water (µg/L)	0.5-20	1,50E-01	1,50E-01	2,08E-01
Soil (mg/kg _{wwt})	0.565-22.6 extremes up to 110.74	9,10E-03	1,27E-03	1,26E-02
Groundwater (µg/L)	1-70	1,74E+00	2,43E-01	2,40E+00

For spreading of sewage sludge on arable land it is assumed that 14% of iodine is transformed into iodide (according to CAR).

Primary and secondary poisoning

Not relevant. Iodine is not bioaccumulative (Kow<3). A direct or indirect exposure of different animals other than treated is considered unlikely.

ES CA:

Primary poisoning

Not relevant. A direct exposure of different animals (birds or mammals) other than treated animal to the biocidal product is considered negligible since there is no direct release of the product in the environment.

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. 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.

2.2.8.3 Risk characterisation

Risk assessment via atmosphere emissions

Conclusion: Risk is not relevant. Emissions of Iodine to air resulting from the product application is not considered relevant (CAR, 2013).

ES CA:
 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.

Risk assessment via manure application after 10 years applications and via Sewage treatment plant (STP) to Aquatic compartment and Terrestrial compartment

	Values for Iodine			Values for Iodide		Values for Iodate	
	Background	PEC	PEC/PNEC*	PEC	PEC/PNEC*	PEC	PEC/PNEC*
Via manure: 10 years application							
Surface water grassland (µg.L ⁻¹)	0.5-20	1.7905	3.0348	1.7905	2.1572	2.4745	0.0423
Surface water arable (µg.L ⁻¹)		0.9824	1.6651	0.9824	1.1836	1.3577	0.0232
In the background level for iodine							
Soil grassland (mg.kg _{wwt} ⁻¹)	0.565-22.6 extremes up to 110.74	0.0515	4.3602	0.0515	11.9651	0.0711	0.2339
Soil arable (mg.kg _{wwt} ⁻¹)		0.0938	7.9466	0.0938	21.8070	0.1296	0.4263
In the background level for iodine							
Groundwater grassland (µg.L ⁻¹)	1-70	17.9051	>0.1	17.9051	>0.1	24.7448	>0.1
Groundwater arable (µg.L ⁻¹)		9.8242	>0.1	9.8242	>0.1	13.5771	>0.1
In or higher than the background level for iodine							

	Values for Iodine			Values for Iodide		Values for Iodate	
	Background	PEC	PEC/PNEC*	PEC	PEC/PNEC*	PEC	PEC/PNEC*
Via STP							
STP (mg.L ⁻¹)	Not relevant	0.0017	0.0006	0.0017	not relevant	0.0024	not relevant
Surface water (µg.L ⁻¹)	0.5-20	0.0002	0.0003	0.0002	0.0002	0.0002	0.000001

		In the background level for iodine					
Soil (mg.kg _{wwt})	0.565-22.6 extremes up to 110.74	0.0017	0.1434	0.0002	0.0551	0.0023	0.0077
		Lower to the background level for iodine					
Groundwater (µg.L ⁻¹)	1-70	0.3231	>0.1	0.0452	<0.1	0.4465	>0.1
		In or lower to the background level for iodine					

**Values in red indicate a risk quotient (PEC/PNEC) > 1*

Risk assessment via manure application after 10 years (Nitrogen standard)

In surface water

The Risk Quotient (RQ) for Iodine and Iodide is > 1. Nevertheless, both Iodine and Iodide PEC_{surface-water} values are in the range of typically background concentrations (0.5 to 20 µg/L) which indicates acceptable risks.

In soil

The Risk Quotient (RQ) for Iodine and Iodide is > 1. Like in Surface water, the PEC_{soil} (for grass and arable land) values are below or in typically background concentrations ranging from 0.565 to 22.6 mg/kg wwt. Conclusion: The risk is acceptable.

In groundwater

In the risk assessment for groundwater, the PEC values are compared with the limit value of 0.1 µg/L provided for pesticides in the Drinking Water Directive 98/83/EC. However, as iodine and iodine compounds are not xenobiotics, this threshold value can be considered as over conservative. Calculated PEC_{gw} values for iodine are higher than the natural background concentrations of 70 µg/L. The estimation of concentrations in groundwater is based on a worst-case assumption taking into account the partitioning equilibrium. In the absence of possible refinement of this methodology, the assessment of estimated concentrations in groundwater cannot be refined. However, no unacceptable risk is expected for groundwater.

Risk assessment via Sewage treatment plant (STP)

In STP

PEC/PNEC value is below 1 which indicates acceptable risk.

In surface water

PEC/PNEC values in surface water are all below 1 or in the background level for iodine in this compartment which indicates acceptable risks.

In soil

PEC_{soil} values are below or in typically background concentrations ranging from 0.565 to 22.6 mg/kg wwt for iodine.

In groundwater

PEC_{gw} are below the maximum natural background concentration of 70 µg/L for iodine.

Risks are acceptable following a theoretical release to the STP. Therefore, releases to the STP from milking parlour are not considered relevant for Spain since many farms are not connected to a municipal STP having their own STP system.

Conclusion: In all cases the risks are acceptable.

Groundwater

For iodine the PEC_{grw} values of the worst-case application as non-medicinal teat dips or sprays were higher than 0.1 µg/L provided for pesticides in the Drinking Water Directive 98/83/EC.

However, it should be noted that the definition of pesticides in the Drinking Water Directive is limited to organic substances and their relevant metabolites, degradation and reaction products. Based on this definition iodine, iodide and iodate are not within the scope of this Directive. Moreover, iodine and its species are not xenobiotic substances but essential nutrients which are needed in relatively high concentration, and for this reason the limit concentration of 0.1 µg/L for pesticides is not considered applicable.

Although the calculated iodine concentration in groundwater is above the mean natural background concentration of 1 µg/L it is still below the maximum natural background concentration of 70 µg/L (up to 400 µg/L in exceptional cases).

It should be noted that the PEC in groundwater were calculated following the TGD using the pore water concentration in soil as indication for the groundwater level (in the following noted as "pore water-approach"), not taking into account any removal processes like e.g. lateral transport or plant uptake. This leads to a large overestimation of the real concentrations in groundwater. FOCUS-modelling for the groundwater (and surface water) to achieve more realistic predictions is not applicable to inorganic substances (see for example EFSA conclusion on sulphur under Dir 91/414/EC; available at <http://www.efsa.europa.eu/en/scdocs/scdoc/221r.htm>).

For comparison, if the groundwater- and surface water concentrations would be calculated for the average natural background concentration of iodine species in soil of 5 mg/kg, using the "pore water- approach" based on the TGD it results in surface- and groundwater concentrations of 0.16 and 1.6 mg/L, respectively which is 10 - 100 fold higher than the concentrations measured in these compartments in the field. This illustrates that the results of the calculations using the "pore water-approach" must be interpreted with caution.

In conclusion given that the derived conservative Upper Intake Level (UL) for children and adults is 250 and 600 µg iodine/day respectively an increase in the natural groundwater iodine levels of up to 65.9 µg/L for iodine/iodide (using nitrogen standard) appears not to be of any concern.

ES CA:

The table below represents the risk assessment via manure application after 10 years applications and via Sewage treatment plant (STP) to Aquatic compartment and Terrestrial compartment with the background levels (as Iodine).

Summary table on calculated PEC and background levels (as iodine)							
	Values for Iodine			Values for Iodide		Values for Iodate	
	Background	PEC	PEC/PNEC	PEC	PEC/PNEC	PEC	PEC/PNEC
Via manure application (10 years applications)							
Surface water grassland ($\mu\text{g}\cdot\text{L}^{-1}$)	0.5-20 $\mu\text{g}/\text{L}$	1,17E+00	1,99E+00	1,17E+00	1,41E+00	1,62E+00	2,77E-02
Surface water arable ($\mu\text{g}\cdot\text{L}^{-1}$)		7,07E-01	1,20E+00	7,07E-01	8,52E-01	9,77E-01	1,67E-02
In the background level for iodine							
Soil grassland (mg.kg _{wwt})	0.565-22.6 mg/kgdwt extremes up to 110.74 mg/kgdwt	6,16E-02	5,22E+00	6,16E-02	1,43E+01	8,51E-02	2,80E-01
Soil arable (mg.kg _{wwt})		3,71E-02	3,14E+00	3,71E-02	8,62E+00	5,12E-02	1,69E-01
Lower the background level for iodine							
Groundwater grassland ($\mu\text{g}\cdot\text{L}^{-1}$)	1-70 $\mu\text{g}/\text{L}$ with extremes up to 400 $\mu\text{g}/\text{L}$	1,18E+01	>0,1 $\mu\text{g}/\text{L}$	1,18E+01	>0,1 $\mu\text{g}/\text{L}$	1,62E+01	>0,1 $\mu\text{g}/\text{L}$
Groundwater arable ($\mu\text{g}\cdot\text{L}^{-1}$)		7,08E+00	>0,1 $\mu\text{g}/\text{L}$	7,08E+00	>0,1 $\mu\text{g}/\text{L}$	9,78E+00	>0,1 $\mu\text{g}/\text{L}$
In the background level for iodine							
Via STP							
Elocal (kg/d)	3,77E-03						
STP (mg/L)	Not relevant	1,51E-03	5,20E-04	1,51E-03	Not relevant	2,09E-03	Not relevant
Surface water ($\mu\text{g}/\text{L}$)	0.5-20 $\mu\text{g}/\text{L}$	1,50E-01	2,55E-01	1,50E-01	1,81E-01	2,08E-01	3,55E-03
Lower to the background level for iodine							
Soil (mg/kg _{wwt})	0.565-22.6 mg/kgdwt extremes up to 110.74 mg/kgdwt	9,10E-03	7,71E-01	1,27E-03	2,96E-01	1,26E-02	4,14E-02
Lower the background level for iodine							
Groundwater ($\mu\text{g}/\text{L}$)	1-70 $\mu\text{g}/\text{L}$ with extremes up to 400 $\mu\text{g}/\text{L}$	1,74E+00	>0,1 $\mu\text{g}/\text{L}$	2,43E-01	>0,1 $\mu\text{g}/\text{L}$	2,40E+00	>0,1 $\mu\text{g}/\text{L}$
In the background level for iodine							

*Values in bold indicate a risk quotient (PEC/PNEC) > 1

Conclusion concerning the risk assessment via manure application after 10 years applications:

In surface water

Although the PEC/PNEC ratios for Iodine and Iodide are > 1, the PEC surface water values for iodine are in the range of typically background concentrations (0.5 to 20 $\mu\text{g}/\text{L}$) which indicates acceptable risks.

In soil

The individual PEC / PNEC ratios for the relevant compartment are higher than 1 for iodine and iodide in grassland and arable land. Iodine is a natural substance, and PEC / PNEC values greater than 1 are acceptable since PEC values are within background concentrations. Iodine is not a xenobiotic substance and is naturally present in soil. Its background concentrations are in the range of 0.565 – 22.6 mg/kgdwt (expressed as iodine).

For cases where it is greater than 1, the highest PEC for iodine is 7.04E-02 mg/l, so it is within the lower range of background iodine concentrations in soil.

Therefore, the emission to soil is considered acceptable.

In groundwater

The concentration in the soil's pore water derived by equilibrium partitioning according to the guidance are above the limit values of 0.1 µg/L provided for pesticides in the Drinking Water Directive 98/83/EC.

It is stated in the CAR (2013) that the trigger value of 0.1 µg/L is limited to organic substances and their relevant metabolites and degradation products. Since iodine and its species are inorganic substances, which are not xenobiotic but essential nutrients, it is concluded in the CAR that the concentration limit of 0.1 µg/L for pesticides is not applicable to iodine.

The predicted concentrations were compared to natural background concentrations. The PECs are expected to be within the natural background level of iodine in groundwater that ranges between 1 and 70 µg/L with extremes up to 400 µg/L. Therefore, emission to groundwater is considered acceptable and no risk mitigation measures are necessary.

Conclusion concerning the risk assessment via STP:

In STP

The individual PEC/PNEC ratio for the assessed scenario is below 1 for iodine, iodide and iodate in the aquatic compartment, exposed via STP. Therefore, there is no unacceptable risk to this compartment for the proposed use of the teat disinfectant product.

In surface water

PEC/PNEC values in surface water are all below 1 in this compartment, which indicates that emission to surface water is considered acceptable.

In soil

The individual PEC / PNEC ratio for the relevant compartment is lower than 1 for all substances when soil is exposed via STP.

Therefore, emission to terrestrial compartment via STP is considered acceptable.

In groundwater

The same approach used previously can be applied.

PECsgw are below the maximum natural background concentration of 70 µg/L for iodine. Therefore, emission to groundwater is considered acceptable.

Primary and secondary poisoning

Primary poisoning

For the proposed use of the active substances in PT3 applications direct exposure of birds and mammals to the active substances or contaminated aquatic and terrestrial organisms is considered negligible.

As iodine is not bioaccumulative and the proposed applications will not result in exposure of surface water and the amounts of iodine delivered into the environment through biocidal uses are within the natural occurring background levels, the risk for the primary and secondary poisoning is considered acceptable. The proposed applications meet the standards for birds and mammals.

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

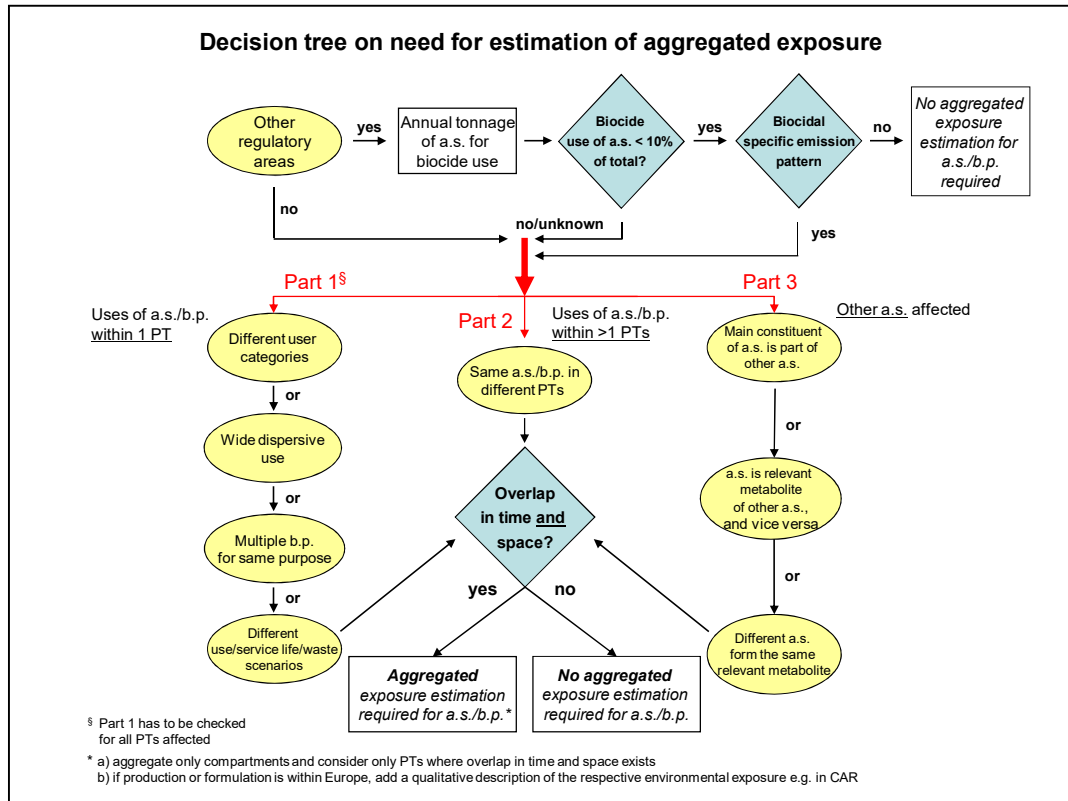
Not relevant. The product only contains one active substance (PVP-Iodine) and no substances of concern. In addition, no active substances from other PTs and no other ingredients that need consideration are contained.

Aggregated exposure (combined for relevant emission sources)

Iodine is also used for disinfection of udders before milking (the manufacturer advises the combination of MAMICAMP SELLADOR[®] with the product YODICAMP ORDEÑO[®], that contains a maximum of 0.25% iodine, diluted to 3% v/v, applying it by towel or sponge before milking), but the amount of iodine contributed in the pre-milking phase is of the order of 5000 times less than post-milking (2.5 ml YODICAMP ORDEÑO[®]/treatment/cow x 3% v/v is equivalent to 0.054 ml of MAMICAMP SELLADOR[®]), and so it is totally negligible against the iodine used in post-milking.

Furthermore, the amount of MAMICAMP SELLADOR[®] used to calculate the environmental risk according the guides (10 ml/treatment/cow) exceeds 2.5 times the actual recommended dose (4 ml/treatment/cow ml), so that iodine provided by the pre-milking phase is considered widely encompassed in the iodine used in post-milking. Therefore, the aggregate exposition study of both milking phases is considered totally unnecessary.

On the other hand, although iodine is released from multiple sources, aggregated exposure assessment is not deemed necessary as there is no overlap in space and time for the current biocidal product family. Iodine as a teat disinfectant is predominantly released to agricultural soils and therefore not mixed with iodine from other anthropogenic sources. See fig.1 for decision tree on the need for estimation of aggregated exposure according CAR (2013)



Overall conclusion on the risk assessment for the environment of the product

As iodine is not bioaccumulative and for the proposed applications (indoor use) the amounts of iodine delivered into the environment through biocidal uses are within the natural occurring background levels, the risk for the environment of the product is considered acceptable.

ES CA:
The use of MAMICAMP SELLADOR can be considered acceptable for the environment according to the results of the risk assessment.
Release via manure results in a PEC:PNEC ratio >1 for surface water and also for soil. The expected concentrations are however within the natural background. The accompanied risks are therefore considered acceptable.
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 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.

It may also be noted that iodine is an essential element to both animals and plants in rather high concentrations (higher than what corresponds to a trace element). It can thus be concluded that the actual risks arising from the use of iodine-containing product should be considered acceptable.

2.2.9 Measures to protect man, animals and the environment

The BP has been classified as: Eye Irrit. 2, and Aquatic Chronic 3, with the next hazard phrases:

H319: Causes serious eye irritation

H412: Harmful to aquatic life with long lasting effects

The risk is acceptable for professional users when gloves and eye protection are worn during the handling of the product.

The use of the product by professional users presents a low potential of exposure for a frequency 2 milking events /day, and 300 days/year. Therefore, with the RMMs included (see section 2.1.5.2), the risk is acceptable including without wear gloves.

The product is classified as Harmful to aquatic life with long lasting effects, it will be recommended in the label the following phrases:

P273: Avoid release to the environment

P501: Dispose of contents and / or containers in accordance with regulations on hazardous waste or packaging and packaging waste respectively.

Finally, it has been demonstrated that this BP at the dose recommended is safe because presents an acceptable risk to man and the environment.

2.2.10 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

2.2.11 Comparative assessment

BACKGROUND

The biocidal product MAMICAMP SELLADOR contains the active substance PVP-iodine. This a.s. does meet the exclusion criteria according to Article 5(1 d) BPR and, therefore, does meet the conditions laid down in Article 10 BPR, and is consequently a candidate for substitution.

In accordance with Article 15(2) 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 review of approval of the active substance iodine and polyvinylpyrrolidone iodine. These substances are identified as having endocrine-disrupting properties.

Therefore, in accordance with Article 23 of Regulation 528/2012 a comparative assessment will be carried out for the biocidal product. This comparative assessment has been carried out by the ES CA using the agreed guidance, including the Technical

Guidance Note on comparative assessment of biocidal products (TNSG-CA i.e. CA-May15-Doc4.3a-final).

1. APPLICATION ADMINISTRATIVE DETAILS

Procedure: NA-APP

Purpose: Authorisation

Case Number in R4BP: BC-AE019732-60

Evaluating Competent Authority: ES CA

Applicant: PRODUCTOS QP S.A

(Prospective) Authorisation holder: PRODUCTOS QP S.A

2. ADMINISTRATIVE INFORMATION OF THE BPF

Trade name(s): MAMICAMP SELLADOR

Product type(s): 03 Veterinary hygiene (Disinfectants)

Active substance(s): Polyvinylpyrrolidone Iodine (CAS: 25655-41-8)

3. SCREENING PHASE

The ES CA began the comparative assessment with the screening phase described in section 6.1 of the TNSG-CA to identify whether the diversity of the active substances - mode of action combination in authorised biocidal products is adequate.

Intended use and properties of the biocidal product

Use 1 – Teats disinfection

Product Type	PT03 – Veterinary hygiene (Disinfectants)
Where relevant, an exact description of the authorised use	Teat disinfection (non-medical) after milking
Target organism (including development stage)	Bacteria and yeasts
Field of use	Indoor
Application method(s)	Manual or automatic dipping cups treatment
Application rate(s) and frequency	Application rate: RTU after milking -daily cows: 4 ml/cow/event -sheep and goats: 2 ml/animal/event Contact time: 5 minutes after milking The frequency of application is: 2 events/day for manual milking or 3 events/day for milking systems for dairy cows, and 1 application per day for ewes or goats.
Category(ies) of users	Trained professional and Professional users
Pack sizes and packaging material	Please see the relevant section.

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

Iodine rapidly penetrates into microorganisms showing a high affinity pattern of adsorption. • Iodine combines with protein substances in the bacterial cell; these could be peptidoglycans in the cell walls or enzymes in the cytoplasm. This results in irreversible coagulation of the protein and consequent loss of function.

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

Iodine reacts with key groups of proteins, in particular the free-sulphur amino acids cysteine and methionine, nucleotides and fatty acids. Iodine Product types 1, 3, 4, 22
December 2013 Page 13 of 107

Iodine interferes at the level of the respiratory chain of the aerobic microorganisms by blocking the transport of electrons through electrophilic reactions with the enzymes of the respiratory chain. The rapid penetration of iodine into microorganisms and its mode of action indicate that the time-delay i.e. contact time required for sufficient efficacy depends on the tolerance of the organism to iodine and the concentration of iodine used for treatment. Iodine is more effective at higher temperatures. The germicidal activity of iodine-containing solutions is characterised by their colour. Amber solutions are active whilst pale yellow or colourless solutions are less effective and must be replaced by new solutions. The efficacy of iodine as a biocide has been demonstrated over 170 years of use and due to this long history of use there are numerous papers demonstrating the microbiocidal activity of iodophor products in laboratory and field tests. An overview on literature reviews describing the efficacy of iodophor products has been provided in Document III-A5. Relevant efficacy data for the different target organisms has been summarised in DOCII-A and II-B. In the confidential annex, tables are included summarising the available efficacy data provided by the respective applicants. Information on resistance: Taking into account the mode of action of iodine which is non-selective, development of resistance against iodine is unlikely. Iodine / iodophors have been used for over 170 years as disinfectants for a variety of applications. Such applications include disinfection of skin in the human hygiene and medical area but also skin of animals using teat dips as well as surfaces such as milk tanks. No reduction in efficacy was reported to the producers of iodine/iodophor based products for such applications indicating that no development of resistant microorganisms or viruses has occurred

3.2. Chemical diversity of the active substances - mode of action combination in authorised biocidal products

According to the information available to the ES CA, there is a biocidal product authorised in Spain under Product Type 03 (Veterinary hygiene (Disinfectants) of the Biocidal Products Directive and Biocidal Products Regulations (including Mutual Recognitions and same product authorisations). There is an active substance **acid lactic** which has been included in authorised PT03 products.

ACID LACTIC

Use: The active substance is intended to be used for cleaning, disinfecting and sealing of the udder/teat hole before and after milking, providing a protective barrier against the entry of germs into the udder through the teat hole, protecting and softening the skin and mucous membranes. Indicated for topical use in dairy cows, ewes, goats and other lactating females.

Target organism: Bacteria and yeast

Category(ies) of users: authorized for Professional and trained professional

Mode of action: In solution, lactic acid exists in a pH-dependent equilibrium between the undissociated and dissociated form. Only in its undissociated state, the acid is able to pass the cell membrane. At a relatively low pH, the uncharged acid enters the cell. Inside the cell, the lactic acid dissociates due to the higher pH. The molecules remain inside the cell, because the resulting ions cannot pass the membrane. The pH inside the cell is lowered and metabolic reactions are inhibited. Further effects are also reported: decrease of the membrane permeability for amino acids, organic acids, phosphates resulting in uncoupling

of both substrate transport and oxidative phosphorylation from the electron transport system. Furthermore, an inhibition of the glycolysis is observed. The bactericidal activity of L(+) lactic acid was investigated by studies performed with the representative biocidal product containing 8% of lactic acid. The performed tests provide reliable results for innate efficacy assessment. L (+) lactic acid shows an innate bactericidal activity on samples of the target organisms (amongst others: Staphylococcus aureus, Streptococcus agalactiae, Streptococcus uberis, Streptococcus dysgalactiae, Escherichia coli) after a contact time of 10-30 minutes at concentrations of 6.1-6.8%. The studies performed are sufficient at the approval stage. However, efficacy shall be reviewed in accordance with the relevant guidance documents in the framework of active substance renewal and relevant data shall be provided in the scope of product authorisation. Development of resistance is considered unlikely due to the non-specific mode of action. Therefore, products based on acid lactic could be eligible as alternative biocidal

3.3 Conclusions on screening phase

In the technical guidance note on comparative assessment of biocidal products, it is stated that:

a suitable number of available active substances having different modes of action on the harmful organism would be necessary to minimise resistance development or selection as a general rule, at least three different and independent "active substance/mode of action" combinations should remain available through authorized BPs for a given use in order to consider that chemical diversity is adequate.

Taking into account the weak diversity of active substances in biocidal products authorized for cleaning, disinfecting and sealing of the udder/teat hole, the ES CA concludes that there is no adequate chemical diversity in line with Article 23(3)(b) and the technical guidance note on comparative assessment.

However as PVP-Iodine meets the exclusion criteria in article 5, it is proposed that the comparative assessment for PVP-Iodine must be taken forward to Tier IB (quantitative analysis) in line with section 6.2 of the TNSG-CA.

4.TIER IB: DETAIL COMPARISON

According to the information available to the ES CA, there is a biocidal product authorised in Spain under Product Type 03 (Veterinary hygiene (Disinfectants) of the Biocidal Products Directive and Biocidal Products Regulations (including Mutual Recognitions and same product authorisations). There is an active substance **acid lactic** which has been included in authorised PT03 products.

As per documents CA-March14-Doc.4.1-Final and CA-Nov14-Doc.4.4-Final, only data available in the PAR associated to the following exclusion/substitution criteria will have to be compared.

4.1. Concerning Human Health

ED PROPERTIES (exclusion criterion)

PVP-IODINE:

In accordance with Article 15(2) 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 review of approval of the active substance iodine and polyvinylpyrrolidone iodine.

Iodine, in excess of physiological needs, meets all the above three criteria – it shows adverse effects (thyroid disorders) in humans; it has an endocrine mode of action (disruption of thyroid hormones metabolism and hypothalamic-pituitary-thyroid axis); and the adverse effects are a consequence of the endocrine mode of action. Therefore, the biocidal active substances, iodine and PVP-iodine, are identified as having endocrine-disrupting properties with respect to humans.

ACID LACTIC:

In accordance with Assessment report, L(+) lactic acid is not considered to have endocrine disrupting properties and does not fulfil criterion (d) of Article 5(1).

It can therefore be considered that the alternative biocidal product on the market have a lower risk to human health compared to MAMICAMP SELLADOR

4.2 Conclusions of Tier IB assessment

The alternative authorised biocidal product provide a significant lower risk to human health but the alternative biocidal product show more economical and practical disadvantages than the biocidal product relevant.

5.OVERALL CONCLUSION. COMPARATIVE ASSESSMENT REPORT

ES CA considers that there is not currently an adequate chemical diversity of active substance-mode of action combinations to minimise the occurrence of resistance in the target organisms.

In addition to identifying economic disadvantages linked to the substitution by alternative biocidal product

The conclusions of the comparative assessment are not sufficiently conclusive to support the prohibition or restriction of biocidal product under Article 23(3) of Regulation 528/2012, and the ES CA proposes that the biocidal product MAMICAMP SELLADOR should be authorised for a period not exceeding 5 years in accordance with Article 23(6) of Regulation 528/2012.

3 ANNEXES

3.1 List of studies for the biocidal product

Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
[REDACTED]	[REDACTED]	Caracterización físico-química de MAMICAMP SELLADOR	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	Estudio de estabilidad a 25°C durante 2 años de MAMICAMP SELLADOR – Validación del método de análisis y determinaciones a 0, 3, 6, 12, 18 y 24 meses	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	ATQ Declaración expert YODICAMP	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	Contenido en Yodo libre y Yoduro MAMICAMP SELLADOR – Determinaciones en muestras a 0 y mas de 24 meses almacenamiento a T ^{amb} .	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	MAMICAMP SELLADOR UN Metal Corrosivity Testing	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	Valoración de la actividad bactericida según norma UNE-EN 1656: JUNIO 2010 (ERRATUM OCTUBRE 2010)	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	Ensayo cuantitativo de superficie para la evaluación de desinfectantes de pezones PT3 utilizados en el área veterinaria. Método de prueba y requisitos (fase 2, etapa 2) con el producto MAMICAMP SELLADOR (Norma PR NF EN 17422:2019, bajo condiciones específicas de la guía BPR:2018)	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	Valoración de actividad levurizada para desinfección de pezones post-ordeño según norma: UNE-EN 1657:2016	Y	PRODUCTOS QP, S.A.
[REDACTED]	[REDACTED]	Ensayo cuantitativo de superficie para la evaluación de la actividad levurizada de desinfectantes de pezones utilizados en el área veterinaria (PT3). Método de prueba y requisitos (fase 2, etapa 2) con el producto MAMICAMP SELLADOR (Basado en norma PR NF EN 17422:2019, bajo las condiciones específicas de la guía BPR:2018)	Y	PRODUCTOS QP, S.A.

European Pharmacopoeia	2004	European Pharmacopoeia, 5th Edition, suplement 5.2, Council of Europe, Strasborg.	N	Public
D.C. Whitehead	1979	Iodine in the UK environment with particular reference to agriculture. <i>Journal of Applied Ecology</i> , Vol. 16, 269-279.	N	Public
E. Rae, S.A. Malik,	1996	The determination of iodine in geochemical samples: The use of pyrohydrolytic decomposition. <i>Chemosphere</i> 33 (1996) 2121.	N	Public
W.S. Kim, J.D. Glothlin and R. E. Kupel.	1981	Sampling and Analysis of Iodine in the Industrial Atmosphere, <i>Am. Ind. Hyg. Assoc. J.</i> , 43, 187-190	N	Public
OSHA	1994	Iodine In Workplace Atmospheres (Impregnated Activated Beaded Carbon) OSHA Method ID-212 May 1994	N	Public
NIOSH	1994	IODINE: METHOD 6005 NIOSH Manual of Analytical Methods (NMAM), Fourth Edition	N	Public
US-EPA	1983	Iodine Method 345.1 <i>Methods for chemical analysis of water and wastes. Cincinnati, OH: U.S Environmental Protection Agency, Environmental Monitoring and Support Laboratory. EPA-600/4-79020.</i>	N	Public
ASTM	1995	1995 Annual book of ASTM Standards. Vol. 11.02. American Society for Testing of Materials. Philadelphia, PA.	N	Public
Jones SD, Spencer CP, Truesdale VW.	1982	Determination of total iodine and iodate-iodine in natural freshwater. <i>Analyst</i> 107:1417-1424. 1982	N	Public
R.E. Moxon	1984	Automatic methods for the determination of total inorganic iodine and free iodide in waters. <i>Analyst</i> 109:425-43, 1984	N	Public
L. Maros, M. Káldy and S. Igaz	1989	Simultaneous determination of bromide and iodide as acetone derivatives by gas chromatography and electron capture detection in natural waters and biological fluids. <i>Anal Chem</i> 61:733-735, 1989	N	Public
H.G.Weinberg and H. Yamada	1997	Sub part-per-billion analysis of bromate, iodate, and chlorite in drinking water using a new post ion chromatography column reaction and UV detection. In: <i>Water quality technology conference proceedings, November 9-12, 1997, Denver, Co., 4B1/1-4B1/13.</i>	N	Public

Benotti J, Benotti N, Pino S, et al.	1 9 6 5	Determination of total iodine in urine, stool, diets and tissues. <i>Clin Chem</i> <i>11:932-936, 1965</i>	N	Public
S. Ohno	1 9 7 1	Determination of iodine and bromine in biological materials by neutron activation analysis. <i>Analyst</i> <i>96:423-426,</i> <i>1971</i>	N	Public
L.L. Oliver, R.V. Nallard, O.K. Manuel	1 9 8 2	¹²⁹ I in Missouri thyroids. <i>Health Phys</i> <i>42:425-432, 1982</i>	N	Public
Verma KK, Jain A, Verma A.	1 9 9 2	Determination of iodide by high- performance liquid chromatography after precolumn derivatization. <i>Anal</i> <i>Chem</i> <i>64:1484-1489, 1992.</i>	N	Public
Hou X, Chai X, Qian Q, et al.	1 9 9 7	Determination of bromine and iodine in normal tissues from Beijing health adults. <i>Biol Trace Elem Res</i> <i>56:225-230,</i> <i>1997</i>	N	Public
Andersson S, Forsman U.	1 9 9 7	Determination of total iodine in biological material by alkaline ashing and column-switching ion-pair liquid chromatography. <i>J Chromatogr B Biomed Appl</i> <i>692:53-59,</i> <i>1997.</i>	N	Public
Sachs BA, Siegel E, Horwitt BN, et al.	1 9 7 2	Bread iodine content and thyroid radioiodine uptake: A tale of two cities. <i>Br Med J</i> <i>1:79-81, 1972.</i>	N	Public
Chadha RK, Lawrence JF.	1 9 9 0	Determination of iodide in dairy products and table salt by ion chromatography with electrochemical detection. <i>J Chromatogr</i> <i>518:268-272,</i> <i>1990.</i>	N	Public
		Valoración de Actividad Bactericida según Norma UNE-EN 1656: junio 2010 (erratum octubre 2010) CONFIDENTIAL REPORT	Y	PRODUCT OS QP, S.A.
		Valoración de Actividad Levaduricida según Norma UNE-EN 1657: marzo 2007 CONFIDENTIAL REPORT	Y	PRODUCT OS QP, S.A.
US -EPA	1 9 8 3	Methods of chemical analysis of water and wastes. US-EPA	N	Public
US-EPA	1 9 8 6	Test methods for evaluating solid waste1A: Laboratory manual physical/chemical methods. Washington, DC: U.S. Environmental Protection Agency.	N	Public
AOAC	1 9 9 5	Association of Official Analytical Chemistry (AOAC). 1995. Official Methods of Analysis of AOAC International, 16th ed. Vol. 1 and 2. AOAC International, Arlington, Virginia.	N	Public

EMMI	1 9 9 7	Environmental monitoring methods index. Version 1.1. PC#4082. Rockville, MD: U.S. Environmental Protection Agency, Government Institutes	N	Public
ECHA-Sweden	2 0 1 3	Assessment Report of Iodine (including PVP-iodine) for Product types 1, 3, 4, 22	N	Public
BPC Ad hoc WG on Human Exposure Assessment	2 0 1 7	Recommendation no. 13 of BPC Ad hoc WG on Human Exposure Assessment of Teat Disinfection Products for Veterinary Hygiene (PT3), version 2, 30 March 2019.	N	Public
EU Scientific Committee on Food (SCF)	2 0 0 2	OPINION OF THE SCIENTIFIC COMMITTEE ON FOOD ON THE TOLERABLE UPPER INTAKE LEVEL OF IODINE Source: European Commission Report No.: SCF/CS/NUT/UPPLEV/26 Final Not GLP; (published) Doc. No.: 592-031	N	Public
Raffael and E. van de Plassche	2 0 1 1	EMISSION SCENARIO DOCUMENT FOR PT 3 ERU-JRC Scientific and Technical Reports Drafted by (SCC) GmbH Revised by the BTechn Meeting Endorsed by the BCAMeeting Edited by B. Raffael and E. van de Plassche EUR25116EN-2011	N	Public

3.2 Output tables from exposure assessment tools

See the attached documents:

HUMAN HEALTH EXPOSURE CALCULATIONS:



HH Scen 1.1.pdf



HH Scen 1.2.pdf



HH Scen 3.1.pdf



HH Dietary exp.pdf



HH Total combined (use+dietary).pdf

ENVIRONMENTAL EXPOSURE CALCULATIONS:



MAMICAMP ERA SCENARIO.pdf



MAMICAMP kdegrsoil - I2.pdf



MAMICAMP PEC via manure 10 YEARS.pc



MAMICAMP PEC via STP.pdf



ESD_calculations_M
AMICAMP_v3.pdf

Justification regarding inhalation exposure towards vapour of Iodine complex-bound.

In the iodine Assessment Report for PTs, 1, 3, 4 and 22 (Sweden 2013) it is clearly detailed in the identity chapter 2.1.1, that an iodophor is a preparation containing iodine complexed with a carrier and/or a solubilizing agent, such as polycarbonic acids, surfactants or polymers as povidone (PVP, Polyvinylpyrrolidone).

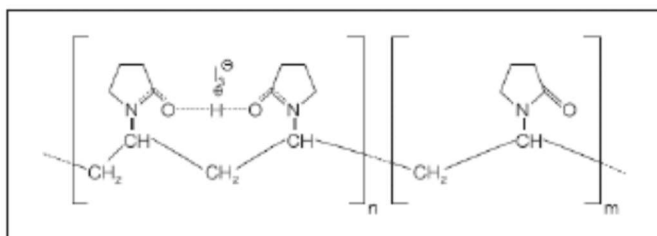
According to G. Görtz, K. Reimer, H. Neef, 1996²:

"PVP-iodine belongs to the group of iodophors. Iodophors are substances which are capable of taking up iodine and transport it. The carrier does not react with the substance taken up via a stable chemical bond but rather takes it up due to its electrochemical configuration in its scaffold. The chemical properties of the individual substances are essentially maintained, the physical properties, i.e. solubility, can in contrast change."

In this way, a controlled release of iodine, that is regarded as the active substance, is accomplished thereby preventing negative effects such as irritation, but keeping sufficient free iodine in the formulation to ensure its efficacy.

Despite the clear description in the iodine dossier, more details on the structure of iodophors and the release of complex-bound iodine from these iodophors are included below.

The predicted structure of solid PVP-iodine as provided in the iodine dossier:



were $m/n = \text{ca } 18$.

As can be seen from the figure, iodine is complex-bound to the carrier in the form of I_3^- , which is an ionic species resulting from the reaction of molecular iodine (I_2) and iodide (I^-). Of note, it is not bound as molecular iodine I_2 , reason why solid PVP-iodine does not smell of iodine and also indicating a tight bound of I_3^- to the carrier molecule.

When discussing iodophor structures and release of complex-bound iodine out of it, the following terms are important to explain first³:

Available iodine (av I_2) = iodine that can be titrated with

² G. Görtz, K. Reimer, H. Neef (1996): Topische Infektionstherapie und Prophylaxe: aktueller Stellenwert von PVP-Iod. Kapitel: Entwicklung, Eigenschaften und Bedeutung von PVP-Iod. Hrsg. von C. Hierholzer ... Unter Mitarb. von R. Achatzy... - Stuttgart; New York : Georg Thieme Verlag

³ TDS BASF – PVP-Iodine grade (2017)

sodium thiosulphate; also the complex bound iodine fraction can be determined

Iodide (I^-) = reaction partner of available iodine in the iodophor

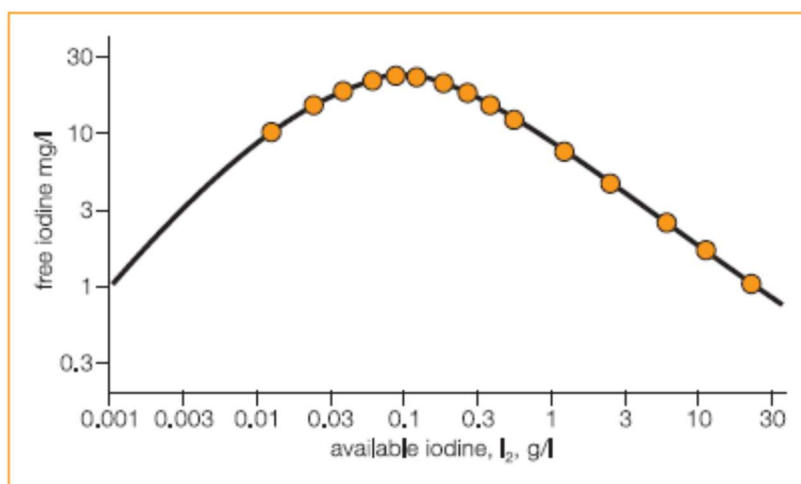
Triiodide (I_3^-) = iodine species bound in iodophor-complex, reaction product of I_2 and I^-

Total iodine = sum of available iodine + iodide content

Free iodine (free I_2) = non-complexed iodine that can be determined via dialysis test or in an electrochemical model.

In aqueous solutions of iodophors, an equilibrium between I_2 , I^- , I_3^- and the polymeric organic molecules are established and the high amount of carrier molecules results in the content of free molecular iodine (I_2) being greatly reduced in such preparations⁴.

The Relationship between the free iodine concentration and the concentration of available iodine in aqueous solution with the commonly used concentrations of PVP-Iodine preparations (1 – 10% PVP-Iodine = 1 – 10 g available iodine/l), is shown below¹⁵.



Looking at this curve, two facts stand out:

The free iodine content is extremely low at 1 – 8 ppm in aqueous solutions of 1 – 10% PVP-Iodine (1-10 g av I_2 /l)

The free iodine content is inversely proportional to the concentration of PVP-Iodine or available iodine in aqueous solutions of more than 0.1 g/l of available iodine.

And tests on micro-organisms have shown that the rate of microbicidal activity is proportional to the free iodine content, the only responsible for disinfection^{15,16}.

Then, at a typical concentration of 0.3% available iodine (3 g/l available I_2), only about 0.0015% free iodine (15 mg/L) are present in solution. Only this minor fraction may contribute to vapour above the solution.

⁴ Tatsuo Kaiho, 2015, Iodine Chemistry and Applications, Wiley, p. 387

So, the content of free iodine (I_2) in solid iodophor complexes is predicted to be zero based on the inverse relationship between available iodine and free iodine. Consequently, no iodine is expected to evaporate from dried residues. In other words: no secondary exposure of the professional user towards iodine vapour is possible when all the water has been evaporated.

Finally, in the chapter 8.3.3.2 Uptake via inhalation of the Iodine Final Doc II-B2 PT3 document for the approval Iodine dossier (please see LoA) the following is mentioned: *"The evaporation of iodine from water-based products is assumed to be very low. Iodine is supposed to react immediately with organic matter (microorganisms, protein substances etc.), also by formation of different iodine species (iodide etc.). For these reasons and with respect of the natural background values in the air (ambient air: 10 to 20 ng/m³. marine air: 100 µg/m³), iodine evaporation and – consequently – contamination of the air is regarded as negligible due to teat disinfection."*

In conclusion:

The iodine used for teat disinfection in PT3 is complexed to iodophors in the form of triiodide (I_3^-).

In aqueous solutions, bound triiodide releases only minute fractions of free (molecular) iodine (I_2).

Free iodine (I_2), the only responsible for disinfection, reacts immediately with organic matter and forms ionic iodine species such as iodide (I^-) that do not tend to evaporate.

Residual free iodine (I_2) in aqueous solutions, if present, is considered to lead to negligible exposure to iodine vapor.

3.3 New information on the active substance

Not applicable.

3.4 Residue behaviour

Not applicable.

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

Summaries of efficacy studies are provided in section 2.2.5.5 and in IUCLID6 part 6.7.

3.6 Confidential annex

Please see confidential annex.

3.7 Other

Not relevant.