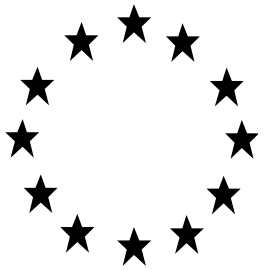
Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Iodine

(including PVP-iodine)

Product types 1, 3, 4, 22

13 December 2013

Sweden

Iodine (PT1, 3, 4, 22)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 13 December 2013

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Principle of evaluation

This assessment report has been established as a result of the evaluation of iodine in product type 1(Human hygiene biocidal products), product type 3 (Veterinary hygiene biocidal products), product type 4 (Food and feed area disinfectants) and in product type 22 (Embalming and taxidermist fluids), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with the original view to the possible inclusion of this substance into Annex I or IA to that Directive.

The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product types 1, 3, 4 and 22 containing iodine that will fulfil the requirements laid down in Article 5(1) b), c) and d) of that Directive.

1.2. Purpose of the assessment

The aim of the assessment report is to support a decision on the approval of iodine for product-types 1, 3, 4 and 22, and should it be approved, to facilitate the authorisation of individual biocidal products in product-types 1, 3, 4 and 22 that contain iodine. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

The conclusions of this report were reached within the framework of the uses that were proposed and supported by the applicants (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Regulation (EU) No 528/2012.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

1.3. Procedure followed

Iodine (CAS no. 7553-56-2) was notified as an existing active substance in product type 1 by Alcoholes Montplet and in product types 3 and 22 by the Iodine Registration Group (IRG), consisting of a task force with twelve companies.

Commission Regulation (EC) No. 1451/2007 of 4 December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, Sweden was designated as Rapporteur Member State (RMS) to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for iodine as an active substance in product types 1 and 3 was 31 July 2007 and for product type 22 it was 31 October 2008, in accordance with Annex V of Regulation (EC) No. 2032/2003[3].

On 31 July 2007, the RMS received a dossier from the applicant IRG in support of iodine in product type 3. The RMS concluded that the PT3 dossier was complete for the purpose of the evaluation on 31 October 2007. On 31 October 2008, the RMS received a dossier from the applicant IRG in support of iodine in product type 22. The RMS concluded that the PT22 dossier was complete for the purpose of the evaluation on 30 January 2009. On 30 November 2009, the RMS received a dossier from the applicant Alcoholes Montplet (a member of the IRG) in support of iodine in product type 1. The RMS concluded that the PT1 dossier was complete for the purpose of the evaluation on 26 February 2010. Most of the underlying data in the PT1 and PT22 dossiers was shared with the dossier for PT3. During the evaluation process, the evaluation period has been extended due to that new data has been awaited and for facilitating the submission of a combined competent authority report (CAR).

On 20 April 2011, the Rapporteur Member State submitted, in accordance with the provisions of Article 10(5) and (7) of Regulation (EC) No. 2032/2003, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 6 May 2011. The competent authority report included a recommendation for the inclusion of iodine in Annex I to the Directive.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission. The first discussion took place at TMII-12 in June 2012, and it was concluded that no further discussions on technical level were necessary. Revisions agreed upon were

2 Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

3 Commission Regulation (EC) No 2032/2003 of 4 November 2003 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/ 8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, and amending Regulation (EC) No 1896/2000. OJ L307, 24.11.2003, p1

presented at technical and competent authority meetings and the competent authority report was amended accordingly.

Towards the end of the evaluation process it became evident that some of the claimed uses that by the time of dossier submission belonged to PT3 now rather belonged to PT4, namely products used in contact with food and feed. After discussions at the 48:th CA meeting in September 2012, it was agreed that the product type affiliation for the former PT3 uses disinfection of milking equipment and milk tanks should be transferred to PT4 and the CAR should be updated accordingly. It was also discussed at the same CA meeting whether disinfection of milking equipment and teat dips falls within the scope of the Directive or if it falls under veterinary legislation. It was declared that disinfection of teats ("teat dips") without therapeutical claims is covered by biocides legislation.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 13 December 2013.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

Overall summary

Product type 1: Iodine is used in biocidal products for hand disinfectants. The representative biocidal product contains an iodophor, i.e. iodine complexed with Polyvinylpyrrolidone (iodophor type 2).

Product type 3: Iodine is used in biocidal products for the disinfection of animals' teats/udder and animal houses. Biocidal products contain iodophors, i.e. either iodine complexed with surfactant (iodophor type 1) or iodine complexed with Polyvinylpyrrolidone (iodophor type 2).

Product type 4: Iodine is used in biocidal products for disinfection of milking equipment and bulk milk tanks. Biocidal products contain iodophors, i.e. iodine complexed with surfactant (iodophor type 1).

Product type 22: Iodine is used in embalming fluids for the short-term preservation and hygienisation of cadavers until burial/cremation. The representative biocidal product contains an iodophor, i.e. iodine 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.

Iodine was present during the primordial development of the earth, but it has been leached from the surface soil by snow, rain, and glaciations and carried into the sea causing a constant decrease of iodine levels in soil and correspondingly, a constant increase of sea water levels.

Background values between 0.5 and 20 mg iodine/kg are found in soil, whereas in ground water a mean concentration of 1µg/L is reported. The background values in surface water (0.5 to 20 µg iodine/L) are considerably lower than in marine water (45 to 60 µg iodine/L). The levels in rain water (0.1 to 15 µg/L) are comparable to those of surface water.

The reduction of iodine background concentrations in soil by leaching has an impact on the iodine level in crops and animals, and consequently in human food. In the last decades, iodine deficiency disorders (IDD) have become recognized as the most common preventable causes not only of e.g. endemic goitre but also of mental retardation worldwide. For this reason, recommendations for the daily intake for humans were established. e.g. by the World Health Organisation (WHO) of 150 – 200 µg/day and the fortification of table salt with iodine has become a means to prevent an undersupply for this essential dietary trace element. On the other

hand, excessive iodine intake can imbalance the synthesis of thyroid hormones and may cause serious health problems.

Because of its great importance for human health, numerous expert panels all over the world have already prepared toxicological profiles of iodine based on a huge data package acquired over many decades, primarily due to its use in human and veterinary disinfectants and drugs. The evaluations of such panels have been taken into consideration.

Since iodine is not a xenobiotic substance but an essential dietary trace element and ubiquitously present in the environment, the recommended upper intake levels and background values have been taken into account in the human health and environmental risk assessments.

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

During the TM-discussions (TM II-2012) it was concluded that in principle iodine should be regarded as the active substance as long as the iodophors are not considered as discrete active substances. In the case of iodophor 1 (iodine complexed with surfactants) the complexed iodine is used for the manufacturing of the biocidal product (the pre-mix may be either prepared on site or bought from suppliers) and it is clear the iodine can be regarded as the active substance with additional information that it is present in stabilized (complexed) form.

Iodophor 2 (PVP-iodine) is added to the biocidal products in the form of a pre-mix which is commercially available. Moreover, there is a separate CAS-No (25655-41-8) assigned to this material. However, the applicant is of the opinion that no real reaction between iodine and PVP is formed but that a complex is built. This is further supported by a publication (G. Görtz, K. Reimer, H. Neef, 1996[4]) in which the following is given (translated from German by the applicant):

“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 addition to this the applicant has further clarified the stabilizing role of the iodophor by stating that “PVP and also the surfactants are used **in the first place** to bring iodine into the formulation in a soluble form. In addition, the iodophor affects the content of reactive iodine in the formulation, thereby preventing negative effects such as irritation, but keeping sufficient free iodine in the formulation to ensure its efficacy. Some call the iodophor-iodine "tamed"

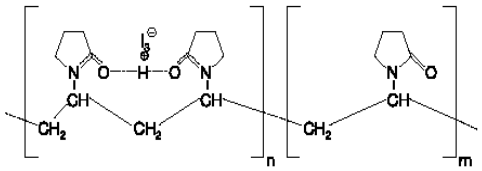
[4] *G. Görtz, K. Reimer, H. Neef (1996): Topische Infektionstherapie und Prophylaxe: aktueller Stellenwert von PVP-Iod. Kapitel: Entwicklung, Eigenschaften und Bedeutung von PVP-Iod. Hrsg. von C. Hierholzer ... Unter Mitarb. von R. Achatzy... - Stuttgart; New York : Georg Thieme Verlag.*

iodine in comparison to Lugol's solution or tincture of iodine. The stabilising effect is considered minor compared to the solubilisation effect of the surfactants and PVP".

In conclusion therefore in the table below iodine is listed as the active substance with additional information on the identity of iodophor 2 (PVP-iodine). Nevertheless, as it appears that the iodophors have some stabilizing effect this should be highlighted for the MS to consider when authorizing products (i.e. in case of application of products containing free non-stabilized iodine).

Table 1: Identity of active substance

CAS-No.	7553-56-2
EC No.	231-442-4
Other No. (CIPAC, ELINCS)	Not assigned
IUPAC Name	iodine
CA Name	iodine
Common name, synonyms	Not relevant
Structural formula	I-I
Molecular formula	I_2
Molecular weight (g/mol)	253.81
Purity of a.s.	min. 995 g/kg (manufactured to the specification of *Ph. Eur*)*
Impurities	Specification according to *Ph. Eur (ver. 7.0, 2010)* and *USP**: 1) Bromides and chlorides (max. 0.25 g/kg) 2) Non-volatile substances (max 1 g/kg) The impurities specified are not considered relevant and as they are either below 1 g/kg (bromide and chlorides) or non-specific (non-volatiles) they should normally not be specified in the reference specification for biocidal purposes. However, in the case of iodine it is considered justified to adopt the specification according to the *Ph. Eur* (see further Document III-A2). It should be noted that in the case of iodine, given that it may be purchased from any manufacturer of *Ph. Eur.* grade active substance, it is considered acceptable that a definite list of sources or 5-batch data for all sources are not provided for a possible Annex I-listing (i.e. certificates of analysis for some of the listed sources have been provided). This is also consistent with the approach taken under the plant protection legislation, where for example it has been agreed not to require 5-batch analyses or a definite list of sources for active substances purchased as

	commodity chemicals (e.g. acetic acid).
Additives	No additives
Representative biocidal products:	
PT 1	Yodi Cura (1.13% w/w iodine in the form of 10.0% PVP-iodine)
PT 3	Masodine 1:3 (1.93% iodine; surfactant stabilized) Io Shield (0.122-0.162% iodine in the form of 1.35% PVP-iodine
PT 4	Masodine 1:3 (1.93% iodine; surfactant stabilized) Io Shield (0.122-0.162% iodine in the form of 1.35% PVP-iodine)
PT 22	AARDBalm arterial fluid (1.15-1.54% iodine in the form of 12.80% PVP-iodine)
Identity details for iodophor 2 (PVP-iodine)	CAS-No: 25655-41-8 EC-No.: not assigned IUPAC Name: Polyvinylpyrrolidone iodine CA Name: 2-Pyrrolidinone, 1-ethenyl-, homopolymer, compd. with iodine Common name, synonyms: PVP-iodine Structural formula: m/n=ca 18  Molecular formula: $(C_6H_9NO)_x * n\ I_2$ Molecular weight: not applicable *Ph. Eur** quality used in representative formulations Specification**: 9.0-12.0% available iodine (dried substance), max 2.0% formic acid, max. 8.0% water, max. 6.0% iodide, loss on drying max 8.0%, sulphated ash max 0.1%

* European Pharmacopoeia (*Ph. Eur*)

** According to the applicant, the manufacturers of *Ph. Eur* grade PVP-iodine use iodine that complies with the *Ph. Eur (ver. 7.0, 2010).* for iodine as specified above even though this is not explicitly outlined in the specification for PVP-iodine.

2.1.1.1. Physico-Chemical Properties

Most phys.chem. properties of the active substance iodine is based on data from Handbooks and alike, which lacks information on quality of test material and test methods used. However, commercially available iodine (as the iodine evaluated) is obtained through sublimation which yields a highly pure grade (≥99.5%). This means that data presented from trustable sources like the Merck Index or the CRC Handbook are believed to be representative for the iodine under evaluation. Moreover, as agreed during the peer-review the weight of evidence approach is used for critical endpoints (seen in parenthesis below). Iodine is a grey-black metallic shining

crystalline solid with a sharp characteristic odour. It is melting at 114°C (n=4) and its relative density is 4.93(n=3). The solubility of iodine at 25°C in water is rather low, 0.3 g/l (pH not stated, n=2), while it is soluble in many organic solvents (n=2) to an extent of between 13.2 g/l (n-hexane) and 230 g/l (methanol). The vapour pressure is 40.7 Pa at 25 °C (n=1, not a critical endpoint) and the Henry's Law Constant was calculated as 34.43 Pa m^3 mol^{-1} at 25 °C (n=1, not a critical endpoint) . The Log K_{ow} has been quoted as 1.89- 2.49 in open literature. However these values seem to be based on QSAR calculations which may not be applicable to a purely inorganic substance like iodine. Hereby, this parameter is instead not considered relevant to iodine (log K_{ow} may be waived for inorganic substance according to REACH). Iodine is not considered to be highly flammable or explosive (theoretical considerations and experience in use). Iodine is oxidizing which render it its biocidal properties. However, iodine is the weakest oxidizer among the halogens and it is currently not classified for oxidizing properties under CLP and and there are no notification for such a classification in the C&L Inventory database at ECHA (as oppose to for chlorine for which there are notification for classification as Ox. Gas 1).

2.1.1.2. Analytical methods

For the determination of both purity of iodine and iodine content in preparations, there exists a well-documented method (titration with sodium thiosulfate) in the European Pharmacopeia. Concerning the residue analysis in the environment, monitoring methods are only considered required for air and food of animal origin (milk) as the PECs calculated for soil and water are low compared to the natural background concentrations in these compartments and as iodine is not classified as toxic or highly toxic. For the environment air is also not considered a relevant compartment but a method could be considered required for the purpose of measuring worker exposure. Acceptable methods have been provided from the open literature for water (IC-ICP-MS) and air (IC-PED). Based on the limited data provided in the draft CAR for the ISO-method for iodide in food of animal origin, ISO 14378, it could not be concluded that it is acceptable. However, during the peer-review the applicant provided supporting validation data for a published interlaboratory testing of the method. The ISO-method is thus considered valid as such. Given the use in PT 3 and PT 4 for teat-dipping and milking equipment disinfection a method seems to be required for milk, based on a preliminary dietary risk assessment. Nevertheless, the final conclusion on the need for such a method and the LOQ to be required has to be referred to the product authorisation stage when the final guidance for dietary risk assessment is available.

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

In addition, in order to facilitate the work of in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

Function

Bactericide, viricide and fungicide. Note: claims for viricide and fungicide functions are not substantiated by key studies and appropriate data has to be submitted for product authorisation.

Field of use envisaged

PT 1: Iodine (as PVP-I) is an antimicrobial active ingredient for use in liquid hand disinfectants (MG01/PT1). The biocidal product Yodi Cura contains 10% PVP-I which in turn contains 11.3% available iodine. Thus, the product contains 1.13% available iodine. The use of Yodi Cura. in PT1 is by professional health care personnel, as well as by the general public. For professional use, both hands and forearms are lathered with the product for up to five minutes and then rinsed off with tap water. The use by the general public is expected to involve smaller application areas and shorter contact times.

PT 3: Iodine is used in veterinary hygiene biocidal products (MG01/PT3) for the purpose of manual or automatic non-medical teat disinfection and udder washes and surface disinfection in animal houses: Concentrations used are 0.0025 – 1.0 % iodine corresponding to 25 – 10,000 ppm iodine.

PT 4: Iodine is used in food and feed area disinfectant biocidal products (MG01/PT4) for the purpose of disinfection of milking equipment and milk tanks. Concentrations used are 0.0025 – 0.010 % iodine corresponding to 25 – 100 ppm iodine.

PT 22: Iodine is used in embalming fluids (MG04/PT22) for the purpose of short-term preservation of cadavers prior to burial/cremation. Concentrations used correspond to 0.29 – 1.54 % available iodine.

For detailed use descriptions, please refer to Document II-B1-B4, chapter 8.

Effects on target organisms

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. 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.

2.1.3. Classification and Labelling

Current classification

Harmonised classification of iodine in Regulation (EC) No 1272/2008, Annex VI, Table 3.2 (in accordance with the criteria in Directive 67/548/EEC)

Xn; R20/21	Harmful by inhalation and in contact with skin
N; R50	Very toxic to aquatic organisms

Labelling (in Annex VI, Table 3.2)

Xn, N

R: 20/21-50

S: (2-)25-23- 61

Harmonised classification of iodine in Regulation (EC) No 1272/2008, Annex VI, Table 3.1 (in accordance with the criteria in that Regulation). The classification for acute toxicity is minimum classification based on a translation in accordance with Annex VII to Regulation (EC) No 1272/2008. The actual hazard class cannot be determined since no LD/LC_{50}-values are available.

Acute Tox. 4 *; H332
Acute Tox. 4 *; H312
Aquatic Acute 1; H400
M=1

Labelling (in Annex VI, Table 3.1)
GHS07, GHS09
Wng
H332, H312, H400

Proposed classification

Active substance

Due to the experience with iodine and observed skin, eye and respiratory irritational effects, the following additional classification is proposed.

In accordance with the criteria in Directive 67/548/EEC:
Xi
R: 36/37/38

In accordance with the criteria in Regulation (EC) No 1272/2008:
Eye irrit. 2; H319
STOT SE 3; H335
Skin Irrit. 2; H315

Products

The proposed classification and labelling of the biocidal product Yodi Cura (PT1) with R41 has been removed. The applicant for Yodi Cura has access to studies performed with a product in PT3 with a higher content of iodine and PVP as carrier. The results do not warrant a classification with R41 (please see DOC III-B6 for PT3).

Consequently, for the representative products in PT1, PT3, PT4 and PT22 no classification is required.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

Iodine is an essential dietary trace element for mammals being required for the synthesis of the thyroid hormones. Ingested iodine is quickly and quantitatively reduced to iodide in the small intestine prior to absorption and then converted to iodine in the thyroid and/or excreted as iodide via the urine. For this reason, studies in which the metabolism is the decisive factor and iodide (not iodine) was administered are also regarded as appropriate to assess the toxicity of iodine in mammals, in particular in humans.

Excessive iodine intakes may bear risks for humans with pre-existing thyroid diseases, pregnant woman and infants, in particular if they are not living in iodine-replete regions. The latter apply to some European countries or regions, all having a mild iodine deficiency according to the WHO criteria. The differences in Europe can be explained by the fact that the legal preconditions for universal voluntary iodised salt prophylaxis and that the additional use of iodised salt in food and animal feed vary considerably. Excessive iodine intake can lead to an underactive thyroid (hypothyroidism) or excessive thyroid activity (hyperthyroidism), with or without goitre.

Basically, no other effects occur at relevant dose levels.

2.2.1.2. Effects assessment

Toxicokinetics, metabolism and distribution including skin absorption

ADME:

Absorption: Ingested iodine and iodate are reduced to iodide prior to absorption and iodide as such is directly absorbed. The absorption, which occurs in the small intestine, is fast and quantitative.

The skin penetration rates of iodine, aqueous solutions of I_2 gas, and iodide are low.

The absorption of iodine or iodide due to inhalation of vapour or inhalable aerosols (<10 µm) is assumed to be quite high. After absorption, practically only iodide reaches the blood circulation and becomes bioavailable.

Distribution: After absorption into the blood stream, iodide is quickly distributed via the blood circulation system, independent of the route of exposure. About 30% of the bioavailable iodide is removed by the thyroid for hormonal synthesis.

The iodide uptake into the thyroid gland is highly sensitive to the iodine/iodate/iodide intake from the diet and the thyroid has mechanisms to adapt to iodide deficiency or excess.

Goitre, hypothyroidism (deficient hormone synthesis) and hyperthyroidism (excessive hormone synthesis) are possible disorders due to an excessive or deficient iodine intake, however, diseases due to an iodide deficiency are much more likely (because of population in iodine deficient areas), than due to excessive intake.

Some iodide is also trapped in the stomach, salivary gland, mammary glands, placenta, and choroid plexus. Iodide passes the placenta barrier supplying the foetal thyroid.

Metabolism: The iodide in the thyroid is converted to iodine and then incorporated in organic compounds as thyroid hormones T_3 and T_4 and their precursors; the smaller proportion is pooled as iodide. The synthesis of the thyroid hormones depends on the supply of iodide and is controlled by two other hormones (TSH, TRH) and regulated by the levels of circulating free thyroid hormones as a negative feedback mechanism.

Degradation of the precursors occurs in the thyroid and degradation of T_3 and T_4 practically in all organs, particularly in the liver and the kidneys by deiodination. Liberated iodide can be re-utilised for the synthesis of thyroid hormones, but is also excreted.

Excretion: The excretion of absorbed iodide is expected to be similar regardless of the route of exposure to inorganic iodine. 97% of the absorbed dose is quickly and effectively excreted via the urine. The excretion of iodide in the urine is a good measure of the intake by diet and the condition of the thyroid.

Smaller quantities of iodide are excreted in faeces, saliva, milk, sweat, tears, bile, other secretions and exhaled air. No data suggest a potential bioaccumulation of iodine / iodide in the body under normal circumstances. Some drugs, chemicals and compounds of plants may induce increased or deficient trapping of iodine / iodide in the thyroid and influence the excretion rates of iodide.

Dermal penetration:

In an in vitro skin penetration study, the percutaneous absorption of total iodine from two biocide formulations (Biocide 1006 and PE 305-1) through human (split-thickness) skin membranes was examined. Biocide 1006 is a formulation, which contains 2.63% total iodine. Biocide 1006 was diluted 4 times one day prior to application, giving an iodine concentration of 0.66%. PE 305-1 is a ready-to-use solution containing PVP-iodine, which contains 0.26% total iodine.
Dermal absorption has been discussed extensively at the Technical Meetings for biocides. Especially the amounts of the compound still retained in the various skin layers, including tape strips have been in focus. At present, provided that levels of the compound still present in the skin levels are included as absorbed, results from in vitro methods seem to adequately reflect those from in vivo experiments.

The inclusion of the amount located in the skin as being absorbed, may result in a conservative estimate of the amount becoming systemically available in vivo. If refinement is needed, it

should be convincingly demonstrated that the skin dose does not become absorbed at a later stage.

For the amounts present in the tape strips, it is not known how much will, or will not, be systemically bioavailable. It has been suggested that the first two layers only should be excluded. Hence, the amounts in the remaining layers (in this case layers 3-15) should be added to the dermal absorption value (that consist of the amounts in the receptor fluid, the receptor compartment, and the amounts in the dermis and epidermis) obtained by the applicant.

To include the amounts still present in the tape strips is further justified, since cumulative absorption data in the dermal penetration study show that absorption continued after 24 h (8 h exposure + 16 h post-exposure)

The mean total absorption was 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 (11.3% for Biocide 1006 and 12.0% for PE 305-1).

Based on these results, a dermal penetration rate of 12% was used for the human health exposure assessment and the subsequent risk characterisation.

Acute toxicity

The acute toxicity data for iodine has been obtained from publications and databases. This is considered to be acceptable in the present case, since iodine is an essential nutritional element and that the upper intake level is known based on human data.

Iodine is not harmful via oral exposure. The results of acute oral toxicity studies performed in animals demonstrate only a very low acute toxicity potential. Iodine has not to be classified and labelled with respect to acute oral toxicity. All non-human LD_{50} values are in the range of 10,000 mg/kg bw or higher and therefore > 2000 mg/kg bw.
Acute dermal and inhalation toxicity studies in animals are waived on the basis that iodine is classified according to the criteria in Directive 67/548/EEC as acutely harmful via dermal and inhalation exposure. The basis for the classification is somewhat unclear, but is likely to be to be linked to the irritating popoerties of concentrated iodine.
Iodine has been used in a number of clinical products, e.g. antiseptics for which the route of exposure is primarily dermal. Because of the low absorption through skin, acute dermal toxicity in man is very unlikely and cases of death due to single application or exposure via dermal route are virtually unknown.

Waiving is also justified by

- the knowledge on the physiological role of iodine as an essential element;
- the available information on strong irritation of skin exposed to crystalline iodine or to certain solutions, even producing damage like chemical burns following dermal exposure (Doc IIIA6.1.4.2).
- the available information on the strong irritation of mucous membranes and of the respiratory tract leading to pulmonary oedema following inhalation exposure.

Although the reliability of the reported irritational effects after inhalation in relation to the concentration in air cannot be verified, the reported experience in humans demonstrates that a concentration of 0.1 ppm (1 mg/m^3) is a concentration not causing irritational effects. This value, although not scientifically assured but derived from human experience, forms the best basis for the definition of a threshold concentration of iodine in the vapour phase.

Irritation and corrosivity

Iodine, in particular in solutions and highly concentrated, is a known human skin irritant but it is not classified as skin irritant according to the criteria in Directive 67/548/EEC

Iodine, as vapour or in higher concentrated solutions, can cause eye irritant effects in humans but it is not classified as eye irritant according to the criteria in Directive 67/548/EEC.

Due to the experience with iodine and observed skin, eye and respiratory irritational effects, a classification with R36/37/38 (EU C&L system) or H315, H319, H335 (GHS C&L system) is proposed by the Applicant in addition to the official classification in Annex VI, Tables 3.1 and 3.2 of the CLP with R20/21 or H332, H312.

Sensitisation

Based on the result of the maximisation test, iodine is not regarded as a skin sensitizer.

Repeated dose toxicity

Repeated administration of iodine via the oral route revealed no evidence for cumulative toxicity in rats. Dose levels of iodine up to 14 mg/kg bw/day and 1.4 mg/kg bw/day did affect the T3/T4 ratios in rats when treated for 10 or 100 days, respectively. Iodide dose levels of 1.4 and 0.42 mg/kg bw/day did not affect the thyroid hormone levels in female rats when treated for 10 or 100 days, respectively. Moreover, for iodide, the thyroid weights of males were significantly increased at a dose level of 1.4 mg/kg bw/day. Hence, the LOAEL in rats is 14 mg/kg bw/day and 1.4 mg/kg bw/day when treated for 10 or 100 days, respectively.

Another state of the art repeated dose study of animals would be of limited values for the hazard and risk assessment in humans for this physiological substrate. Instead, experience in humans for iodine/iodide that also were the basis for the deduction of an Upper Intake Level in humans represents more valuable information to address this data requirement.

Studies are available in where supplemental doses of 1500 µg iodine/day in humans produced small but significant changes in the thyroid parameters. The changes are likely to represent normal feedback processes rather than adverse effects because nearly all values remained within the normal range. Considering the basic intake via diet of 200-300 µg iodine/day, estimated intakes of 1700 and 1800 µg/day represent the LOEL. The Upper Intake Level of 600 µg/day, deduced by the Scientific Committee on Food (SCF), considers to be safe in

conjunction with longer-term/chronic exposure to additional low doses, in particular in regions with mild iodine deficiency (to be found in many European countries).

For the dermal route and exposure via inhalation no study is available but waivers are provided.

For a subchronic oral toxicity study in dog (2nd Species) a waiver is provided. Further animal studies are not justified due to animal welfare reasons, but also for scientific reasons, since more reliable human data is available. An upper intake level in humans is already available since long. Based on the above mentioned arguments, further animal studies would be of limited value.

Genotoxicity

The mutagenic potency of iodine was studied *in vitro* in bacteria and mammalian cells and in *in vivo* test systems in Chinese hamsters and mice. The potential genotoxicity of iodine was comprehensively investigated and a complete data package of *in vitro* genotoxicity data of iodine is available, although some tests have deficiently / limitation.

In one study, a potential clastogenic effect in human lymphocytes was observed when tested without metabolic activation after 24 hours exposure. Neither in presence of metabolic activation nor at a previous time point (4 hours) and without metabolic activation this effect was observed. Findings in the presence of metabolic activation are more relevant because they more resemble the *in vivo* situation.

Furthermore, all other study findings are negative. This is supported by the results of the *in vivo* genotoxicity testing which were all negative. Consequently, based on the overall weight of evidence of all of all *in vitro* and *in vivo* genotoxicity studies, no genotoxic potential of iodine can be identified.

Several expert groups which have evaluated the available data base have concluded that iodine is not considered to be a mutagen *in vivo*.

Carcinogenicity

Some increase in squamous cell carcinomas (SCCs) in the salivary gland following the chronic oral exposure to iodine were noted at the highest dose tested. However the biological meaning of this finding can hardly be evaluated. The highest dose was 764 ppm, equivalent to 41and 51 mg iodide/kg day in male and female rats, respectively.

This dose is 2900-3600 times higher than the Upper Intake Level of 600 µg/day. No clear dose-response relationship is evident. Since iodine is a local irritant and as no genotoxic potential has been identified, the mechanism of the SCC is likely to be mediated by sustained irritation through chronic exposure followed by reparative cell proliferation resulting in possible metaplasia in the salivary gland which is known to concentrate iodine/iodide (factor 20-100 above plasma levels). As the effects are likely be linked to the irritative nature of iodine, a risk of humans considering the recommended daily intake (150-200 µg/day) or the Upper Intake Level (600 µg/day) is not expected. This specific study did not raise concern with regard to carcinogenicity by the different expert groups which have evaluated the toxicity data of iodine.

Though there are some discussions about rare cases of potential carcinogenic effect due to deficiency or excess of iodine in humans (e.g. with regard to the thyroid), for the general population however, none of the expert groups considered the substance to present a risk with regard to carcinogenicity.

Taken into account the local effects of iodine and sustained local irritation/inflammation on the site of contact, a C&L with respect to carcinogenicity seems not warranted. The harmonized C&L of iodine will be discussed and adopted during the evaluation of the CLH report by the RAC Committee of ECHA.

Reproductive toxicity

Teratogenicity

Two studies were submitted. One in which PVP-iodine was administrated and one in which iodide was administrated. The fact that iodide was tested has no impact on the acceptability of the study, since iodine is quickly and quantitatively reduced to iodide in the small intestine prior to absorption and then converted to iodine in the thyroid and / or excreted as iodide via the urine. Very high doses were administrated in the studies, about 750 and 12150, respectively, times the upper intake level for humans (upper intake level is 600 ug/day, equivalent to 10 ug/kg bw/day, assuming a body weight of 60 kg). despite this fact, iodine did not reveal teratogenic effects under test conditions.

Fertility

One study is available, comprising several different experiments and endpoints, relevant for assessing reprotoxicity. The dose levels are about 2800 – 12150 times higher than the upper intake level in humans (which is 10 µg/kg bw/day assuming a body weight of 60 kg). The study is, although it is old, considered to be acceptable, especially in conjunction with the rabbit teratogenicity study.

The NO(A)EL derived from reprotoxicity studies in rats is < 28 mg/kg bw/day for F_0 and F_1 due to diminished milk secretion and therefore decreased survival of pups. No other effects are reported. This finding including NO(A)EL deduction corresponds to the findings of the 100-day study in female rats receiving different doses of iodine via drinking-water, where T_3 was found significantly decreased and T_4/T_3 significantly increased at 10 mg/kg bw/day. T_3 is a very important (if not the most important) hormone at the cellular level. Its decrease may cause decreased energy consumption, lethargy, bodyweight gain, etc. and can explain the effects noted in this study at a systemically high dose.

Neurotoxicity

The chemical structure of iodine is of no specific concern with regard to neurotoxicity. Furthermore, neither acute nor chronic toxicity has to be expected based on effects noted in other studies. Potential indirect effects of high doses of iodine in sensitive subpopulations cannot be excluded. Excessive oral iodine intake by the mother may cause iodine-induced hypothyroidism and potentially secondary neurological effects in foetus or newborn infants because thyroid hormones are essential to the development of the neuromuscular system and brain. However, even at high doses no such effects have been noted so far for in older children or adults and are therefore not likely.

Human data

Iodine is an essential dietary element and therefore a lot of human toxicity data are available. For iodine, recommended daily intakes and upper intake levels based on study findings in humans are already established. Two studies in humans (prisoners) were presented which might have been supportive for the deduction of the Upper Intake Level of 600 µg/day (SCF). No effect on tyroid hormone T_4 levels or formation of neonatal goitre were noted in the prisoners or infants born from mothers, respectively, that were exposed to additional iodine via drinking water. Furthermore, no sensitisation reactions and no iodism were seen.

2.2.1.3. Exposure assessment

Product Type 1:

The sole path of exposure to iodine from its use in liquid hand disinfectants is via skin contact. Liquid soaps are rinse-off products that allow only for a short contact time.

Iodine as a 1.13% aqueous solution as in the biocidal product is only semi-volatile.

The generation of an inhalable mist during hand washing can be excluded. Therefore, iodine vapour is the only relevant source of inhalation exposure.

Exposure via hand-to-mouth contact is unlikely because the product is rinsed off so that the skin surface is free of saliva-dislodgeable iodine. Furthermore, hand-to-mouth contact can be precluded in a professional health care setting.

The general public uses iodine-containing products for hand disinfection but at a much lower frequency than health-care professionals. The use of iodine-containing products like Yodi Cura for first-aid disinfection of small wounds is not within the scope of Directive 98/8/EC and will not be assessed in this dossier.

Exposure to iodine of the general public will predominantly occur orally via iodine-supplemented table salt and food containing it. This is not within the scope of Directive 98/8/EC and will not be assessed or discussed in this context.

Iodine-containing hand disinfectant will be used by health care professionals. Therefore, multiple uses per workday are anticipated. It is recognised that the individual use frequency and duration may vary substantially from user to user.

Liquid hand disinfectant (ca 6.9 g) will be applied to both hands and forearms; the suds are left on skin for up to 5 minutes and then rinsed off with tap water.

As reference values for the human health risk assessments for dermal, inhalation and oral exposure, the Upper Intake Levels for iodine established by the EU Scientific Committee on Food were used, i.e. 600 µg iodine/day for adults (corresponding to 0.01 mg/kg bw/day with a mean bodyweight of 60 kg).

Product Type 3:

Iodine-based biocidal products for veterinary hygiene (Product Type 3) are used in many different professional applications. In respect of exposure assessments, the exposure assessment was focused on the following two main uses:

- teat disinfection
- disinfection of animals houses

Relevant routes of **primary exposure** to biocidal iodine are dermal contact and inhalation. Oral exposure is not relevant because the users of biocidal iodine are always professionals.

Secondary oral exposure can be due to the consumption of milk which contains iodine residues from teats disinfectants, udder washes or from milking equipment disinfection. Exposure to iodine residues via consumption of meat from food producing animals is considered to be covered by the uptake via milk since the transfer of iodine to milk is considerably higher than the transfer to meat. Secondary dermal exposure *via* contact with freshly treated surfaces may be relevant for children on farms where biocidal iodine products are used. Secondary exposure by inhalation is considered to be negligible.

As reference values for the human health risk assessments for dermal, inhalation and oral exposure, the Upper Intake Levels for iodine established by the EU Scientific Committee on Food were used, i.e. 600 µg iodine/day for adults (corresponding to 0.01 mg/kg bw/day with a mean bodyweight of 60 kg) and 250 µg/day for a 6-year old child. Local effects (irritation of the respiratory tract) were also evaluated for inhalation exposure, using the OEL value of 0.1 ppm.

Product Type 4:

Biocidal products of product type 4 containing iodine are designed for different uses in food and feed area disinfection. The uses considered in this dossier are professional uses only. Amateur/non-professional uses are not relevant in the intended applications addressed in this dossier.

Human exposure assessments were performed for the following relevant application/use:

- Disinfection of milk storage tanks by spraying and brushing.

For the following application/use, no separate exposure assessments were performed because the exposure in this use is obviously lower than the exposure in the use listed above and because of the same concentration in the application solution which is used less frequently:

- Disinfection of milking machine systems

As reference values for the human health risk assessments for dermal, inhalation and oral exposure, the Upper Intake Levels for iodine established by the EU Scientific Committee on Food were used, i.e. 600 µg iodine/day for adults (corresponding to 0.01 mg/kg bw/day with a mean bodyweight of 60 kg) and 250 µg/day for a 6-year old child. Local effects (irritation of

the respiratory tract) were also evaluated for inhalation exposure, using the OEL value of 0.1 ppm.

Secondary exposure: Not relevant in PT4 due to removal of the disinfectant by rinsing water before use and because of the low iodine concentration of 55 ppm, potential residues are regarded as negligible.

Product Type 22:

Relevant routes of **primary exposure** to iodine during embalming procedures are dermal contact and inhalation. Oral exposure is not relevant because the users of biocidal iodine are always professionals.

The general public (bystanders/non-professionals) might only be exposed in **secondary exposure** scenarios towards iodine as a result of dermal and inhalation exposure during handling of treated cadavers and cleaning of surfaces after the embalming procedure.

For the assessment of the human health risk following application of the biocidal product described in this dossier, AARDbalm arterial fluid, in the primary and secondary (dermal and inhalation) exposure scenarios within PT22, the Upper Intake Level established for iodine by the EU Scientific Committee on Food iodine (600 µg iodine/day or 10 µg/kg bw/day for adults) was used as the reference value. Likewise, the occupational exposure limit of 0.1 ppm (1 mg/m^3) derived for iodine was used as the reference figure for an assessment of the inhalation exposure during the intended uses within PT 22.

2.2.1.4. Risk characterisation

Product Type 1:

Yodi Cura (1.13% available iodine) is sold to professionals and non-professionals. The biocidal use of Yodi Cura by non-professionals is qualitatively identical to the professional use. However, the daily use rate is going to be lower than 8 per day and also the contact time is less than 5 minutes. Hence, the exposure of professionals constitutes a worst-case scenario that also covers amateurs. No designated calculations for non-professionals are conducted. The primary exposure resulting from daily hand-washing procedures was calculated using the default scenario of ConsExpo 4.1 assuming a body weight of 60 kg and a permeability constant of 7.7×10^{-6} cm/h. Iodine can evaporate from the wet hands with a mass transfer rate of 0.207 m/min (Thibodeaux's method). The annual use frequency is 1825 which is equivalent to 8 uses per day for a user with 228 workdays per year. 6.9 g of the product are applied to 1980 cm^2 skin surface (hands and forearms). The contact time is five minutes.

The relevant routes of primary exposure are the inhalation and dermal route. There is no relevant secondary exposure scenario resulting from the use iodine in PT1.

For a 60-kg user, the chronic systemic exposure of 6.6 µg/kg bw/day is equivalent to a daily iodine intake of 414 µg. This is **69%** of the upper intake levels for adults (600 µg/day) recommended by the EU SCF.

The risk assessment for professionals serves as a worst case for the use of the biocidal product by non-professionals.

When the upper frame of recommended daily intake of 150-200 µg/person/day via diet has been taken into account, the exposure is 9.9 µg/kg bw/day, which is 99% of the UL. However, as presented elsewhere in this CAR, healthy adults can tolerate iodine intakes of more than 1000 µg per day without any adverse side effects.

The conclusions are that the proposed use of iodine (as PVP-I) in hand disinfection products is safe for human health.

Product Type 3:

For all primary and secondary exposure scenarios assessed in Doc IIB8.3, including secondary exposure *via* milk, the calculated exposure was below the above mentioned maximum intake levels and, thus, these uses comply with the criteria of safe use. Only in cases of combined exposure (teat disinfection and considering the highest median dietary iodine intake from milk), the Upper Intake Level of 600 µg/day will be exceeded. This scenario, however, has to be regarded as an overestimation, as residues from teat disinfectants are already included in the highest median dietary intake. In addition, also for children and pupils for which the Upper Intake Level is lower than that for adults (200-250 µg/day for children and 300-450 µg/day for pupils), no adverse effects due to potential additional iodine from teat dip products are likely as no source for an additional iodine exposure, e.g. *via* primary exposure following application as a teat disinfectant, can be identified for this special part of the population.

As reference value for local exposure via the inhalation route, the occupational exposure limit for iodine of 0.1 ppm (1 mg/m^3) was used. Based on the calculation in Doc II, all biocidal uses of iodine comply with the criteria of safe use. However, spray application of iodine containing biocides may lead to relevant inhalation exposure and relevant systemic availability of iodine. For such uses, the use of a mask is to be recommended.

Teat disinfection with iodine-based disinfectants by dipping results in moderate systemic exposure, corresponding to 35% of the Upper Uptake Level if it is applied at a representative concentration of 5000 ppm. When additionally considering the daily dietary iodine intake, the estimated systemic exposure corresponds to 60% of the Upper Uptake Level. Even if teat disinfection is performed twice per day, the systemic exposure results in a maximum of 99.6% of the Upper Uptake Level. Following disinfection by spraying exposure was calculated to result in an acceptable systemic exposure, even if the product is applied twice per day in the absence of PPE. Regardless of daily use frequency and application type, the highest exposure was always identified for teat disinfection when mixing/loading operations were performed by pumping.

Disinfection of animal houses by spraying or fogging in the absence of PPE once per day results in a maximum exposure of ~ 60% of the Upper Intake Level when the daily iodine intake is taken into account in parallel. During application the uptake through skin was calculated to be higher than the uptake by inhalation both in the absence and presence of PPE. For all exposure scenarios, it could be shown that the dermal exposure contributed most to the overall systemic exposure

In addition, a comparison of the estimated inhalation exposure in all primary exposure scenarios with the OEL of 0.1 ppm (1 mg/m^3) derived for iodine demonstrated no exceedance of this tolerable (local) exposure level.

Secondary exposure through dermal contact with treated surfaces or equipment can be considered to be not relevant because iodine is considered to be inactivated upon contact with organic matter (micro-organisms, protein substances). The exposure calculated for a worst case scenario for an about six year old child resulted in a maximum systemic exposure utilizing **39.8%** of the Upper Intake Level of iodine considering an uptake through dermal contact with freshly treated walls and subsequently mouthing. For this use, secondary exposure *via* inhalation of evaporated iodine is regarded as negligible as iodine is quickly and sufficiently diluted by the ambient air.

Adverse effects in adults and children due to iodine from teat dip applications into milk are also very unlikely as the iodine content in milk as such (from cows that are not treated with teat disinfectants) reveals strong natural variation depending on feed, season etc. Furthermore, it could be demonstrated that upper intake levels are not exceeded: Through daily consumption of 0.5 L milk the Upper Intake Level is utilized to up to **14.5%** for an adult and up to **44%** for a child, respectively.

The conclusions are that the proposed use of iodine as teat disinfectant is safe for human health.

Combined exposure

As a hypothetical worst case scenario, a farmer is considered who is exposed to iodine during teat disinfection by spray application (more than one time per day; PPE is worn; RPE should in this case be used during spraying. Gloves are automatically included in the models used in exposure estimations and moreover, gloves are used to reduce the risk of possible cross contamination (hence not primarily in order to reduce exposure)) as well as through the uptake of milk containing iodine from the use of iodine as a disinfectant. In addition, he is considered to have a dietary iodine intake corresponding to the highest median dietary intake, calculated for the UK. Although in this exposure scenario the Upper Intake Level will be exceeded, this is considered to be an overestimation as residues from teat disinfection are already included in the highest median dietary intake and the latter one might also already include intake *via* milk.

In the context of the exposure estimations and risk characterizations performed it has additionally to be pointed out that the UL of 600 µg/person/day is based on data in humans applying an over-conservative uncertainty factor of 3 to the dose where only minimal effects were observed in humans. Thus, the UL of 600 µg iodine/day is a conservative reference figure

and a slight exceedance of this figure would not be associated with an unacceptable health risk for humans. Healthy adults can tolerate iodine intakes of more than 1000 µg/person per day without any adverse side effects and can be considered as "safe" (in particular for healthy professionals).

Product Type 4:

All calculated exposure values were below the upper intake levels and, thus, these uses in PT4 comply with the criteria of safe use

Usually, the milk bulk storage tanks are cleaned automatically but may be done once a month manually by brushing and spraying. Due to the low iodine concentration of 55 ppm (0.0055%) in the application solution, the estimated systemic dose ranges from 0.528% (automatic spraying and brushing) to 9.67% (pumping followed by manual brushing) of the Upper Intake Level. Considering in addition the daily dietary iodine intake, the estimated systemic dose ranges from 25.5% (automatic cleaning) to 34.7% (pumping followed by manual brushing) of the Upper Intake Level, respectively.

Although PPE is generally recommended in use descriptions, no PPE was considered in the exposure estimations (as first tier), except gloves when diluting the concentrate.

In addition, the local exposure of iodine in the air during the disinfection of milk storage tanks by spraying or brushing was estimated to be in the range of 0.42% to 38.5% of the occupational exposure limit of 1 mg/m^3 for iodine.

Product Type 22:

For the embalming of a single cadaver with a 1:3 or 1:1 dilution of AARDBalm arterial fluid for arterial injection and with undiluted AARDBalm arterial fluid for cavity injection, the systemic exposure of a professional embalmer resulting from dermal and inhalation exposure towards iodine was estimated to be in the range of **17.44 – 18.43%** (50.8-51.8% of the UL when the dietary intake is taken into account)of the tolerable upper intake level (UL) of 0.01 mg/kg bw/day (600 µg/person/day) derived for iodine. A major part of the total exposure (about 13%) resulted from post-application procedures comprising washing of the cadaver and cleaning of surfaces such as the embalming table while exposure during the mixing/loading process when the injections solutions are prepared constitutes only about 4-5% of the total systemic exposure.

Thus, a professional embalmer was shown to be safe during the different stages of the embalming process and no unacceptable health risk could be identified even if more than 2 embalmings are performed by an individual embalmer per day.

Furthermore, the exposure estimation of the application of AARDBalm arterial fluid demonstrated that the overall inhalation exposure which was calculated to be 0.163 - 0.167 mg iodine/m^3 during the entire embalming procedure and which also takes into account the washing of cadavers and cleaning of surfaces, does not result in an exceedance of the occupational exposure level of 1 mg iodine/m^3.

Secondary exposure (dermal and inhalation) to iodine from its use in an embalming fluid is extremely unlikely. Even when the embalming procedure is performed by a travelling embalmer in a private home, it is not usual that non-professionals/bystanders (i.e. family members, especially children) are present during the embalming. Furthermore, any potential secondary inhalation exposure possibly experienced by bystanders would not be higher than that of the professional embalmer during the embalming procedure and represents, thus, a worst case.

When a travelling embalmer performs the arterial injection procedure only and the handling of the treated cadaver is performed by other persons, a secondary dermal and inhalation exposure scenario cannot be excluded and has to be considered during washing of cadavers and cleaning of the embalming table.

The combined secondary dermal and inhalation exposure during the washing of the cadaver and cleaning of the embalming table was estimated to correspond to **12.9%** of the tolerable upper intake level (UL) of 0.01 mg iodine/kg bw/day (or 600 µg iodine/person/day**)** and, thus, demonstrates no exceedance of the acceptable exposure level for humans. The secondary exposure assessment further shows that persons other than the professional embalmer could perform these washing and cleaning procedures several times per day without being exposed to unacceptably high iodine doses even if the recommended daily intake of 200 µg/person/day corresponding to 0.003 mg/kg bw/day or 33.3% of the UL for a person of 60 kg is taken into account.

Therefore, the secondary dermal and inhalation exposure was demonstrated to be safe and no exceedance of the UL derived for iodine was identified.

The level of inhalation exposure during washing of cadavers and cleaning of surfaces such as the embalming table was estimated to amount to 0.145 mg iodine/m^3 and does not result in an exceedance of the occupational exposure level of 1 mg/m^3.

The combined dermal and inhalation exposure of a professional embalmer resulting from applications of iodine within PT22 (about 18% of the tolerable upper intake level of 0.01 mg iodine/kg bw/day) as well as the oral exposure towards iodine from its use as an essential nutrient (33% of the UL) results in an overall utilisation of 51% of the UL for this scenario. The results of the primary exposure assessment demonstrate further that a professional embalmer may perform up to the maximum number of **3** embalming procedures per day (resulting in a total systemic exposure corresponding to **87%** of the UL of iodine). Even in case 4 embalming procedures are performed on a single day (resulting in a total systemic exposure corresponding to 105% of the UL of iodine when the daily iodine intake is added), the resulting overall systemic exposure is considered to be still acceptable taking into account both the safety factor used in the deduction of the UL and that adults can tolerate iodine intakes of more than 1000 µg per day (corresponding to about 0.017 mg/kg bw/day) without any adverse side effects.

Similarly, the combined secondary dermal and inhalation exposure during handling of treated cadavers (about 0.00129 mg/kg bw/day or **13%** of the UL of iodine) as well as the oral exposure towards iodine from its use as an essential nutrient (33% of the UL) results in an overall utilisation of about **46%** of the UL for this scenario. This shows that the handling of

cadavers that were treated with iodine for preservation and the subsequent cleaning of embalming tables may be performed up to about 5 times per day (resulting in a total systemic exposure corresponding to 97.5% of the UL of iodine) without exceeding the UL for iodine when considering also the recommended daily intake of 200 µg iodine/person/day corresponding to 0.0033 mg/kg bw/day or 33% of the UL for a person of 60 kg.

For hygienic reasons it is standard practice to use at least gloves and protective clothing. Additional PPE frequently used is wellingtons, apron, forearm protectors, head and face protection. Facemasks are medical rather than respiratory protective equipment for this use. In embalming theatres, there may be exhaust ventilation around the embalming table and there is general ventilation.

The conclusions are that the proposed use of iodine (as PVP-I) as embalming fluid is safe for human health.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Iodine and iodine compounds are ubiquitously distributed and there is a natural cycle of iodine species in the environment (see figure 2.2.2-1 below). Consequently, a lot of research has been made on the fate and distribution of iodine in the environment and all information presented in the dossier for this section is based on open literature, except for the adsorption to soil, for which a study has been conducted. Accordingly, environmental background values as presented in the table below are likely to be encountered for soil, water and air. It should be noted that the RMS has not made a comprehensive literature search, but has mainly adopted the values quoted in the overview articles submitted by the applicant and in some cases added values from additional references.

Table 2.2.2.1

Compartment	**Background level (as iodine)**
Soil	Typically 0.5 - 20 mg/kg dw but with extremes up to 98 mg/kg Global mean value of 5 mg/kg
Groundwater	Mean concentration: 1 µg/l Range: < 1-70 µg/l with extremes up to 400 µg/l
Freshwater (river and lake)	0.5 - 20 µg/l
Marine water	45 - 60 µg/L
Rainwater	0.1-15 µg/l
Freshwater sediment	Typically: 6 mg/kg
Marine sediment	Typically: 3-400 mg/kg

Compartment	Background level (as iodine)
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)

Figure 2.2.2-1: Diagram of the global iodine cycle at steady state. The figure shows environmental compartments, compartment inventories in grams (g), transport pathways, and fluxes in grams per year (g/year).

Whereas the term degradation is not applicable to an element, iodine may undergo different hydrolytical, photolytical and microbial transformation processes (i.e. speciation) in the different compartments. The presence of different forms of iodine is largely dependent on redox potential and pH. Iodide and iodate are the dominant iodine species in soil. Iodate is the dominant chemical form of iodine in the soil solution under non-flooded conditions whilst under flooded conditions iodide is the dominant chemical form. In water, the prevalent iodine forms are iodide (I^-) and iodate (IO_3^-). In surface waters, the proportion of iodide to iodate will vary depending on microbial activity and the release of iodine species from terrestrial sources. Microbial action converts iodide to organic forms of iodine, primarily methyl iodide (CH_3I). Its high vapour pressure and limited solubility in water leads to volatilisation of methyl iodide

from surface waters to the surrounding atmosphere. Also, microbial activity and photochemical reactions with iodide or iodate can lead to the formation of iodine, which evaporates to the atmosphere. At ordinary pressures and temperature, methyl iodide and iodine will exist, predominately in a free gaseous form, in air. Both iodine and methyl iodide undergo photochemical reactions to form iodine radicals, which can form a number of other iodine species.

Iodine as an element does not undergo biodegradation processes and although biotic transformation processes may be involved in the formation of the different iodine species no studies have been provided on the significance of such processes. It is likely that the magnitude of the natural occurrence of iodine species in the environment renders for example the formation of methyl iodide from biocidal use of iodine to be insignificant.

Hydrolysis of iodine takes place in a series of reactions and leads to the formation of iodide and iodate. Natural waters, particularly marine waters, contain iodine mainly in the form of iodide and iodate. Iodide (oxidation state -1) is the dominant iodine species in surface waters whilst iodate (oxidation state +5), the second most abundant form of iodine in aqueous systems, is found predominantly under alkaline and well oxidized conditions. In water, photolytic dissociation of methyl iodide can result in the formation of elemental iodine and inorganic iodine species. Also, photochemical production of iodine from a reaction between iodide and iodate upon irradiation with UV-light at sea level may occur. However, iodine production via this pathway may be regarded as insignificant.

The earth's oceans contain 8.1×10^{16} g of iodine at an average concentration of between 45 and 60 µg/L and it is estimated that iodine in the earth's surface amounts to 6.3×10^{18} g. The concentration of iodine in bedrock varies between 0.5 and 380 ppm. The major source of iodine in soil originates from the volatilisation of iodine from the ocean surface transported as ocean spray, rainwater and snow to terrestrial surface, but also weathering of rock contributes to the iodine content of the terrestrial surface. Within the soil profile, the highest levels of iodine are often found in the upper layers, where also the organic content is highest. The level of iodine is generally high in peat soils and in mineral soils, the highest levels of iodine are found in the organic layers.

Adsorption data for iodine has been acquired from an adsorption screening test according to OECD 106 and from publicly available information. A geometrical mean K_{oc} of 165.8 cm^3/g was calculated from the OECD 106 test. However, the adsorption of iodine to soil is not only attributed to organic matter, even though this type of adsorption seems to be predominant at pH > 6. A different approach is therefore applied, i.e. to use measured partitioning coefficients K_d (or Kp_{comp} as given in the TGD) for soil and suspended matter directly. In conclusion, and in agreement with the statement in section 2.2.5.3 in the TGD that for ionic substances measured adsorption coefficients are needed, the solids-water adsorption coefficients to be used the environmental exposure calculations are Kp_{soil} = 5.8 cm^3/g and $Kp_{susp} = 2.2 \times 10^2$ cm^3/g.

When assessing the distribution of iodine species in sewage treatment plants (STP), it was established that the Simple Treat model normally used, and that resulted in a sludge retention factor of 1.93%, was not appropriate. Molecular iodine is a chemically unstable element with oxidizing properties and it is assumed that when iodine reaches the wastewater stream it will speciate into iodate and iodide. Therefore, sludge retention factors are based on literature data

and laboratory and field experiments, which range between 20 and 80% retention. Considering that iodide is not highly adsorbed to sludge under typical conditions and iodate can form complexes with calcium which easily adsorb to negatively charged particle surfaces, the majority of the iodine that passes an STP will most probably not be retained in sludge and a sludge retention factor of 20% is chosen for the risk assessment (i.e. 80% of the iodine discharged to the STP remains in the effluent). Exposure to air is not considered as iodide and iodate are assumed not to be volatile.

Bioaccumulation (BCF) values for iodine are generally low, although values up to 10000 have been found. However, the reported values should be treated with caution, since they are not acquired from bioaccumulation studies, but are merely a comparison of iodine content in the source and in the organism. Estimation of Kow and bioaccumulation potential for an inorganic substance such as iodine is not considered relevant. High intracellular iodine concentrations may have other explanations, e.g. physiological processes like active transport and intracellular enzymatic reactions.

2.2.2.2. Effects assessment

For the aquatic compartment, three OECD guideline studies have been submitted, namely on fish, invertebrates and algae. In addition, two disinfection efficacy tests with fish have been performed, which partly may be used to evaluate ecotoxicity, but they have not been used in the risk assessment. The most sensitive aquatic organism was the invertebrate *Daphnia*, for which the lowest EC_{50} 0.59 mg/L was derived with iodine. In addition, a *Daphnia* study with PVP-iodine (PT1 product Yodi Cura) resulted in an even lower EC_{50} of 0.315 mg/L. Also, a respiration inhibition test with sewage sludge micro-organisms has been submitted. The results are summarised in table 2.2.2.2a below and the effect values are expressed as mg iodine/L.

Table 2.2.2.2a

Aquatic tests	**Results, L/EC_{50} (mg/L)**		
	iodide	**iodate**	**iodine**
Oncorhynchus mykiss, acute toxicity, 96 h LC_{50}	3780	220	1.67
Daphnia magna, acute toxicity/immobilisation, 48 h L/EC_{50} (key study)	0.83	58.5	0.59
Daphnia magna, acute toxicity/immobilisation, 48 h L/EC_{50} (key study PT1)	-	-	0.315
Desmodesmus subspicatus, growth inhibition, 72 h E_rC_{50}	-	-	1.3
Activated sewage sludge micro-organisms, respiration inhibition, 3 h EC_{50}	-	-	290

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.

Acute terrestrial toxicity tests have been submitted for earthworms, non target plants and soil micro-organisms with non target plants being most sensitive. In the study on terrestrial plants

six different species were tested and the results were rather similar for all six, the EC_{50} values ranging between 13.4 and 26.6 mg/kg. The most sensitive species was *Avena sativa*, with an EC_{50} of 13.4 mg iodine/kg dry soil for the most sensitive parameter shoot fresh weight. The results are summarised in table 2.2.2.2b below and the effect values are expressed as mg iodine/kg dry soil.

Table 2.2.2.2b

Terrestrial tests	**Results, L/EC_{50} (mg/kg dwt)**		
	iodide	**iodate**	**iodine**
Eisenia fetida, acute test, 14 d LC_{50}	-	-	>1000
Avena sativa, seedling emergence & growth, 21 d EC_{50} (key study)	-	-	13.4
Soil microorganisms, respiration inhibition, 28 d EC_{50}	-	-	148.7
Soil microorganisms, nitrate formation, 28 d EC_{50}	-	-	82.6

At TMII-12, which was held in June 2012 in Somma Lombardo, Member States expressed concern that the ecotoxicity data set was rather limited, and that additional tests are available in the literature, e.g. on fish toxicity. However, it was concluded that these tests do not add information that would lead to a modification of the PNEC. It was also concluded that at the moment it was unnecessary to perform new tests. It was further concluded that it is desirable to gain insight into natural background levels of iodine in relation to the background levels in the ecotoxicity studies. An attempt to do this has been done by RMS, which is reported in Doc III-A7. The conclusion was that the background levels used in the tests are not likely to have affected the outcome of the tests.

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. In the case of PT22, it could be mentioned that the working process of a crematorium is regulated by national law and given limit values have to be observed. Therefore the dusts and gases which are formed during incineration are filtered before release to air. Also, in the embalming process most of the iodine is oxidised to iodate, which is not volatile. Consequently, air is not an environmental compartment of concern and the potential effect on the ozone layer could be considered as negligible.

As the amounts of iodine potentially released into the environment through biocidal uses are within the natural occurring background levels, there is no concern with respect to secondary poisoning.

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 excess iodine 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.

2.2.2.3. PBT assessment

The RMS considers that a comprehensive PBT assessment is not relevant in the case of iodine. The term persistence is not appropriate, since iodine is an element and not degradable. Estimation of bioaccumulation potential for iodine is not considered relevant. In the concerned environmental compartments iodine speciates into the ionic forms iodide and iodate. In line with what has been discussed for inorganic metals (e.g. Ni and Zn), bioaccumulation is not relevant because these substances (and iodine) are regulated in animals of several taxonomic groups. The acute toxicity to mammals is low, but iodine is very toxic to aquatic organisms. However, the screening T criterion (L(E)C50 to aquatic organisms less than 0.1 mg/L) is not fulfilled, and there is no chronic data available, which is needed to assess the T criterion.

2.2.2.4. Exposure assessment

Product Type 1:

Yodi Cura contains iodine complexed with polyvinylpyrrolidone, and the fraction of free iodine is 1.13%. It is intended to be used in hospitals and medical practice by professional users. Skin antiseptics are applied and used in very short time. After maximum five minutes the product is rinsed off with fresh water and released to wastewater. Consequently, sewage treatment plants (STP) are an important emission pathway. Release of STP effluents containing potential iodine residues leads to emissions to surface water and sediment, both freshwater and marine. Emissions to soil could arise indirectly, via the application of STP sludge and via aerial deposition. Furthermore, soil porewater concentrations as an indicator for potential groundwater levels will be assessed.

The emission scenario document for PT 1 products, when employed by professionals, presents a use scenario in hospitals. A typical hospital, being responsible for the health care of 10000 inhabitants, has 400 beds, 75% of them (i.e., 300 beds) are occupied. The exposure assessment is based on the average consumption of disinfectants per bed. In the absence of empirical data, the average consumption of Yodi Cura per occupied bed was set to 0.13 g a.i. per day by default. The above scenario can be considered to represent an absolute worst case, and two further scenarios are presented by the applicant to represent more realistic conditions. Given the uncertainties in the amount of iodine released in healthcare per occupied bed and day shown in a recent EU-survey, the RMS has used the worst case scenario. This approach was also agreed to by the Technical meeting (TM II 2012).

PEC values for iodine are calculated using EUSES 2.1 based on available data on solids-water partition coefficients and sludge retention factor, and are summarised in table 2.2.2.4a below.

Table 2.2.2.4b. PEC values for PT1.

Compartment	Abbreviation [unit]	PEC value
Sewage treatment plant	PEC_{STP} [µg/L]	15.6
Surface water	PEC_{water} [µg/L]	1.55
	PEC_{sed} [mg/kg wwt]	0.076
Marine environment	$PEC_{seawater}$ [µg/L]	0.16
	$PEC_{marine\ sed}$ [mg/kgwwt]	0.0076
Terrestrial compartment	PEC_{soil} [mg/kg wwt]	0.0966 (iodate 0.13 ; iodide 0.0135)
	$PEC_{groundwater}$ [µg/L]	18.1 (25.0 iodate, 2.53 iodide)
Air	PEC_{air} [ng/m^3]	not relevant.
Biota	PEC_{biota} [mg/kg]	not applicable

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

Product Type 3:

Within PT3, the following uses for the typical products (Masodine and Io Shield) are assessed:

PT3a: Manual non-medical teat disinfection and udder washes.
PT3b: Automatic teat disinfection (covered by PT3a).
PT3c: Animal house disinfection by spraying or fogging (pigs, veal cattle, ducks and turkeys has been identified as relevant and thus further considered).

The route of exposure of iodine to the environment is either via application of manure/slurry to agricultural land or by release from the facility drain to an STP and subsequent compartments. Relevant receiving compartments are soil, groundwater and surface water. PEC values are reported as iodine, iodide and iodate. The reason is that it is assumed that iodine is transformed to iodide in the alkaline anaerobic conditions in the manure, whilst when it is spread and mixed into the top layer of agricultural soil it will predominantly be transformed into iodate. In the case of release via STP iodine will be transformed into iodide and iodate, depending on the redox conditions. PEC_{soil}, PEC_{gw} and PEC_{sw} values were calculated for application to grassland and arable land, each based on phosphate and nitrogen standards. It should be noted that the nitrogen standard is the most relevant in Europe and the focus during the evaluation of iodine species is put on the nitrogen standard. PEC values in the different compartments are summarised below, partly in tabular form (tables 2.2.2.4c-e).

For release to STP from use category PT3a/b PEC values are calculated to 1.23 and 1.70 µg/L for iodine/iodide and iodate, respectively, whilst the corresponding PEC values for PT3c are 11.2 and 15.5 µg/L for iodine/iodide and iodate, respectively..

Table 2.2.2.4c. PEC values for PT3, soil.

Terrestrial		spreading of manure/slurry PEC_{soil} [mg/kg_{wwt}]				spreading of sewage sludge PEC_{soil} [mg/kg_{wwt}]
		phosphate standard		nitrogen standard		
iodine species	**product type**	**grassland**	**arable land**	**grassland**	**arable land**	
iodine/ iodide	PT3a/b	0.023	0.018	0.011	0.011	0.0076
	PT3c:					
	Pigs (sows in group)	0.0014	0.0008	0.0018	0.0013	n r.
	Veal cattle	0.0027	0.0010	0.0025	0.0012	n r.
	Ducks	0.0019	0.0015	0.0017	0.0017	n.c.
	Turkeys	0.0011	0.0002	0.0008	0.0002	0.07 iodine 0.01 iodide
iodate	PT3a/b	0.032	0.025	0.015	0.015	0.011
	PT3c					
	Pigs (sows in group)	0.0020	0.0012	0.0024	0.0018	n r.
	Veal cattle	0.0037	0.0014	0.0034	0.0017	n r.
	Ducks	0.0026	0.0020	0.0024	0.0024	n.c.
	Turkeys	0.0015	0.0003	0.0011	0.0003	0.10

n.r. = not relevant
n.c. = not calculated (covered by the worst case scenario 'turkeys')

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

It should be noted that the above calculated iodine concentrations in soil are far below the natural background concentration of 0.5 – 20 mg/kg soil (see 8.4.1).

Table 2.2.2.4d. PEC values for PT3, groundwater.

Groundwater		spreading of manure/slurry PEC_{gw} [µg/L]				spreading of sewage sludge PEC_{gw} [µg/L]
		phosphate standard		nitrogen standard		
iodine species	**product type**	**grassland**	**arable land**	**grassland**	**arable land**	

Groundwater		spreading of manure/slurry PEC_{gw} [µg/L]				spreading of sewage sludge PEC_{gw} [µg/L]
		phosphate standard		nitrogen standard		
iodine species	product type	grassland	arable land	grassland	arable land	
iodine/ iodide	PT3a/b	4.43	3.42	2.11	2.11	1.43 iodine 0.20 iodide
	PT3c:					
	Pigs (sows in group)	0.28	0.16	0.33	0.25	n r.
	Veal cattle	0.51	0.20	0.47	0.23	n r.
	Ducks	0.36	0.28	0.33	0.33	n.c.
	Turkeys	0.21	0.04	0.16	0.04	12.9 iodine 1.81 iodide
iodate	PT3a/b	6.12	4.73	2.92	2.92	1.97
	PT3c:					
	Pigs (sows in group)	0.38	0.22	0.46	0.35	n r.
	Veal cattle	0.70	0.27	0.65	0.32	n r.
	Ducks	0.50	0.39	0.46	0.46	n.c.
	Turkeys	0.29	0.06	0.22	0.05	17.8

n.r. = not relevant
n.c. = not calculated (covered by the worst case scenario 'turkeys')

PEC_{gw} values were calculated based on the PEC_{soil} for application to grassland and arable land. Although the above calculated iodine concentrations in groundwater are above the mean natural background concentration of 1 µg/L they are still far below the maximum natural background concentration of 70 µg/L.

Table 2.2.2.4e. PEC values for PT3, surface water.

Surface water		runoff from agricultural land PEC_{sw} [µg/L]				release via STP PEC_{sw} [µg/L]
		phosphate standard		nitrogen standard		
iodine species	product type	grassland	arable land	grassland	arable land	
iodine/ iodide	PT3a/b	0.44	0.34	0.21	0.21	0.12
	PT3c					
	Pigs (sows in group)	0.028	0.016	0.033	0.025	n r.
	Veal cattle	0.051	0.020	0.047	0.023	n r.

Surface water		runoff from agricultural land PEC_{sw} [µg/L]				release via STP PEC_{sw} [µg/L]
		phosphate standard		nitrogen standard		
iodine species	product type	grassland	arable land	grassland	arable land	
	Ducks	0.036	0.028	0.033	0.033	n.c.
	Turkeys	0.021	0.004	0.016	0.004	1.1
iodate	PT3a/b	0.61	0.47	0.29	0.29	0.17
	PT3c					
	Pigs (sows in group)	0.038	0.022	0.046	0.035	n r.
	Veal cattle	0.07	0.03	0.07	0.03	n r.
	Ducks	0.05	0.04	0.05	0.05	n.c.
	Turkeys	0.03	0.01	0.02	0.01	1.5

n.r. = not relevant
n.c. = not calculated (covered by the worst case scenario 'turkeys')

PEC_{sw} values were calculated based on the PEC_{gw} for application to grassland and arable land. The reported iodine concentrations in surface water are in the range of natural background concentrations in river waters of 0.5 to 20 µg/L. 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. Accordingly, also the PEC's calculated for freshwater and marine sediments are negligible compared to the natural background levels and not further summarised here.

Product Type 4:

Within PT4, the following uses for the typical product (Masodine) are assessed:

PT4a/b: Disinfection of milking machine systems (pipelines, claws) and other milking equipment and disinfection of bulk milk storage tanks.

The route of exposure of iodine to the environment is by release from the facility drain to an STP and subsequent compartments. Relevant receiving compartments are soil, groundwater and surface water. PEC values are reported as iodine, iodide and iodate (table 2.2.2.4f).

Table 2.2.2.4f. PEC values for PT4.

Compartment	Abbreviation [unit]	PEC value
Sewage treatment plant	PEC_{STP} [µg/L]	4.00
Surface water	PEC_{water} [µg/L]	0.40 iodine/iodide (0.55 iodate)
	PEC_{sed} [mg/kg wwt]	0.02
Marine environment	$PEC_{seawater}$ [µg/L]	0.04
	$PEC_{marine\ sed}$ [mg/kgwwt]	0.002
Terrestrial compartment	PEC_{soil} [mg/kg wwt]	0.025 (iodate 0.034 ; iodide 3.5 $x10^{-3}$)
	$PEC_{groundwater}$ [µg/L]	4.64 (iodate 6.41, iodide 0.65)
Air	PEC_{air} [ng/m^3]	not relevant.
Biota	PEC_{biota} [mg/kg]	not applicable

Product Type 22:

The iodine containing product AARDBalm arterial fluid is used for the embalming of cadavers for short-term preservation until burial/cremation. The iodine content in the product is 0.039% for arterial injection (diluted 1:3) and 0.154% for cavity injection (undiluted). The following emission pathways are relevant for iodine:

- A: Release during the embalming process. Small quantities of iodine can be released during arterial and cavity injection via the sewer system and STP into the environment.
- B: Release in cemeteries. When the embalmed cadavers are buried on a cemetery, iodine can be released directly to soil and groundwater.

PEC values calculated for the different environmental compartments are summarised in the table 2.2.2.4g

Table 2.2.2.4g. PEC values for PT22.

Environmental compartment	Unit	Calculated PEC for relevant compartments for PT 22.2	
		Case A Release during the embalming process	**Case B** Release in cemeteries
Freshwater			
Surface water ($PEC_{aquatic}$)	µg/L	0.186	n.a.
Freshwater sediment ($PEC_{sediment}$)	mg/kg_{wwt}	0.009	n.a.
Marine			

Seawater ($PEC_{aquatic}$)	µg/L	0.019	n.a.
Marine sediment ($PEC_{sediment}$)	mg/kg_{wwt}	0.0009	n.a.
Terrestrial			
Local PEC in agricultural soil averaged over 30 days (PEC_{soil})	mg/kg_{wwt}	0.012 (iodine) 0.017 (iodate) 0.0017 (iodide)	n.a.
PEC in cemetery soil	mg/kg_{wwt}	n.a.	iodine **0.11 (revised equation)*** 3.02 (original ESD)* iodate **0.16 (revised equation)*** 4.17 (original ESD)* iodide **0.016 (revised equation)*** 0.423 (original ESD)*
Groundwater			
Groundwater under agricultural soil (PEC_{gw})	µg/L	2.16	n.a.
Groundwater under cemetery soil (PEC_{gw2})	µg/L	n.a.	iodine **21.8 (revised equation)*** 576.8 (original equation of the ESD)* iodate **30.2 (revised equation)*** 797 (original equation of the ESD)* iodide **0.30 (revised equation)*** 80.7 (original ESD)*
STP			
Sewage treatment plant (PEC_{STP})	µg/L	1.86	n.a.

n.a. = not applicable

*: It was decided during TM discussion (TM II 2012) that the revised equation (taken into account exponential decay) proposed by RMS should be used. The original ESD calculation (based on the calculation of a plateau concentration which it takes ~100 years to reach) is kept for comparison.

For the calculation of PECsoil it is assumed that 100% of iodine is transformed into iodate and 14% into iodide.

In accordance with the ESD for PT22 no risk assessment should be made for the soil compartment under the cemetery, but the PEC_{soil} for iodate and iodide (as well as for iodine in the table above) are presented only for the sake of completeness: Case A PEC_{soil}(iodate) = 0.017 mg/kg_{wwt} and PEC_{soil}(iodide) = 0.0017 mg/kg_{wwt} and the corresponding figures for case B are PEC_{soil}(iodate) = 0.16 mg/kg_{wwt} and PEC_{soil}(iodide) = 0.016 mg/kg_{wwt}.

The iodine concentrations in pore water of agricultural soil (after application of sewage sludge – case A) or in the pore water of cemetery soil (due to direct release from buried embalmed corpses – case B) are taken as indication of potential groundwater levels, assuming that the concentration in soil pore water is identical to the concentration in groundwater. PEC_{gw} values are thus calculated using this "porewater approach" based on PEC_{soil}. PEC_{gw} values for iodate (30.2 µg/L) and iodide (0.30 µg/L) are presented for the sake of completeness. Also for PT22 resulting groundwater levels are above the mean natural background concentration of 1 µg/L but far below the maximum natural background concentration of 70 µg/L. However, iodine leaching out from a cemetery is not considered relevant for the assessment of human exposure or risk due to drinking water for the following reasons. 1) Special local regulations apply for the locations of cemeteries, taking into account the local geology in order to prevent possible drinking water contaminations. 2) Groundwater layers used as source for drinking water have much larger capturing sizes than the 500-1000 m^3 for which an assessment was made, are often in deeper groundwater horizons and are usually not located directly under a cemetery. At TMII-12 it was confirmed that cemeteries can be regarded as isolated places according to national regulations applied within the EU and that even though higher pore water concentrations than natural background levels are reached, the risk can be disregarded.

Cumulative exposure:

It is possible that iodine is used simultaneously in different product types and that this leads to higher loads of iodine to the respective environmental compartments due to cumulative exposure. No specific guidance is available on how to take care of this in the evaluation of biocidal substances. However, an attempt is made to calculate worst case values for cumulative exposure. The simplest and most straightforward way of doing this is to add emissions calculated from the uses of four separate product types. This requires that it is realistic that all four product types are used within the same local area within the same time period as may at least theoretically be the case for release into an STP. In the following RMS has considered that this is the case and presents the following calculations: $PEC_{cumulative\_comp} = PEC_{PT1} + PEC_{PT3} + PEC_{PT4} + PEC_{PT22}$. To be able to use comparable data from all product types the figures for iodine are used except for soil where data from all three iodine species are available.

To STP: $PEC_{cumulative\_STP}$ = 15.6 + (1.23 + 11.2) + 4.0 + 1.86 = **33.9 µg/L (iodine)**

For soil application of manure from different domestic animals onto the same field is not considered relevant. Furthermore, it is not assumed that both manure and sewage sludge are applied to the same piece of land. In PT3 both emission to manure and STP is possible. Exposure of soil through application of manure should be considered separately. Therefore, a cumulative exposure assessment for soil is only performed for uses with emission to STP.

$PEC_{cumulative\_soil}$ = 0.0966 + (+ 0.0076 + 0.07) + 0.025 + 0.012 = **0.21 mg/kg wwt (iodine)**

$PEC_{cumulative\_soil}$ = 0.13 + (+ 0.011 + 0.10) + 0.034 + 0.017 = **0.29 mg/kg wwt (iodate)**

$PEC_{cumulative\_soil}$ = 0.0135 + (+ 0.0076 + 0.01) + 0.0035 + 0.0017 = **0.036 mg/kg wwt (iodide)**

Since the groundwater assessment is based on the PECsoil, the same reasoning would apply as for soil. As described above, direct exposure to groundwater under a cemetery is not assumed.

$PEC_{cumulative\_groundwater}$ = 18.1 + (+ 1.43 + 12.9) + 4.64 + 2.16 = **39.2 µg/L (iodine)**

For surface water both release from STP and runoff from agricultural land (grassland, nitrogen standard) may be considered in the cumulative exposure assessment. In this case, care must be taken not to add up the PEC values resulting from application of manure and from application of sewage sludge since to a piece of land it is likely that either manure or sewage sludge is applied. Furthermore, it would not be realistic to add up the PEC values resulting from the application of manure from different animal species, and thus only the PEC value for veal cattle is used. For cumulative surface water assessment the following calculation is proposed: .

$PEC_{cumulative\_surface\_water}$ = 1.55 + (0.21 + 0.047 + 0.12 + 1.1) + 0.40 + 0.186 = **3.61 µg/L (iodine)**

Certain circumstances make iodine a special substance, mainly that in most environmental compartments the background concentration is high and that iodine is essential in rather high concentrations to both animals and plants.

2.2.2.5. Risk characterisation

PNEC derivation:

The derivation of PNEC values has been done as described in Document II-A with the exception of the $PNEC_{aquatic}$ for iodine in PT1, which was derived from a product study. The PNEC values used in the risk assessment are summarised in table 2.2.2.5a below.

Table 2.2.2.5a. PNEC values.

Environmental compartment		iodine species	PNEC
Aquatic, freshwater	Surface water	iodine (I_2)	0.00059 mg/L
		iodine (I_2 in product)	0.00032 mg/L (PT1)
		iodate(IO_3^-)	0.0585 mg/L
		iodide(I^-)	0.00083 mg/L
	Freshwater sediment	-	not used in the risk assessment
Aquatic, marine	Seawater	iodine (I_2)	0.000059 mg/L
		iodine (I_2 in product)	0.000032 mg/L (PT1)
		iodate(IO_3^-)	0.00585 mg/L
		iodide(I^-)	0.000083 mg/L
	Marine sediment	-	not used in the risk assessment
Terrestrial		iodine (I_2)	0.0118 mg/kg_{wwt}
		iodate(IO_3^-)	0.304 mg/kg
		iodide(I^-)	0.0043 mg/kg
STP		iodine (I_2)	2.9 mg/L

Product Type 1:

The risk assessment of iodine in PT1 has led to the following PEC/PNEC ratios, as described in table 2.2.2.5b below:

Table 2.2.2.5b. Risk quotients for PT1.

Environmental compartment	PEC/PNEC
Freshwater & marine	
Surface water	**4.84**
Sediment	**4.84**
Terrestrial	
Soil	**8.2** (iodine) 0.43 (iodate) **3.14** (iodide)
STP	
Sewage treatment plant	0.0054

The PEC/PNEC ratios for iodine for the freshwater and the marine environment indicate unacceptable risk. However the calculated PEC is well within the natural background levels of 0.5-20 µg/L in surface water with up to 60 µg/L in seawater and the established PNEC values may be regarded as truly worst case and not realistic as indicators of the toxicity of iodine in the form it is present in the environment. Additionally, iodine is assumed to speciate into iodide and iodate within the waste water stream, which would mean that for the risk assessment of surface water and marine water the PEC should be compared to the PNEC for iodide and iodate. If the PNEC values for iodide are used as a worst case it means that the PEC/PNEC ratios are reduced to 1.87. As also indicated by the comparison of the natural background levels of iodine with the PNEC's for the different inorganic forms of iodine, a significant part of the iodine in the aquatic compartment appears to be present as dissolved organic iodine (DOI), indicating that the risk characterisation for the aquatic compartment based only on inorganic iodine species is of quite low relevance.

The PEC value of 76 µg/kg for sediment calculated for freshwater is well below the natural background level which is typically 6 mg/kg. For seawater the concentration is 10 times lower, which is also well within the natural background levels in marine sediment. 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.

The PEC/PNEC ratios for soil are above 1 for both iodine and iodide indicating unacceptable risk. However, as indicated above, scenario 1 may not represent realistic European conditions. Under conditions more close to reality, the risk for soil organisms related to the use of iodine in PT1 as the product Yodi Cura may be considered as acceptable.

The risk quotient for STP is clearly below 1, even using conservative worst-case assumptions for the calculation (scenario 1). This result indicates acceptable risk for the micro-organisms in a STP due to the use of Yodi Cura as human disinfectant.

The relevant value for the risk assessment of groundwater is the PEC_{gw} of 18.1 µg/L. This value is above the limit value of 0.1 µg/L provided for pesticides in the Drinking Water Directive 98/83/EC.

Product Type 3:

An overview on the results of the aquatic risk assessment for iodine, iodide and iodate is provided below, partly in tabular form (Tables 2.2.2.5c, d). The PEC/PNEC ratios for seawater are not explicitly reported here since they would be the same as those for freshwater taking into account both that the PNEC values are 10 times higher and that a dilution factor of 10 is applied on the PEC.

Table 2.2.2.5c. Risk quotients for PT3, surface water.

Surface water	**runoff from agricultural land** **PEC/PNEC**	**release via STP** **PEC/PNEC**

		phosphate standard		nitrogen standard		
iodine species	**product type**	**grassland**	**arable land**	**grassland**	**arable land**	
iodine	PT3a/b	0.75	0.58	0.36	0.36	0.20
	PT3c:					
	Pigs (sows in group)	0.05	0.03	0.06	0.04	n.r.
	Veal cattle	0.09	0.03	0.08	0.04	n.r.
	Ducks	0.06	0.05	0.06	0.06	n.c.
	Turkeys	0,04	0,01	0,03	0,01	**1,86**
iodide	PT3a/b	0.53	0.41	0.25	0.25	0.14
	PT3c :					
	Pigs (sows in group)	0.03	0.02	0.04	0.03	n.r.
	Veal cattle	0.06	0.02	0.06	0.03	n.r.
	Ducks	0.043	0.034	0.040	0.040	n.c.
	Turkeys	0.025	0.005	0.019	0.005	**1.33**
iodate	PT3a/b	0.010	0.008	0.005	0.005	0.003
	PT3c:					
	Pigs (sows in group)	0.0006	0.0004	0.0008	0.0006	n.r.
	Veal cattle	0.0012	0.0005	0.0012	0.0005	n.r.
	Ducks	0.0009	0.0007	0.0009	0.0009	n.c.
	Turkeys	0.0005	0.0002	0.0003	0.0002	0.03

n.r. = not relevant
n.c. = not calculated (covered by the worst case scenario 'turkeys')

Table 2.2.2.5d. Risk quotients for PT3, soil.

Terrestrial		**spreading of manure/slurry PEC/PNEC**				**spreading of sewage sludge PEC/PNEC**
		phosphate standard		**nitrogen standard**		
iodine species	**product type**	**grassland**	**arable land**	**grassland**	**arable land**	
iodine	PT3a/b	**1.95**	**1.53**	0.93	0.93	0.65
	PT3c :					
	Pigs (sows in group)	0.12	0.07	0.15	0.11	n.r.
	Veal cattle	0.23	0.08	0.21	0.10	n.r.
	Ducks	0.16	0.13	0.14	0.14	n.c.
	Turkeys	0.093	0.017	0.068	0.017	**5.93**

Terrestrial		spreading of manure/slurry PEC/PNEC				spreading of sewage sludge PEC/PNEC
		phosphate standard		nitrogen standard		
iodine species	**product type**	**grassland**	**arable land**	**grassland**	**arable land**	
iodide	PT3a/b	**5.35**	**4.19**	**2.56**	**2.56**	**1.77**
	PT3c :					
	Pigs (sows in group)	0.33	0.19	0.42	0.30	n.r.
	Veal cattle	0.63	0.23	0.58	0.28	n.r.
	Ducks	0.44	0.35	0.40	0.40	n.c.
	Turkeys	0,256	0,047	0,186	0,047	**2.33**
iodate	PT3a/b	0.11	0.082	0.049	0.049	0.036
	PT3c :					
	Pigs (sows in group)	0.007	0.004	0.008	0.006	n.r.
	Veal cattle	0.012	0.005	0.011	0.006	n.r.
	Ducks	0.009	0.007	0.008	0.008	n.c.
	Turkeys	0.005	0.001	0.004	0.001	0.329

n.r. = not relevant
n.c. = not calculated (covered by the worst case scenario 'turkeys')

The risk assessment for sewage treatment plants resulted in PEC/PNEC ratios of 4.2×10^{-4} to 3.9×10^{-3} which indicate acceptable risk. Also, the risk assessment of surface water as a result of runoff from agricultural land and release from STP indicates acceptable risk except for the disinfection of animal houses (turkeys) where risk quotients of 1.9 and 1.3 are calculated for iodine and iodide respectively (0.03 for iodate).

For soil, PEC/PNEC values in soil are all below 1 for iodate, the relevant species of iodine under aerobic conditions, indicating acceptable risk. For iodide, PEC/PNEC values in soil above 1 have been identified for PT3a/b for spreading of manure/slurry on grassland and arable land and for spreading of sewage sludge as well as in PT3c for spreading of sewage sludge. Correspondingly, for iodine PEC/PNEC values in soil above 1 have been identified for PT3a/b for spreading of manure/slurry on grassland and arable land when the phosphate standard is considered as well as in PT3c for spreading of sewage sludge.

For groundwater, PEC_{gw} values have been calculated for iodine, iodide and iodate. Maximum PEC_{gw} values of 12.9 µg/L, 17.8 and 4.43µg/L for iodine, iodate and iodide, respectively. Although the above calculated iodine concentrations in groundwater are above the mean natural background concentration of 1 µg/L they are still far below the maximum natural background concentration of 70 µg/L.

The PNEC values are based on acute or short-term studies using the standard assessment factor of 1000. For a non-xenobiotic substance, this seems to be an over-conservative approach when taking into account the fact that the natural background concentrations are higher than the calculated PECs, which most probably do not cause any risk to terrestrial or aquatic species in the environment.

Product Type 4:

An overview on the results of the risk assessment for iodine, iodide and iodate is provided below, partly in tabular form (Table 2.2.2.5e). The PEC/PNEC ratios for seawater are not explicitly reported here since they would be the same as those for freshwater taking into account both that the PNEC values are 10 times higher and that a dilution factor of 10 is applied on the PEC.

Table 2.2.2.5e. Risk quotients for PT4.

Environmental compartment	**PEC/PNEC**
Freshwater & marine	
Surface water	0.68 (iodine) 0.009 (iodate) 0.48 (iodide)
Terrestrial	
Soil	**2.1** (iodine) 0.11 (iodate) 0.81 (iodide)
STP	
Sewage treatment plant	0.0014 (iodine)

The calculated PEC/PNEC values for the aquatic environment are all below 1, which indicates acceptable risks. A risk assessment for sediment was not conducted since the PEC as well as the PNEC values for sediment would have been calculated using the equilibrium partitioning method, consequently the results would be the same as described for surface water.

The risk assessment for the terrestrial environment concerns spreading of sewage sludge from STP. For iodate, the predominant iodine species in soil under non-flooded conditions, and for iodide, the above results show that the PEC/PNEC values are below 1, which indicates acceptable risk. The PEC/PNEC value is above 1 for iodine in soil, which would indicate unacceptable risk for this scenario.

It should be noted that iodine is not a xenobiotic substance and that the predicted iodine concentrations in soil are below the natural background concentration of 0.5 – 20 mg/kg soil.

For groundwater, PECgw values have been calculated for iodine, iodide and iodate. Maximum PECgw values of 4.64 µg/L, 6.41 and 0.65 µg/L for iodine, iodate and iodide respectively. Although these concentrations in groundwater are above the mean natural background

concentration of 1 µg/L they are still far below the maximum natural background concentration of 70 µg/L.

Product Type 22:

The risk assessment for iodine in PT22.2 has led to the following PEC/PNEC ratios (Table 2.2.2.5f).

Table 2.2.2.5f. Risk quotients for PT22.

Environmental compartment	**PEC/PNEC ratios for relevant compartments for PT 22.2**	
	Case A Release during the embalming process	**Case B** Release in cemeteries
Freshwater & marine		
Surface water	0.32	n.a.
Sediment	0.32	n.a.
Terrestrial		
Agricultural soil	1.0 (iodine) 0.056 (iodate) 0.40 (iodide)	n.a.
Cemetery soil	n.a.	9.3 (iodine) 0.53 (iodate) 3.7 (iodide)
STP		
Sewage treatment plant	6.4×10^{-4}	n.a.

The PEC/PNEC values for iodine and iodide in cemetery soil are above 1, which would indicate unacceptable risk. However, in the ESD for PT22 it is proposed to estimate only the concentration of the active substance in groundwater and not in soil. Since the PEC in groundwater is calculated on the basis of the PEC_{soil} and resulting pore water concentration in soil, the exposure assessment for the soil compartment in a cemetery was included only for the sake of completeness. Considering the risk assessment for groundwater, the calculated PEC_{gw} (max 30 µg/L for iodate) is above the mean natural background concentration of 1 µg/L but below the maximum natural background concentration of 70 µg/L

Conclusions:

For all four product types, including cumulative assessment, the risk for STP microorganisms is acceptable. Air is not considered as a compartment of concern and no risk assessment has been performed for air.

In the risk assessment of groundwater the PEC_{gw} values are compared with the limit value of 0.1 µg/L provided for pesticides in the Drinking Water Directive 98/83/EC. The maximum PEC_{gw} values for iodine are 18.1 µg/L (PT1), 17.7 µg/L (PT3), 4.64 µg/L (PT4) and 21.8 µg/L (PT22). The calculated cumulative PEC_{gw} value is 39.2 µg/L. It should be noted that the PEC values in groundwater were calculated following the TGD using the porewater concentration in soil as indication for the groundwater concentration, 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. For comparison, the groundwater and surface water concentrations were calculated for the natural background concentration of iodine species in soil of 5 mg/kg, using this "porewater approach" based on the TGD. This resulted in surface and groundwater concentrations of 0.16 and 1.6 mg/L, respectively which is 10- to 100-fold higher than the concentrations measured in these compartments in the field. This illustrates that the results of the calculations using the "porewater approach" should be interpreted with caution.

It should also be noted that the definition of pesticides in the Drinking Water Directive 98/83/EC is limited to organic substances and their relevant metabolites, degradation and reaction products, and thus iodine, iodide and iodate would not fall 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 value of 0.1 µg/L is not considered applicable. Although the PEC_{gw} is above the mean natural background concentration of 1 µg/L it is still far below the maximum natural background concentration of 70 µg/L. Furthermore, given that the derived conservative upper intake levels (UL) for children and adults are 250 and 600 µg iodine/day, respectively, an increase in the natural groundwater iodine levels of up to 30 µg/L appears not to be of any concern.

The PEC/PNEC ratio for iodine for the freshwater and the marine environment for PT1 indicates unacceptable risk and in the case of cumulative exposure the contribution from the other PTs would lead to a marginal increase in risk. However the calculated PECs are well within the natural background levels of 0.5-20 µg/L. Also, considering that iodine is an essential element to both animals and plants in rather high concentrations, the standard assessment factors applied to the aquatic test results may be considered as overly conservative.

For soil, PEC/PNEC ratios above 1 have been found for PT1 and PT3 both for iodine and iodide and in PT4 for iodine only, which is indicative of unacceptable risk. If cumulative exposure is considered, the following PEC/PNEC ratios are calculated: 18 (iodine), 0.9 (iodate) and 8.4 (iodide). Simple addition of PECs from different compartments may not reflect realistic conditions, since iodine, as described previously, prevails in different forms at different pH and redox conditions being characteristic of the different compartments. Also, in line with what was discussed for aquatic test on iodine, the use of standard assessment factors applied to the terrestrial test results may be considered as overly conservative.

At TMII-12, it was concluded that the approach taken by RMS, i.e. that the risk can be disregarded if the PECs added are assumed to be not relevant compared to the background levels, and there is no evidence for overtime accumulation, is accepted. For the assessment of relevance it is necessary to have insight into natural background levels of iodine in relation to the background levels in the ecotoxicity studies and the levels of essentiality.

To conclude the risk assessment for iodine several conditions should be taken into account. The background iodine concentrations in the environmental compartments concerned are high and the PEC values resulting from the use of the concerned iodine containing products are well within these ranges of background values. Also, the iodine forms that prevail in the different compartments are not primarily iodine (I_2), but rather iodate or iodide, and the risks calculated for these forms are all lower, in some cases much lower, than for iodine. 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). RMS SE thus concludes that the actual risks arising from the use of iodine containing products in product types 1, 3, 4 and 22 should be considered to be acceptable.

2.2.3. List of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. PROPOSED DECISION

3.1. Background to the proposed Decision

Iodine is an essential nutritional dietary element. It is required for the synthesis of the thyroid hormones, which control metabolism and play an important role in reproduction, growth and development. Recommendations for the daily intake for humans were established. e.g. by the World Health Organisation (WHO) of 150 – 200 µg/day and the fortification of table salt with iodine has become a means to prevent an undersupply.

However, also excessive iodine intakes may bear risks for humans, especially for individuals with pre-existing thyroid diseases, pregnant woman and infants, in particular if they are living in iodine-deplete regions. The latter apply to some European countries or regions, all having a mild iodine deficiency according to the WHO criteria.

Normally, healthy adults can tolerate iodine intakes of more than 1000 µg per day without any side effects and the WHO (2004) expressed Upper Intake Levels of 1800 µg/day for (adults) and 2400 µg/day (pregnant and lactating women) for iodine sufficient regions. The situations for regions with known iodine deficiency might be different.

A more conservative Upper Intake Level of 600 µg/day was established by the EU Scientific Committee on Food (SCF) for iodine to account for possible increased sensitivity of some individuals in iodine deficient regions.

Since iodine is not a xenobiotic substance but an essential dietary trace element and ubiquitously present in the environment, the recommended upper intake levels and background values have been taken into account in the human health and environmental risk assessments.

The representative biocidal products evaluated in the present CAR contain iodophors, i.e. either iodine complexed with surfactant (iodophor type 1) or iodine complexed with polyvinylpyrrolidone (iodophor type 2).

The iodophor 2 (PVP-iodine) is placed on the market as such and this material has a separate CAS-No (25655-41-8), whereas iodophor 1 (surfactant complexed iodine) may be formed during the manufacture of the biocidal product. For clarity it is considered important to explicitly state that the evaluation covers iodine and PVP-iodine (polyvinylpyrrolidone iodine).

Also for biocidal products containing stabilized iodine, for example PVP-iodine, the outcome of the risk assessment is determined by the equivalent amount of molecular iodine which must therefore have been quantified.

The present CAR comprises the evaluation of the use of representative products containing iodine or PVP-iodine in product type (PT) 1 in which iodine is used in biocidal products for skin disinfection, in PT 3 in which iodine is used in biocidal products for the disinfection of animals' teats/udder as well as for disinfection of animal houses, in PT 4 in which iodine is used for disinfection of milking equipment and milk storage tanks and in PT 22 in which iodine

is used in embalming fluids for the short-term preservation and hygienisation of cadavers until burial/cremation.

The risk characterisation for human health shows that the proposed uses (in addition to iodine intake via the diet) do not lead to exposure levels which are above the Upper Intake Level, which has been established by scientific panels based on human data. Also the occupational exposure limit (OEL 1 mg/m^3), protecting for local effects by the inhalation pathway, is not exceeded. Hence, the proposed uses are considered to be safe.

For the environment risks have been identified for surface water, soil and groundwater. However, these risks are based on standard risk assessment procedures which include conservative assessment factors and limit values which are not considered appropriate for this kind of substance. Background levels of iodine in the different compartments concerned are: for surface water 0.5-20 µg/L with up to 65 µg/L in seawater; for soil 0.5 – 20 with a mean value of 5 mg/kg dw and; for groundwater typically up to 70 µg/l with a mean value of 1 µg/l. PEC values resulting from the use of the concerned iodine containing products are well within these ranges of background values. In conclusion, taking into account the high background iodine concentrations in the environmental compartments concerned and that iodine is an essential element to both animals and plants in rather high concentrations (higher than what corresponds to a trace element), the actual risks to the environment arising from the use of iodine containing products in product types 1, 3, 4 and 22 is considered to be acceptable.

3.2. Proposed Decision

The overall conclusion from the evaluation of iodine for use in product type 1 (Human hygiene biocidal products), product type 3 (Veterinary hygiene biocidal products), product type 4 (Food and feed area disinfectants) and in product type 22 (Embalming and taxidermist fluids), is that it may be possible to issue authorisations of products containing iodine including PVP-iodine in accordance with the conditions laid down in Article 5(1) b), c) and d) of Dir. 98/8/EC.

It is therefore proposed to approve iodine including PVP-iodine as an active substance for use in product type 1 (Human hygiene biocidal products), product type 3 (Veterinary hygiene biocidal products), product type 4 (Food and feed area disinfectants) and in product type 22 (Embalming and taxidermist fluids), subject to the following specific conditions:

Iodine for the use as biocidal product shall have a minimal purity of 995 g/kg and shall comply with the requirements in the EUROPEAN PHARMACOPOEIA (Ph. Eur.) with regards to the impurity levels specified therein.

For PT 1 :

The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

For PT 3 :

The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

Authorisations are subject to the following condition:

1) For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 of the European Parliament and of the Council or Regulation (EC) No 396/2005 of the European Parliament and of the Council shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

For PT 4 :

The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

Authorisations are subject to the following condition:

1) For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 of the European Parliament and of the Council or Regulation (EC) No 396/2005 of the European Parliament and of the Council shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

2) Products containing iodine shall not be incorporated in materials and articles intended to come into contact with food within the meaning of Article 1(1) of Regulation (EC) No 1935/2004, unless the Commission has established specific limits on the migration of iodine into food or it has been established pursuant to that Regulation that such limits are not necessary.

For PT 22 :

The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not adressed in the Union level risk assessment of the active substance.

Authorisations are subject to the following condition:

For professional users, safe operational procedures and appropriate organizational measures shall be established. Where exposure cannot be reduced to an acceptable level by other means, products shall be used with appropriate personal protective equipment

3.3. Elements to be taken into account when authorising products

The waiver for acute toxicity studies on birds has been accepted at Annex I level for all three product types. However, at the product authorisation stage Member States may require acute studies on birds for products in PT3 that are intended to be used in poultry farms.

Some studies were not finalized during the assessment and may be required at product authorization stage. This is the case for

PT 1:	Shelf-life stability
PT 3-IoShield:	Shelf-life stability study
PT 3, PT 4-Masodine:	Shelf-life stability study
PT 22:	Shelf-life stability and method and validation for determination of active substance in formulation

For product types 1, 3, 4 and 22 efficacy should be further assessed on a case by case basis, depending on the intended use, at product authorisation stage. For instance, efficacy needs to be assessed for products in PT 1 that are intended to be used by non-professionals.

For the approval stage, iodine in PT 3, PT 4 and PT 22 was only assessed for professional uses. Products in PT 1 were assessed for professionals as well as by non-professionals.

In the representative biocidal products evaluated, iodine is present in stabilized form, either by surfactants or by polyvinylpyrrolidone (Povidone, PVP). Special considerations with regard to safety and efficacy may be required when authorising products containing free non-stabilized iodine.

When iodine is present in stabilized form the nature of the stablizer should be reported in the application and considered when authorizing products. In particular, in products containing PVP-iodine, the presence of polyvinylpyrrolidone (PVP) should be considered when authorising products. For products containing stabilized iodine, the active ingredient content should be expressed as the equivalent amount of iodine. For products containing PVP-Iodine, the content of PVP-Iodine should be indicated, as well as the equivalent amount of iodine present in the product.

For use in PT 1, respiratory protection is recommended in case of insufficient ventilation. For protection against splashes it is recommended to wear goggles with lateral protection.

Usually no specific PPE is needed during use in PT 3. However, disposable gloves are worn during application to avoid cross contamination (cow / worker / cow). Eye/face protection may also be used when handling the concentrate. The use of RPE is recommended during spray application more than once a day to avoid a potential exceeding of the UL.

For use in PT 22 it is, for hygienic reasons, standard practice to use at least gloves and protective clothing. Additional PPE frequently used is wellingtons, apron, forearm protectors, head and face protection. Facemasks are medical rather than respiratory protective equipment for this use. In embalming theatres, there may be exhaust ventilation around the embalming table and there is general ventilation.

Inhalation exposure of non-professionals has not been included in the risk characterisation.

A refinement of the dietary risk assessment is needed at Member State level when authorising products, since trigger values according to the Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products prepared by DRAWG (Dietary Risk Assessment working group) were exceeded for certain scenarios (e.g., surface disinfection of animal houses).

Dermal absorption values used in the applications for product authorisation should be justified, if available by the submission of specific dermal absorption data on the product, or by read-across to existing data if scientifically justified, or by using default values.

Regarding resistance, so far no reduction in efficacy has been reported indicating that no development of resistance has occurred.

Regarding the assessment of aggregated exposure, i.e. contribution of iodine exposure from different PTs and other sources, when guidance is available for aggregated risk assessment, such guidance should be incorporated in the risk assessment at product authorisation.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the approval of iodine in accordance with Article 9 of Regulation (EU) No 528/2012.

3.5. Updating this Assessment Report

This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information submitted in relation with Regulation (EU) No 528/2012. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the approval of iodine.

Appendix I: List of endpoints

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	Iodine
Function (*e.g.* fungicide)	Bactericide, fungicide and viricide
Rapporteur Member State	Sweden

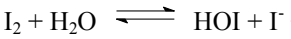
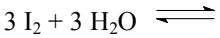
Identity (Annex IIA, point II.)

Chemical name (IUPAC)	Iodine
Chemical name (CA)	Iodine
CAS No	7553-56-2 (PVP-iodine used as carrier for iodine in biocidal formulations: 25655-41-8)
EC No	231-442-4
Other substance No.	No other identification numbers are available.
Minimum purity of the active substance as manufactured (g/kg or g/l)	995 g/kg of iodine (manufactured according to the European Pharmacopoeia) For PVP-iodine, the iodine content shall have a minimum purity of 995 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Limits according to the European Pharmacopoeia 1) Bromides and chlorides ≤ 0.25 g/kg 2) Non-volatile substances ≤ 1 g/kg
Molecular formula	I_2
Molecular mass	253.81 g/mol
Structural formula	I-I

Physical and chemical properties (Annex IIA, point III., unless otherwise indicated)

Melting point (state purity)	113.5-113.7°C; Data taken from several sources (n=4) such as Handbooks (e.g. CRC Handbook of Chemistry and Physics) or alike. No information is available on purity of test material or test method used. However, given that several sources reports approximately the same results the data is considered representative for the iodine under evaluation (min. purity 99.5%)
Boiling point (state purity)	184.24-184.5°C; Data taken from several sources (n=4) such as Handbooks (e.g. CRC Handbook of Chemistry and Physics) or alike. No information is available on purity of test material or test method used. However, given that several sources reports approximately the same results the data is considered representative for the iodine under evaluation (min. purity 99.5%)
Temperature of decomposition	I_2 has a melting point of approx. 114 °C and a boiling point of approx. 185 °C. No decomposition occurs, however iodine tends to sublimate before boiling into brown/purple vapours.
Appearance (state purity)	Solid; grey-black, metallic shine; characteristic, sharp, irritating odour, Data from open literature and no information on purity or test method. This is considered acceptable as it is not a critical parameter
Relative density (state purity)	D_4^{20}: 4.93-4.94 Data taken from several sources (n=3) such as Handbooks (e.g. CRC Handbook of Chemistry and Physics) or alike. No information is available on purity of test material or test method used. However, given that several sources reports approximately the same results the data is considered representative for the iodine under evaluation (min. purity 99.5%)
Surface tension	Not available and not considered required since the active is a purely inorganic substance which is solid at room temperature (i.e. data not relevant for the risk assessment).
Vapour pressure (in Pa, state temperature)	0.030 mmHg (4 Pa) at 0°C 0.305 mmHg (40.7 Pa) at 25 °C 2.154 mmHg (287 Pa) at 50°C,

	26.78 mmHg (3600 Pa) at 90°C Data from a Handbook (Merck index). No information is available on purity of test material or test method used. However, the data is from a trustable source and believed to be representative for the iodine under evaluation (min. purity 99.5%). The data is not considered critical (only used in the risk assessment at one instance (human exposure for PT 1 via vapours)).
Henry's law constant (Pa m^3 mol^{-1})	34.43 Pa m^3 mol^{-1} at 25 °C Data calculated from vapour pressure and water solubility at 25°C (0.3 g/l). Vapour pressure is only availble from one source. This is considered acceptable as this is not a critical parameter (not used in the environmental exposure calculations)
Solubility in water (g/l or mg/l, state temperature)	0.29 g/L at 20 °C 0.30-0.33 g/L at 25 °C 0.78 g/L at 50 °C Data taken from two sources (n=2) such as Handbooks (e.g. CRC Handbook of Chemistry and Physics) or alike. No information is available on purity of test material or test method used. However, given that several sources reports approximately the same results the data is considered representative for the iodine under evaluation (min. purity 99.5%)
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	230 g/L methanol at 25 °C 206 g/L in ether at 17 °C 164.6 g/L in benzene at 25 °C 157 g/kg in ethyl acetate at 25 °C 182.5 g/kg in toluene at 25 °C 17.3 g/kg in n-heptane at 25 °C 13.2 g/kg in n-hexane at 25 °C Data taken from two sources such as Handbooks (e.g. CRC Handbook of Chemistry and Physics) or alike. No information is available on purity of test material or test method used. However, given that several sources reports approximately the same results the data is considered representative for the iodine under evaluation (min. purity 99.5%)
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Not determined as iodine as manufactured does not include an organic solvent.
Partition coefficient (log P_{OW}) (state temperature)	Not relevant to a a purely inorganic substance like iodine
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	In natural water, I^-, IO_3^-, and I_2 are coexisting whereas iodide strongly prevails (see below). Degradation of these three species does not occur, only slight shifts of the equilibrium may happen, depending on the pH, potential reactions partners, and/or organisms incorporating and metabolising iodine species.

Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	The determination of a pKa or pKb is not relevant for iodine, as it is neither an acid nor a base. The solubility of elemental iodine (I2) in water is low (0.3 g/L at 20 deg C). I_2 disproportionates in aqueous solutions according to the following equation:  $K = 5.44 \times 10^{-13}$ HOI disproportionates further in a very slow reaction:  The two reactions can be described by the following overall equation:  $K = 4.07 \times 10^{-47}$
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Absorption maximum between 530 and 550 nm (from open literature; generated on 99.5% pure iodine).
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	In natural water, I^-, IO_3^-, and I_2 are coexisting whereas iodide strongly prevails. Molecular iodine may photolytically be formed from iodide or iodate in water.
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	Not applicable.
Flammability	Iodine is not considered flammable based on theoretical considerations
Explosive properties	Not explosive based on theoretical considerations, however contact of iodine with the following substances results in the risk of explosion (examples): acetylene, ammonia, alkali metals. Furthermore, iodine reacts exothermically under the formation of heat with (examples): iron powder, lithium, phosphorous.

Classification and proposed labelling (Annex IIA, point IX.)

	Directive 67/548/EEC (DSD)	Regulation (EC) No 1272/2008 (CLP)
with regard to physical/chemical data	None	None
with regard to toxicological data	Xn; R20/21 S: (2-)25-23- 61 Due to the experience with iodine and observed skin, eye and respiratory irritational effects, the following additional classification is proposed: Xi R: 36/37/38	Acute Tox. 4 *; H332 Acute Tox. 4 *; H312 Eye irrit. 2; H319 STOT SE 3; H335 Skin Irrit. 2; H315 GHS07, GHS09 Wng
with regard to fate and behaviour data	None	None
with regard to ecotoxicological data	N; R50	Aquatic Acute 1; H400 M=1

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	Titration with sodium thiosulphate using starch solution as indicator.
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Determination/Quantification of bromides and chlorides by opalescence. Determination/Quantification (gravimetrically) of non-volatile substances after sublimation.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	No fully acceptable method available – not required as the calculated PECs from the biocidal uses evaluated are just a fraction of natural background concentrations
Air (principle of method and LOQ) (Annex IIA, point 4.2)	In air sampling tubes, I_2 is partially but stoichiometrically converted to iodide. Iodide is determined by IC-PED. In case of high relative humidity, the use of impingers or bubblers for air sampling is recommended. LOQ = 0.001 ppm LOD = 0.0004 ppm
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Acceptable methods are available: Synthetic drinking water, industrial and domestic sewage water (iodide): Ion chromatographic separation (IC) and conductivity or UV detection: LOQ = 0.1 mg/L Tap water and surface water (iodide and iodate separately): Ion chromatographic separation and inductively coupled plasma mass spectrographic detection (IC-ICP-MS):

	LOQ: At least 5 µg/L Drinking water (iodide and iodate separately): IC-ICP-MS LOQ: at least 6.4 and 8.8 µg/L for I^- and IO_3^- respectively No method required as the calculated PECs from the biocidal uses evaluated are just a fraction of natural background concentrations
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Not necessary, because iodine (iodide) is not classified as toxic or highly toxic.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not necessary, because iodine-based products or materials treated with such products are not used in a manner which may cause contact with such materials.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Determination of iodide in milk and milk powder: HPLC with electrochemical detection (ISO 14378), Applicability range in whole milk: 0.03 µg/g to 1 µg/g Applicability range in dried skim milk: 0.3 µg/g to 10.0 µg/g Method acceptable as such. Nevertheless, the final conclusion on the need for such a method and the LOQ to be required has to be referred to the product authorisation stage when the final guidance for dietary risk assessment is available.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	Iodine is quickly reduced to iodide by nonenzymatic reactions. Iodide is readily and (almost) completely absorbed. The bioavailability after orally administration is > 90%.
Rate and extent of dermal absorption:	Percentage dermal absorption: 11.3 – 12.0% Mean maximal flux rate: 0.020 – 0.128 µg.cm^{-2}.h^{-1} Tested formulations: Biocide 1006 is a formulation, which contains 2.63% total iodine (concentration in the study: 0.66%). PE 305-1 is a formulation containing PVP-iodine, which contains 0.26% total iodine
Distribution:	Iodine is distributed via the blood circulation system and is trapped and concentrated primarily by the thyroid gland, but also by the stomach (gastric mucosa), salivary gland, mammary glands, placenta, choroid plexus, and sweat.
Potential for accumulation:	No bioaccumulation. Iodide in excess of physiological requirement is excreted mainly via the urine, and in smaller quantities via faeces, saliva, milk, sweat, tears, bile, other secretions and exhaled air.
Rate and extent of excretion:	Urinary excretion normally accounts for > 97% of the elimination of absorbed iodide, while faecal excretion accounts for approximately 1–2%. Normal renal excretion in humans is about 20-100 µg/day.
Toxicologically significant metabolite	None

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	> 2000 mg/kg bw
Rat LD_{50} dermal	Estimated based on R21 classification: 400 < LD_{50}< 2000 mg/kg
Rat LC_{50} inhalation	Estimated based on R20 classification: 2 < LC_{50}< 10 mg/L/4h
Skin irritation	Iodine is a skin irritant.
Eye irritation	Iodine is a strong eye irritant.
Skin sensitization (test method used and result)	Iodine is not-sensitising (Guinea pig maximisation test; Directive 96/54/EC, B.6)

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	human / thyroid / inhibitory effect on the thyroid secretion
Lowest relevant oral NOAEL / LOAEL	Europe: NO(A)EL = 600 µg/day / LOEL = 1800 µg/day (USA: NO(A)EL = 1200 µg/day / LOEL = 1800 µg/day)
Lowest relevant dermal NOAEL / LOAEL	Study not available. Waiver is provided.

Lowest relevant inhalation NOAEL / LOAEL	NO(A)EL = 1 mg/m^3 (0.1 ppm)

Genotoxicity (Annex IIA, point 6.6)	No evidence for a genotoxic potential in *in vitro* and *in vivo* tests.

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	No indications for carcinogenicity available from subchronic, genotoxicity or cancerogenicity studies. Some increase in squamous cell carcinomas (SCCs) in the sublingual and parotid gland after oral exposure in rats are likely be linked to the irritative nature of iodine.
lowest dose with tumours	41 mg iodide/kg day (males)

Reproductive toxicity (Annex IIA, point 6.8)

Species / Reproduction target / critical effect	Rat Parents: diminished milk secretion Pups: reduced viability due to diminished milk secretion
Lowest relevant reproductive NOAEL	< 28 mg/kg bw/day
Species / Developmental target / critical effect	Rabbit: No teratogenic effects. Dams: Maternal: reduced body weight
Lowest relevant developmental NOAEL	Dams: 35 mg PVP-iodine/kg bw/day, equivalent to 3.5 mg available iodine/kg bw/day Pups: ≥ 75 mg PVP-iodine/kg bw/day, equivalent to 7.5 mg available iodine/kg bw/day (highest dose tested)

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect	No study available. Effects in foetus or newborn infants cannot be excluded because thyroid hormones are essential to the development of the neuromuscular system and brain. However, even at high doses no such effects have been noted so far for in older children or adults and are therefore not likely.
Lowest relevant NOAEL	Not applicable

Other toxicological studies (Annex IIIA, VI/XI)

Toxic effects on livestock and pets	Iodine intakes in excess to pregnant animals caused abortions, premature births, weak or abnormal newborn at birth, stillbirths, goitrous offspring, enlarged thyroids, newborn with bone weakness including elevated phosphorus and alkaline phosphatase content in the blood possibly indicating a severe disturbance in the bone metabolism, and skeletal aberrations in horses,

	cows and pigs.
Studies related to the exposure of the a.s. to humans	Long-term studies in humans that were exposed to iodine via drinking water showed that doses of 30 µg/kg bw /day (average) had no effect on T_4 levels. Neither sensitisation nor iodism was noted. No neonatal goitre was observed in infants born from mothers that were exposed to iodine at the same (average) dose.
Food and feeding stuffs	Results in respect of teat dip application: (1) Compared to samples of control days, the residues in milk sampled on experimental days were 15 – 20 % higher. However, the overall variation in the iodine content of milk by far exceeds the increase noted in this study. (2) The average increase of milk iodine content in the publications was about 50 – 174 µg/L, i.e. within the natural variation of the iodine content of milk noted in untreated animals. (3) Iodine content in milk may contribute to the compensation of iodine deficiency in food. If the daily dietary intake of iodine exceeds the daily requirements up to 1000 µg/day, it is eliminated without signs of toxicity. Consequently, even very high levels of iodine in milk are of no concern for children.
Other tests related to exposure of the a.s. to human considered to be necessary	Further studies are not necessary for the purpose of a comprehensive evaluation of the a.s.
Tests to assess toxic effects from metabolites of treated plants	Iodine in products considered in this dossier is not used for action against plants.
Mechanistic studies	The mechanism of excessive iodine in humans is scientifically not fully understood but some data (together with the knowledge on metabolism) and hypotheses on e.g. physiological triggers of the dysregulation of thyroid hormone production are available. Therefore, additional studies are not required to address this point.
Further human health related studies	Further studies are not necessary for the purpose of a comprehensive evaluation of the a.s.

Medical data (Annex IIA, point 6.9)

Medical data in anonymous form	Long-time experiences with PVP-iodine, e.g. regularly used for hand washing in hospitals etc. are available. After regular and intensive exposure to intact skin a slight elevation of thyroid hormone levels may occur.
Direct observations, e.g. clinical cases, poisoning incidents	Acute oral exposure in humans LD_{LO} (human): 0.0197 g/kg bw
Health records	No adverse reactions have been reported with teat dips containing PVP-iodine during the period of observation (1996-2006).

Epidemiological Study	Result: Some regions in Europe have a deficient nutritional status of iodine. The positive effects due to additional iodine uptake by iodinated salt prevail.
Diagnosis of poisoning including specific signs of poisoning and clinical tests	Eyes: brown discoloration of the cornea due to saturated vapours, rejection of this layer and complete renewal within a few days; strong irritation through to chemical burns by alcoholic solutions (from about 5 % upwards) Skin: moderate through to serious irritation to affected areas, possibly inflammatory reactions or damage resembling burning with blistering following contact with concentrated solutions; absorptive-toxic effects following massive contact in particular with preinjured skin; more seldom allergic reactions. Inhalation: vapours are irritant to the mucous membranes. The reported experience in humans demonstrates that a concentration of 0.1 ppm (1 mg/m3) is a concentration not causing irritational effects Ingestion: serious irritation to mucous membranes affected, emesis, diarrhoea, gastritis, systemic effects Absorption: tachycardia, in the ECG idioventricular rhythm, salivation, headache, impaired vision, vertigo, unconsciousness, cramps, cyanosis, functional disturbances to the kidneys, hyperthyroidism, changes to blood (hemolytic anemia), metabolic disturbances (acidosis). Possible (allergic) hypersensitivity reactions to the skin.
Sensitization/allergenicity observations	In very rare cases, (pseudo)allergic reactions to human pharmaceuticals are reported but not for biocides.
Specific treatment in case of an accident or poisoning: first aid measures and medial treatment	Inhalation: While protecting yourself, remove the victim from the hazardous area and bring him into fresh air. Lay the victim down in a quiet place; avoid hypothermia. In case of breathing difficulties, administer oxygen to victim. As soon as possible have the victim repeatedly take deep breaths of a glucocorticoid inhalation spray. If the victim is unconscious but breathing, lay him on his side in a stable position. If the victim has stopped breathing, give mouth to nose resuscitation. If this is not possible use mouth to mouth resuscitation. Keep respiratory tract clear. seek medical care. Ingestion: Rinse mouth and spit out fluids. Slowly administer 1 - 2 glasses of water. Do not administer cooking oil, castor oil, milk or alcohol under any circumstances. Do not induce vomiting. Obtain medical treatment immediately and show container label. Eye: Immediately rinse with plenty of water, control by a specialist. Skin: Remove affected clothing and wash all exposed skin areas with mild soap, water, followed by warm water rinse.
Prognosis following poisoning	Lethal effects due to poising with single doses of iodine are not likely. Furthermore, recovery is expected when exposure is discontinued and proper medication is applied.

Summary (Annex IIA, point 6.10)	Value	Study	Safety factor
Recommended daily intake	150-200 µg/day	-	-
AEL (Operator/Worker Exposure) = Upper Intake Level (UL) (The AEL (=UL) includes all time frames)	Europe: 600 µg/day (0.01 mg/kg bw/d.) (USA: 1200 µg/day, 0.02 mg/kg bw/d.) AEC (inhalative) (OEL): 0.1 ppm / 1 mg/m3	see above	3 (1.5)
Drinking water limit	30 µg/L *)	-	-
ARfD (acute reference dose)	Not applicable. Substance is not acute toxic or harmful.	-	-

*) No drinking water limit is established. Calculation is based on 10% Upper Intake Level and a daily intake of 2 L drinking water.

Acceptable exposure scenarios (including method of calculation)

Professional users	No risk identified for proposed uses (according to models provided by TNsG of Human Exposure).
Non-professional users	No risk identified for proposed uses (according to models provided by TNsG of Human Exposure).
Indirect exposure as a result of use	It has been demonstrated that indirect exposure via milk is of no concern. No upper intake level has been established for infants (< 1 year). However, iodine intake via cows milk is in the same range as the content in infant formulas as well as in breast milk from humans.

Chapter 4: Fate and Behavior in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	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 specie.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	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.
Readily biodegradable (yes/no)	Not applicable because iodine is an element
Biodegradation in seawater	Not applicable because iodine is an element
Non-extractable residues	Not applicable because iodine is an element
Distribution in water / sediment systems (active substance)	In natural water/sediment system, iodide would be the predominant species under aerobic conditions. Iodine can enter sediments through accumulation of plant matter or fixation of iodide in water to humic substances. Weaker and reversible binding of iodide to inorganic components in sediments may also occur (Kd values ranging from -0.22 mL/g for chlorite minerals to 15.14 mL/g for iolite minerals).
Distribution in water / sediment systems (metabolites)	See above.

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

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

applied a.i. (range and maximum)	
Soil accumulation and plateau concentration	No data available and no data required

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

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> Kp_{susp}= 220 cm^3/g (geometrical mean) Kp_{soil} = 0.01- 580 cm^3/g; 6.9 cm^3/g (geometrical mean)

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

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 ($400 < \lambda < 700$ 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_3I) probably being the most important one.

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No data available for the biocidal use. Natural background levels (total iodine) typically in the range 0.5 - 20 mg/kg dw but with extremes up to 98 mg/kg Global mean value of 5 mg/kg
Surface water (indicate location and type of study)	No data available for the biocidal use. Natural background levels (total iodine) in the range 0.5-20 µg/l
Ground water (indicate location and type of study)	No data available for the biocidal use. Natural background levels (total iodine) in the range <1-70 µg/l with extremes up to 400 µg/l Global mean concentration: 1 µg/l
Air (indicate location and type of study)	No data available for the biocidal use. Natural atmospheric background levels (total iodine) in the range 10-20 ng/m^3.

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 hours	LC_{50} (iodide)	3780 mg iodine/L
		LC_{50} (iodate)	220 mg iodine /L
		LC_{50} (iodine)	1.67 mg iodine /L
Invertebrates			
Daphnia magna	48 hours	LC_{50} (iodide)	0.83 mg iodine /L
		LC_{50} (iodate)	58.5 mg iodine /L
		LC_{50} (iodine)	0.59 mg iodine /L
		LC_{50} (PVP-iodine PT1)	0.32 mg iodine /L
Algae			
Desmodesmus subspicatus	72 hours	E_rC_{50} (iodine)	1.3 mg/L
		E_bC_{50} (iodine)	0.62 mg/L
Microorganisms			
Mixed population of activated sewage sludge micro-organisms	3 hours	EC_{50} (iodine)	290 mg/L

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia fetida*.
(Annex IIIA, point XIII.3.2)

NOEC (iodine)	125 mg/kg_{dwt}	93 mg/kg_{wwt}
LC_{50} (iodine)	>1000 mg/kg_{dwt}	>740 mg/kg_{wwt}

Acute toxicity *to non-target plants.*
(Annex IIIA, point XIII.3.2)

Seedling emergence and seedling growth test: most sensitive parameter was shoot fresh weight.

species	NOEC [mg/kg_{dwt}]	LOEC [mg/kg_{dwt}]	E/LC50 [mg/kg_{dwt}]	E/LC50 [mg/kg_{wwt}]
Avena sativa	7.4	22.2	**13.4**	11.8
Allium cepa	7.4	22.2	26.6	23.4
Brassica napus	7.4	22.2	22.1	19.4
Helianthus annuus	7.4	22.2	16.5	14.5
Lycopersicon esculentum	7.4	22.2	16.2	14.3
Cucumis sativa	7.4	22.2	14.2	12.5

Reproductive toxicity to …… (Annex IIIA, point XIII.3.2)	No data available and no data required

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrate formation	NOEC (iodine)	10 mg/kg_{dwt}	8.4 mg/kg_{wwt}
	EC_{50} (iodine)	82.6 mg/kg_{dwt}	69.4 mg/kg_{wwt}
Carbon mineralization	NOEC (iodine)	31.6 mg/kg_{dwt}	26.5 mg/kg_{wwt}
	EC_{50} (iodine)	148.7 mg/kg_{dwt}	125 mg/kg_{wwt}

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	No data available and no data required
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	No data available and no data required
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	No data available and no data required
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	No data available and no data required

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	No data available and no data required
Acute contact toxicity	No data available and no data required

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	No data available and no data required
Acute contact toxicity	No data available and no data required
Acute toxicity to ……..	No data available and no data required

Bioconcentration (Annex IIA, point 7.5)

	The logK_{ow} (< 3, see above) indicates that iodine has a low potential for bio-concentration and bioaccumulation (according to guideline OECD 117, log K_{OW} values below 3 are regarded to be indicators of low accumulation potential).
Bioconcentration factor (BCF)	BCF factors are generally low (0.001 to 810 for freshwater and marine fish, freshwater and marine invertebrates, marine and terrestrial plants). These figures are not based on standard bioconcentration tests.
Depuration time(DT_{50}) (DT_{90})	Not applicable: no test performed

Level of metabolites (%) in organisms accounting for > 10 % of residues	Not applicable due to the fact that iodine is an element

Chapter 6: Other End Points

No other endpoints.

Appendix II: List of Intended Uses

Summary of intended uses5

Iodine-based products are used as bactericide, fungicide and viricide for the following uses. Concentrated products can be diluted in water, if needed.

Product type and application type	Member state or Country	Application technique	Number and timing of application	Concentration in application solution	Remarks
PT1 Skin disinfection (surgical handrub)	**EU**	Hand and forearms are lathered with the product for up to five minutes and then rinsed off with tap water	Once, up to 8 times per day when required	10% PVP-Iodine, equivalent to 1.13 % available iodine (w/w).	--
PT3 Manual teat disinfection	**EU**	Teat skin disinfection using a ready-to-use formulation or a dilution of a concentrated product.	Once*, totally up to four times a day	Iodophor type 1: 900-10,000 ppm available iodine Iodophor type 2: 1000-4000 ppm available iodine	--
PT3 Udder washing	**EU**	Udder disinfection using a dilution of a concentrated product.	Udder washing is not a routine procedure.	Iodophor type 1: 25-50 ppm available iodine Iodophor type 2: Udder washing has not been identified as a use for which iodophor type 2 is used	--
PT3 Automatic** disinfection of teats by spraying (CIP)	**EU**	Teat skin disinfection using a ready-to-use formulation or a dilution of a concentrated product.	Once*, totally up to four times a day	Iodophor type 1: 900-10,000 ppm available iodine Iodophor type 2: Automatic teat disinfection has not been identified as a use for which iodophor type 2 is used.	--
PT3 Disinfection of animal houses	**EU**	Surface disinfection using a dilution	The frequency is generally two times per year and per animal	Iodophor type 1 12.5 ppm to 200 ppm available	--

Product type and application type	Member state or Country	Application technique	Number and timing of application	Concentration in application solution	Remarks
		of a concentrated product.	housing. However, more frequent applications are also possible: weekly applications (cattle and calving pens, some areas of pig housing) and every 6 weeks (poultry housing).	iodine Iodophor type 2: Disinfection of animal houses has not been identified as a use for which iodophor type 2 is used.	
PT4 Manual or automatic** disinfection of milking machine systems (pipelines, claws) and other milking equipment	**EU**	Surface disinfection (CIP) using a dilution of a concentrated product.	Daily between milking different cows.	Iodophor type 1: 25-55 ppm available iodine Iodophor type 2: Manual or automatic disinfection of milking machine systems has not been identified as a use for which iodophor type 2 is used.	--
PT4 Manual or automatic** disinfection of bulk milk storage tanks	**EU**	Surface disinfection using a dilution of a concentrated product.	Manual: monthly (12 times per year) at maximum Automatic: daily or each 2-3 days (max. 353 times per year)	Iodophor type 1: manual: 12.5-65 ppm available iodine automatic: 12.5-100 ppm available iodine Iodophor type 2: Manual or automatic disinfection of bulk milk storage tanks has not been identified as a use for which iodophor type 2 is used.	--
PT22 Embalming of cadavers	EU	Arterial injection of diluted product and injection into the abdominal cavity of undiluted product.	36 cadavers are embalmed per 10,000 inhabitants per year. Based on data from the UK, this translates to 98 cadavers per embalmer per year.	Iodophor type 2: **Arterial injection:** 3.2 % PVP-I (w/w), equivalent to 0.29 - 0.39 % available iodine (w/w) 32,000 ppm PVP-Iodine, equivalent to 2,880-3,850 ppm available iodine **Injection into the abdominal cavity:** 12.8 % PVP-I (w/w), equivalent to	--

Product type and application type	Member state or Country	Application technique	Number and timing of application	Concentration in application solution	Remarks
				1.15 – 1.54 % available iodine (w/w). 128,000 ppm PVP-Iodine, equivalent to 11,150 – 15,400 ppm available iodine.	

adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

Remark: the application rates given for PT3 and PT4 (e.g. concerning the disinfection of animal houses, udder washing) are not supported by key-studies and have to be substantiated at the product authorisation stage by appropriate studies.

* According to Service contract for the development of environmental emission scenarios for active substances used in certain biocidal products; Draft final report to European Commission, Directorate General Environment, January 2007; (AEAT/ED48587/R1

**Automatic teat disinfection is just the automated version of manual disinfection. It increases throughput on farms and reduces human exposure. Special products are used for this purpose.

Appendix III: List of studies

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A1/01	Bervoets, A.	2002	ECB EMAIL TO EVANS - PRELIMINARY NOTIFICATION NUMBER - [N266]EVANS VANODINE INTERNATIONAL PLC-[7553-56-2] Source: EC Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 987-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A2.6/01	Anonymous	1995	CD RÖMPP CHEMIE LEXIKON - IOD Source: CE Römpp Chemie Lexikon, Version 1.0, 1995 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-006	No	N.R.
A2.7/01	Anonymous	2004	EUROPEAN PHARMACOPOEIA - IODINE Source: European Pharmacopoeia, Fifth Edition, Supplement 5.2, ISBN: 92-871-5414-7	No	N.R.
A2.7/02	Turton, R.G. Wilcox	N.I.	SPECIFICATION - IODINE PRILLS PH. EUR. Source: Blagden Chemicals Marketing Report No.: I001/0800 : CR2646/ISSUE NO.2 Not GLP; (unpublished)	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A2.7/03	Anonymous	1992	PRILLED IODINE - TYPICAL SPECIFICATIONS Source: SQM Iodine Europe N.V., Belgium	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A2.7/04	Anonymous	1999	CERTIFICATE OF ANALYSIS - PRILLED IODINE Source: acf minera s.a. Chile Report No.: 01-36 190046 Not GLP; (unpublished)	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A2.8.9/01	Anonymous	2004	EUROPEAN PHARMACOPOEIA - IODINE Source: European Pharmacopoeia, Fifth Edition, Supplement 5.2, ISBN: 92-871-5414-7	No	N.R.
A2.8.9/02	Anonymous	2003	IODINE SPECIFICATION - IODINE I-1 Source: Not applicable Report No.: Not indicated Not GLP; (unpublished)	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A3.1.1/01	Weast, R.C.	1990	CRC HANDBOOK OF CHEMISTRY AND PHYSICS - PHYSICAL CONSTANTS OF INORGANIC COMPOUNDS Source: CRC Handbook of Chemistry and Physics, 70th Edition Report No.: Not applicable Not GLP; (published) Doc. No.: 192-001	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A3.1.1/02	Holleman, A.F. Wiberg, E.	1985	LEHRBUCH DER ANORGANISCHEN CHEMIE - GRUPPE DER HALOGENE Source: Lehrbuch der Anorganischen Chemie, 91-100 Auflage, 1985, 400-401, 434-436, 442-443 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-005	No	N.R.
A3.1.1/03	Anonymous	1995	CD RÖMPP CHEMIE LEXIKON - IOD Source: CE Römpp Chemie Lexikon, Version 1.0, 1995 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-006	No	N.R.
A3.1.1/04	Anonymous	N.I.	DATA BASE REPORT - IODINE - CAS NO. [7553-56-2] Source: Not indicated Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 119-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A3.2/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A3.3.3/01	Anonymous	2006	HSDB DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: HSDB Database search - http://toxnet nlm nih.gov/ Report No.: Not applicable Not GLP; (published) Doc. No.: 591-004	No	N.R.
A3.4/01	Saiz-Lopez, A. et al.	2004	ABSOLUTE ABSORPTION CROSS-SECTION AND PHOTOLYSIS RATE OF I2 Source: Atmos. Chem. Phys. Discuss., 4, 2379-2403, 2004 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-007	No	N.R.
A3.6/01	Lee, S.K. Zhai, H. Maibach, H.I.	2005	ALLERGIC CONTACT DERMATITIS FROM IODINE PREPARATIONS - A CONUNDRUM Source: Contact Dermatitis, 2005, 52, 184-187 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-046	No	N.R.
A3.6/02	Nagy, K. Körtvélyesi, T. Nagypál, I.	2003	IODINE HYDROLYSIS EQUILIBRIUM Source: Journal of Solution Chemistry, 32, 5, May 2003, 385-393 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-005	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A3.9/01	Anonymous	N.I.	EPIWIN CALCULATION OF THE OCTANOL / WATER PARTITION COEFFICIENT OF IODINE Source: Not indicated Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 114-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A3.11/01	Anonymous	2007	GESTIS STOFFDATENBANK - IOD Source: Gestis - Stoffdatenbank Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 191-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A3.11/02	Riedel, E.	1990	ANORGANISCHE CHEMIE - OXIDE DER HALOGENE Source: Anorganische Chemie, 2, 1990, 385-388 Report No.: Not indicated Not GLP; (published) Doc. No.: 192-008	No	N.R.
A3.17/01	Dehouck, P.	N.I.	PACKING SPECIFICATIONS IODINE Source: Cid Lines Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 162-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Cid Lines
A4.1/01	Anonymous	2004	EUROPEAN PHARMACOPOEIA - IODINE Source: European Pharmacopoeia, Fifth Edition, Supplement 5.2, ISBN: 92-871-5414-7 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-010	No	N.R.
A4.2a/01	Günzler, H. et al.	1997	SPURENANALYTIK VON IOD IN BÖDEN UND PFLANZEN Source: Analytiker Taschenbuch 15, 1997, 122-145, Springer Verlag Report No.: Not applicable Not GLP; (published) Doc. No.: 492-009	No	N.R.
A4.2a/02	Günzler, H. et al.	1997	ANWENDUNG DER ICP-MS FÜR DIE SPURENELEMENTBESTIMMUNG IN BIOLOGISCHEN MATERIALIEN Source: Analytiker Taschenbuch, 1997, 15, 90-120 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-008	No	N.R.
A4.2a/03	Knoch, E.	2009	IODINE - DEVELOPMENT AND VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF IODINE IN SOIL SGS Institut Fresenius GmbH, Taunusstein, Germany Report No.: IF-09/01396479 GLP, unpublished Doc. No.: 434-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A4.2a/04	Mani, D. et al.	2007	RAPID DETERMINATION OF IODINE IN SOILS USING INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY Current science, 2007, 93 (9), 1219-1221 Report No.: Not applicable Not GLP, published Doc. No.: 492-016	No	N.R.
A4.2a/05	Yamada, H. et al.	1996	DETERMINATION OF TOTAL IODINE IN SOILS BY INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY Soil Science and Plant Nutrition, 1996, 42 (4), 859-966 Report No.: na Not GLP, published Doc. No.: 492-017	No	N.R.
A4.2b/01	Anonymous	2006	IODINE IN WORKPLACE ATMOSPHERES - IMPREGNATED ACTIVATED BEADED CARBON Source: From website: http://www.osha.gov/ Report No.: Not applicable Not GLP; (published) Doc. No.: 592-036	No	N.R.
A4.2c/01	Anonymous	1997	DETERMINATION OF DISSOLVED ANIONS IN WATER BY LIQUID CHROMATOGRAPHY OF IONS - PART 3 - DETERMINATION OF CHROMATE, IODIDE, SULFITE, THIOCYANATE AND THIOSULFATE Source: Deutsche Norm, DIN EN ISO 10304-3, November 1997 Report No.: DIN EN ISO 10304-3 : 1997-11 ICS 13.060.01 Not GLP; (published) Doc. No.: 492-004	No	N.R.
A4.2c/02	Günzler, H. et al.	1997	SPURENANALYTIK VON IOD IN BÖDEN UND PFLANZEN Source: Analytiker Taschenbuch 15, 1997, 122-145, Springer Verlag Report No.: Not applicable Not GLP; (published) Doc. No.: 492-009	No	N.R.
A4.2c/03	Günzler, H. et al.	1997	ANWENDUNG DER ICP-MS FÜR DIE SPURENELEMENTBESTIMMUNG IN BIOLOGISCHEN MATERIALIEN Source: Analytiker Taschenbuch, 1997, 15, 90-120 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-008	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A4.2c/04	Kirchner, S. Stelz, A. Muskat, E.	1996	BEITRAG NATÜRLICHER MINERALWÄSSER ZUR IODIDVERSORGUNG DER BEVÖLKERUNG Source: Z Lebensm Unters Forsch, 1996, 203, 311-315 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-006	No	N.R.
A4.2c/05	Yoshida, S. et al.	2007	DETERMINATION OF THE CHEMICAL FORMS OF IODINE WITH IC-ICP-MS AND ITS APPLICATION TO ENVIRONMENTAL SAMPLES Journal of Radioanalytical and Nuclear Chemistry, 2007, 273 (1), 211-214 Report No.: na Not GLP, published Doc. No.: 492-018	No	N.R.
A4.2c/06	Sacher, F. et al.	2005	ANALYSIS OF IODINATED X-RAY CONTRAST AGENTS IN WATER SAMPLES BY ION CHROMATOGRAPHY AND INDUCTIVELY-COUPLED PLASMA MASS SPECTROMETRY Journal of Chromatography A, 2005, 1085, 117-123 Report No.: na Not GLP, published Doc. No.: 492-021	No	N.R.
A4.2c/07	Liu, W. et al.	2010	DETERMINATION OF BROMINE AND IODINE SPECIATION IN DRINKING WATER USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY-INDUCTIVELY COUPLED PLASMA-MASS SPECTROMETRY Geostandards and Geoanalytical Research, 2010, 35 (1), 69-74 Report No.: na Not GLP, published Doc. No.: 492-022	No	N.R.
A4.3/01	Anonymous	2000	MILK AND DRIED MILK - DETERMINATION OF IODIDE CONTENT - METHOD USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY Source: ISO 14378, 2000, 1-14 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-013	No	N.R.
A4.3/01a	Sertl, D. Malone, W.	1993	LIQUID CHROMATOGRAPHIC METHOD FOR DETERMINATION OF IODINE IN MILK: COLLABORATIVE STUDY Journal of AOAC International, 76 (4), 1993, 711-719 Report No.: na Not GLP, published Doc. No.: 492-023	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A4.3/02	Rädlinger, G. Heumann, K.G.	1998	IODINE DETERMINATION IN FOOD SAMPLES USING INDUCTIVELY COUPLED PLASMA ISOTOPE DILUTION MASS SPECTROMETRY Analytical Chemistry, 1998, 70 (11), 2221-2224 Report No.: na Not GLP, published Doc. No.: 492-019	No	N.R.
A5/01	Chang, S.L. Morris, J.C.	1953	ELEMENTAL IODINE AS A DISINFECTANT FOR DRINKING WATER Source: Industrial and Engineering Chemistry, 45, 5, May 1953, 1009-1012 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-056	No	N.R.
A5 Attachment 1	Fotheringham, V.J.C.	2007	BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD Source: Evans Vanodine International PLC Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 381-017	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A5.3.1/01	Selvaggi, G. et al.	2003	THE ROLE OF IODINE IN ANTISEPSIS AND WOUND MANAGEMENT : A REAPPRAISAL Source: Acta chir belg., 2003, 103, 241-247 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-055	No	N.R.
A5.3.1/02	Spann, C.T. Taylor, S.C. Weinberg, J.M.	2003	TOPICAL ANTIMICROBIAL AGENTS IN DERMATOLOGY Source: Clinics in Dermatology, 2003, 21, 70-77 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-049	No	N.R.
A5.3.1/03	Shiraishi, T. Nakagawa, Y.	1993	REVIEW OF DISINFECTANT SUSCEPTIBILITY OF BACTERIA ISOLATED IN HOSPITAL TO COMMONLY USED DISINFECTANTS Source: Postgrad Med J, 1993, 69, 70-77 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-057	No	N.R.
A5.3.1/04	Russell, A.D. Hugo, W.B. Ayliffe, G.A.J.	1999	VIRICIDAL ACTIVITY OF BIOCIDES - ACTIVITY AGAINST HUMAN VIRUSES Source: Principles and practice of Disinfection, Preservation and Sterilization, Third Edition, pp Chapter 6: 168, 178, 193; Chapter 2: 5, 45, 46 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-048	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A5.3.1/05	Anonymous	1999	THE COMPLETE DRUG REFERENCE - IODINE Source: Martindale, Thirty-second edition, Pharmaceutical Press, 1493-1494 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-047	No	N.R.
A5.3.1/06	Anonymous	N.I.	CHEMICAL DISINFECTANTS, ANTISEPTICS AND PRESERVATIVES Source: Pharmaceutical Microbiology, Sixth Edition, 10, 201 and 219 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-046	No	N.R.
A5.3.1/07	Jeffrey, D.J.	1995	CHEMICALS USED AS DISINFECTANTS: ACTIVE INGREDIENTS AND ENHANCING ADDITIVES Source: Rev. Sci. Tech. Off. Int. Epiz., 1995, 14,1, 57-74 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-045	No	N.R.
A5.3.1/08	Anonymous	N.I.	DISINFECTANTS AND ANTISEPTICS Source: The Pharmaceutical Codex, 577+582 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-050	No	N.R.
A5.3.1/09	Russell, A.D.	1990	BACTERIAL SPORES AND CHEMICAL SPORICIDAL AGENTS Source: Clinical Microbiology Reviews, Apr. 1990, 99-119 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-058	No	N.R.
A5.3.1/10	Bruce, J.	1981	THE BACTERIAL FLORA OF IN-USE TEAT DIPS Source: Society for applied Bacteriology, 1981, 16, 177-182 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-051	No	N.R.
A5.3.1/11	Cousins, C.M.	N.I.	THE INACTIVATION OF VEGETATIVE MICRO-ORGANISMS BY CHEMICALS IN THE DAIRYING INDUSTRY Source: Inhibition and Inactivation of Vegetative Microbes, Academic Press, 13-30 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-052	No	N.R.
A5.3.1/12	Twomey, A.	1969	IODOPHORS: THEIR PHYSICAL, CHEMICAL AND BACTERICIDAL PROPERTIES, AND USE IN THE DAIRY INDUSTRY - A REVIEW Source: The Australian Journal of Dairy Technology, March 1969 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-053	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A5.3.1/13	Rubbo, D.S. Gardner, J.F.	N.I.	CHEMICAL DISINFECTANTS AND ANTISEPTICS Source: A Review of Sterilization and Disinfection, Lloyd-Luke, Chapter XIII, 143-144 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-054	No	N.R.
A5.3.1/14	Chang, S.L. Morris, J.C.	1953	ELEMENTAL IODINE AS A DISINFECTANT FOR DRINKING WATER Source: Industrial and Engineering Chemistry, 45, 5, May 1953, 1009-1012 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-056	No	N.R.
A5.3.1/15	Rasmussen, M.D. Galton, D.M. Petersson, L.G.	1991	EFFECTS OF PREMILKING TEAT PREPARATION ON SPORES OF ANAEROBES, BACTERIA, AND IODINE RESIDUES IN MILK Source: J. Dairy Sci., 1991, Vol. 74, pp. 2472-2478 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-028	No	N.R.
A5.3.1/16	Anonymous	N.I.	TECHNICAL FILE - XXX Source: ECOLAB INC, Ecolab Center, St. Paul, MN Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 381-015	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	ECOLAB
A5.3.1/17	Evans, D.H. Stuart, P. Roberts, D.H.	1977	DISINFECTION OF ANIMAL VIRUSES Source: Br. Vet. J., 1977, 133, 356-359 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-019	No	N.R.
A5.3.1/18	Anonymous	N.I.	PIG DISINFECTION PROGRAMME Source: EVANS brochure Report No.: Not applicable Not GLP; (published) Doc. No.: 392-005	No	N.R.
A5.3.1/19	Anonymous	1996	35TH ANNUAL MEETING - NATIONAL MASTITIS COUNCIL, INC.: SUMMARY OF PEER-REVIEWED PUBLICATIONS ON EFFICACY OF PREMILKING AND POSTMILKING TEAT DISINFECTANTS PUBLISHED SINCE 1980 Source: National Mastitis Council Annual Meeting Proceedings, 1996, 245-256 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-030	No	N.R.
A5.6/01	Anonymous	N.I.	VIDEO ZUR ANWENDUNG VON TEAT DIPS (U.S. VERSION) (1 CD-ROM) Source: Not indicated Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 998-005	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	ECOLAB

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A5.8/01	Anonymous	N.I.	IODINE WORLD DEMAND BY APPLICATION IN 2006 (ESTIMATION) Source: Not applicable Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 031-013	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Evans
A6.1.1/01	Anonymous	2006	HSDB DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: HSDB Database search - http://toxnet nlm nih.gov/ Report No.: Not applicable Not GLP; (published) Doc. No.: 591-004	No	N.R.
A6.1.1/02	Lewis, R.J.	1992	SAX´S DANGEROUS PROPERTIES OF INDUSTRIAL MATERIALS - IODINE Source: Sax´s Dangerous Properties of Industrial Materials, 1992,1988-1989, 8, 1-3, Report No.: Not applicable Not GLP; (published) Doc. No.: 592-054	No	N.R.
A6.1.1/03	Anonymous	2006	IODINE - IDLH DOCUMENTATION - CAS NO. [7553562] Source: From Website: http://www.cdc.gov/NIOSH/idlh/7553562 html Report No.: Not applicable Not GLP; (published) Doc. No.: 592-035	No	N.R.
A6.1.1/04	de Angelis, L.	1979	IOPAMIDOL - RADIOPAQUE CONTRAST MEDIUM Source: Drugs of the Future, Vol. IV, No. 12, 1979, 876-881 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-018	No	N.R.
A6.1.1/05	Anonymous	2001	RTECS DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: RTECS Database search Report No.: Not applicable Not GLP; (published) Doc. No.: 591-002	No	N.R.
A6.1.1/06	Kishiyama, J.	2005	SUMMARY OF TOXICOLOGY DATA - IODINE Source: California Environmental Protection Agency Department of Pesticide Regulation, Medical Toxicology Branch, USA Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-013	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.1.2/01	Anonymous	2006	ECB - ESIS DATABASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: ECB - ESIS (European chemical Substances Information System) Report No.: Not applicable Not GLP; (published) Doc. No.: 991-003	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.1.3/01	Anonymous	2006	ECB - ESIS DATABASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: ECB - ESIS (European chemical Substances Information System) Report No.: Not applicable Not GLP; (published) Doc. No.: 991-003	No	N.R.
A6.1.3/02	Lewis, R.J.	1992	SAX´S DANGEROUS PROPERTIES OF INDUSTRIAL MATERIALS - IODINE Source: Sax´s Dangerous Properties of Industrial Materials, 1992,1988-1989, 8, 1-3, Report No.: Not applicable Not GLP; (published) Doc. No.: 592-054	No	N.R.
A6.1.3/03	Anonymous	2001	RTECS DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: RTECS Database search Report No.: Not applicable Not GLP; (published) Doc. No.: 591-002	No	N.R.
A6.1.3/04	Flury, F. Zernik, F.	1931	SCHÄDLICHE GASE - DÄMPFE, NEBEL, RAUCH- UND STAUBARTEN - JOD Source: Schädliche Gase - Dämpfe, Nebel, Rauch- und Staubarten, 1931, 123-124 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-068	No	N.R.
A6.1.3/05	Anonymous	2001	IODINE - LITERATURE SEARCH - VARIOUS INFORMATION ON IODINE Source: Literature search A:\f[16].htm (local) - no further information available Report No.: Not applicable Not GLP; (published) Doc. No.: 091-001	No	N.R.
A6.1.3/06	Anonymous	2006	IODINE - IDLH DOCUMENTATION - CAS NO. [7553562] Source: From Website: http://www.cdc.gov/NIOSH/idlh/7553562 html Report No.: Not applicable Not GLP; (published) Doc. No.: 592-035	No	N.R.
A6.1.3/07	Anonymous	1975	GESUNDHEITSSCHÄDLICHE ARBEITSSTOFFE - TOXIKOLOGISCH-ARBEITSMEDIZINISCHE BEGRÜNDUNG VON MAK-WERTEN: JOD Source: DFG Evaluation for MAK Values; The MAK-Collection for Occupational Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, 1975, ISBN 3-527-19030-9 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-051	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.1.3/08	Anonymous	2006	HSDB DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: HSDB Database search - http://toxnet nlm nih.gov/ Report No.: Not applicable Not GLP; (published) Doc. No.: 591-004	No	N.R.
A6.1.4.1/01	Anonymous	2006	HSDB DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: HSDB Database search - http://toxnet nlm nih.gov/ Report No.: Not applicable Not GLP; (published) Doc. No.: 591-004	No	N.R.
A6.1.4.1/02	Anonymous	2006	WHO/FAO JOINT EXPERT COMMITTEE ON FOOD ADDITIVES (1989) TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS Source: WHO Food Additives Series, No. 24, Geneva: World Health Organization http://www.inchem.org/documents/pims/pharm/iodine htm Report No.: Not applicable Not GLP; (published) Doc. No.: 591-008	No	N.R.
A6.1.4.1/03	Anonymous	2003	OCCUPATIONAL HEALTH AND FIRST AID Source: GESTIS Data Base on hazardous substances of the German institutions for statuory accident insurance and prevention (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-050	No	N.R.
A6.1.4.1/04	Anonymous	2006	ECB - ESIS DATABASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: ECB - ESIS (European chemical Substances Information System) Report No.: Not applicable Not GLP; (published) Doc. No.: 991-003	No	N.R.
A6.1.4.2/01	Anonymous	2006	HSDB DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: HSDB Database search - http://toxnet nlm nih.gov/ Report No.: Not applicable Not GLP; (published) Doc. No.: 591-004	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.1.4.2/02	Anonymous	2006	WHO/FAO JOINT EXPERT COMMITTEE ON FOOD ADDITIVES (1989) TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS Source: WHO Food Additives Series, No. 24, Geneva: World Health Organization http://www.inchem.org/documents/pims/pharm/iodine htm Report No.: Not applicable Not GLP; (published) Doc. No.: 591-008	No	N.R.
A6.1.4.2/03	Anonymous	2003	OCCUPATIONAL HEALTH AND FIRST AID Source: GESTIS Data Base on hazardous substances of the German institutions for statuory accident insurance and prevention (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-050	No	N.R.
A6.1.4.2/04	Anonymous	2006	ECB - ESIS DATABASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: ECB - ESIS (European chemical Substances Information System) Report No.: Not applicable Not GLP; (published) Doc. No.: 991-003	No	N.R.
A6.1.4.2/05	Lee, S.K. Zhai, H. Maibach, H.I.	2005	ALLERGIC CONTACT DERMATITIS FROM IODINE PREPARATIONS - A CONUNDRUM Source: Contact Dermatitis, 2005, 52, 184-187 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-046	No	N.R.
A6.1.5/01	NN	2002	IODINE - SKIN SENSITISATION IN THE GUINEA PIG - MAGNUSSON AND KLIGMAN MAXIMISATION METHOD Source: NN Report No.: XX GLP; (unpublished) Doc. No.: 567-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.2/01	Anonymous	2002	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	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.2/02	Anonymous	2006	WHO/FAO JOINT EXPERT COMMITTEE ON FOOD ADDITIVES (1989) TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS Source: WHO Food Additives Series, No. 24, Geneva: World Health Organization http://www.inchem.org/documents/pims/pharm/iodine htm Report No.: Not applicable Not GLP; (published) Doc. No.: 591-008	No	N.R.
A6.2/03	Anonymous	2006	WHO/FAO JOINT EXPERT COMMITTEE ON FOOD ADDITIVES (1989) TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS Source: WHO Food Additives Series, No. 24, Geneva: World Health Organization http://www.inchem.org/documents/pims/pharm/iodine htm Report No.: Not applicable Not GLP; (published) Doc. No.: 591-008	No	N.R.
A6.2/04	Anonymous	2003	OCCUPATIONAL HEALTH AND FIRST AID Source: GESTIS Data Base on hazardous substances of the German institutions for statuory accident insurance and prevention (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-050	No	N.R.
A6.2/05	Forth, W. Henschler, D. Rummel, W.	1985	SCHILDDRÜSENHORMONE UND THYREOSTATIKA Source: Allgemeine und spezielle Pharmakologie und Toxikologie, 1985, 4th edition, 389-396 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-052	No	N.R.
A6.2/06	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.2/07	Anonymous	1975	GESUNDHEITSSCHÄDLICHE ARBEITSSTOFFE - TOXIKOLOGISCH-ARBEITSMEDIZINISCHE BEGRÜNDUNG VON MAK-WERTEN: JOD Source: DFG Evaluation for MAK Values; The MAK-Collection for Occupational Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, 1975, ISBN 3-527-19030-9 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-051	No	N.R.
A6.2/08	Anonymous	2001	DIETARY REFERENCE INTAKES FOR VITAMIN A, VITAMIN K, ARSENIC, BORON, CHROMIUM, COPPER, IODINE, IRON, MANGANESE, MOLYBDENUM, NICKEL, SILICON, VANADIUM AND ZINC - A REPORT OF THE PANEL OF MICRONUTRIENTS Source: Food and Nutrition Board, Institute of Medicine, National Academy Press, Washingtion, D.C., 2002 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-032	No	N.R.
A6.2/09	Köhl, W. Kirbach, I.	2006	EXPERT EVALUATION - PROVIDED FOR DOSSIER PREPARATION IN ACCORDANCE WITH DIRECTIVE 98/8/EC - ADME OF IODINE Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 519-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.2/10	de Ligt, R.A.F.	2009	IN VITRO PERCUTANEOUS ABSORPTION OF TOTAL IODINE FROM TWO BIOCIDE FORMULATIONS THROUGH HUMAN SKIN MEMBRANES TNO, Nutrition and Food Research, Zeist, The Netherlands Report No.: V8124 031.13710 GLP, unpublished Doc. No.: 511-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.3.1/01	Gardner, D.F. Centor, R.M. Utiger, R.D.	1988	EFFECTS OF LOW DOSE ORAL IODIDE SUPPLEMENTATION ON THYROID FUNCTION IN NORMAL MEN Source: Clinical Endocrinology, 1988, 28, 283-288 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-036	No	N.R.
A6.3.1/02	Anonymous	2001	DIETARY REFERENCE INTAKES FOR VITAMIN A, VITAMIN K, ARSENIC, BORON, CHROMIUM, COPPER, IODINE, IRON, MANGANESE, MOLYBDENUM, NICKEL, SILICON, VANADIUM AND ZINC - A REPORT OF THE PANEL OF MICRONUTRIENTS Source: Food and Nutrition Board, Institute of Medicine, National Academy Press, Washingtion, D.C., 2002 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-032	No	N.R.
A6.3.1/03	Anonymous	2002	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	No	N.R.
A6.3.1/04	Domke, A. et al.	2006	USE OF MINERALS IN FOODS - TOXICOLOGICAL AND NUTRITIONAL-PHYSIOLOGICAL ASPECTS Source: BfR Wissenschaft, 2006, ISSN 1614-3795 ISBN 3-938163-11-9 (http://www.bfr.bund.de/cm/238/use_of_minerals_in_foods.pdf) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-080	No	N.R.
A6.3.1/05	Paul, T. et al.	1988	THE EFFECT OF SMALL INCREASES IN DIETARY IODINE ON THYROID FUNCTION IN EUTHYROID SUBJECTS Source: Metabolism, February 1988, 37, 2, 121-124 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-037	No	N.R.
A6.4.1/01	Sherer, T.T. Thrall, K.D. Bull, R.J.	1991	COMPARISON OF TOXICITY INDUCED BY IODINE AND IODIDE IN MALE AND FEMALE RATS Source: Journal of Toxicology and Environmental Health, Vol. 32, pp. 89-101, 1991 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-027	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.6.1/01	Thompson, P.W.	2002	IODINE - REVERSE MUTATION ASSAY "AMES TEST" USING SALMONELLA TYPHIMURIUM Source: Safepharm Laboratories Limited, Derby Report No.: 1580/003 GLP; (unpublished) Doc. No.: 557-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.2/01	Wright, N.P.	2002	IODINE - CHROMOSOME ABERRATION TEST IN HUMAN LYMPHOCYTES IN VITRO Source: Safepharm Laboratories Limited, Derby Report No.: 1580/002 GLP; (unpublished) Doc. No.: 557-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.3/01	Kessler, F.K.	1980	ASSESSMENT OF SOMATOGENOTOXICITY OF POVIDONE-IODINE USING TWO IN VITRO ASSAYS Source: Journal of Environmental Pathology and Toxicology, 4-2,3:327-335 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-019	No	N.R.
A6.6.3/02	Kishiyama, J.	2005	SUMMARY OF TOXICOLOGY DATA - IODINE Source: California Environmental Protection Agency Department of Pesticide Regulation, Medical Toxicology Branch, USA Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-013	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.3/03	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.3/04	Langman, M.	2003	SAFE UPPER LEVELS FOR VITAMINS AND MINERALS - EXPERT GROUP ON VITAMINS AND MINERALS Source: Published by Food Standards Agency, May 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.
A6.6.4/01	Merkle, J. Zeller, H.	1979	ABSENCE OF POVIDONE-IODINE-INDUCED MUTAGENICITY IN MICE AND HAMSTERS Source: Journal of Pharmaceutical Sciences, Vol. 68, No. 1, January 1979, pp. 100-102 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-017	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.6.4/02	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.4/03	Langman, M.	2003	SAFE UPPER LEVELS FOR VITAMINS AND MINERALS - EXPERT GROUP ON VITAMINS AND MINERALS Source: Published by Food Standards Agency, May 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.
A6.6.5.1/01	Merkle, J. Zeller, H.	1979	ABSENCE OF POVIDONE-IODINE-INDUCED MUTAGENICITY IN MICE AND HAMSTERS Source: Journal of Pharmaceutical Sciences, Vol. 68, No. 1, January 1979, pp. 100-102 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-017	No	N.R.
A6.6.5.1/02	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.5.1/03	Langman, M.	2003	SAFE UPPER LEVELS FOR VITAMINS AND MINERALS - EXPERT GROUP ON VITAMINS AND MINERALS Source: Published by Food Standards Agency, May 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.
A6.6.6/01	Merkle, J. Zeller, H.	1979	ABSENCE OF POVIDONE-IODINE-INDUCED MUTAGENICITY IN MICE AND HAMSTERS Source: Journal of Pharmaceutical Sciences, Vol. 68, No. 1, January 1979, pp. 100-102 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-017	No	N.R.
A6.6.6/02	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.6/03	Langman, M.	2003	SAFE UPPER LEVELS FOR VITAMINS AND MINERALS - EXPERT GROUP ON VITAMINS AND MINERALS Source: Published by Food Standards Agency, May 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.6.7/01	Kessler, F.K.	1980	ASSESSMENT OF SOMATOGENOTOXICITY OF POVIDONE-IODINE USING TWO IN VITRO ASSAYS Source: Journal of Environmental Pathology and Toxicology, 4-2,3:327-335 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-019	No	N.R.
A6.6.7/02	Kishiyama, J.	2005	SUMMARY OF TOXICOLOGY DATA - IODINE Source: California Environmental Protection Agency Department of Pesticide Regulation, Medical Toxicology Branch, USA Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-013	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.7/03	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.6.7/04	Langman, M.	2003	SAFE UPPER LEVELS FOR VITAMINS AND MINERALS - EXPERT GROUP ON VITAMINS AND MINERALS Source: Published by Food Standards Agency, May 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.
A6.7/01	Takegawa, K. et al.	1998	INDUCTION OF SQUAMOUS CELL CARCINOMAS IN THE SALIVARY GLANDS OF RATS BY POTASSIUM IODIDE Source: Jpn. J. Cancer Res., February 1998, 89, 105-109 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-082	No	N.R.
A6.7/02	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.8.1/01	Siegemund, B. Weyers, W.	1987	TERATOLOGISCHE UNTERSUCHUNGEN EINES NIEDERMOLEKULAREN POLYVINYLPYRROLIDON-JOD-KOMPLEXES AN KANINCHEN Source: Arzneim.-Forsch./ Drug Res., 1987, 37 (I), Nr. 3, 340-341 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-066	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.8.1/02	Ammerman, C.B. et al.	1964	REPRODUCTION AND LACTATION IN RATS FED EXCESSIVE IODINE Source: J. Nutrition, Vol. 84, 1964, pp. 107-112 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-011	No	N.R.
A6.8.2/01	Ammerman, C.B. et al.	1964	REPRODUCTION AND LACTATION IN RATS FED EXCESSIVE IODINE Source: J. Nutrition, Vol. 84, 1964, pp. 107-112 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-011	No	N.R.
A6.8.2/02	Ammerman, C.B. et al.	1964	REPRODUCTION AND LACTATION IN RATS FED EXCESSIVE IODINE Source: J. Nutrition, Vol. 84, 1964, pp. 107-112 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-011	No	N.R.
A6.8.2/03	Ammerman, C.B. et al.	1964	REPRODUCTION AND LACTATION IN RATS FED EXCESSIVE IODINE Source: J. Nutrition, Vol. 84, 1964, pp. 107-112 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-011	No	N.R.
A6.9.1/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.10/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.1/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.2/01	Anonymous	2002	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	No	N.R.
A6.12.2/02	Moore, M.	1938	THE INGESTION OF IODINE AS A METHOD OF ATTEMPTED SUICIDE Source: The New England Journal of Medicine, Vol. 219, No. 11, pp. 383-388 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-007	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.12.2/03	Anonymous	2001	RTECS DATA BASE SEARCH - IODINE - CAS NO. [7553-56-2] Source: RTECS Database search Report No.: Not applicable Not GLP; (published) Doc. No.: 591-002	No	N.R.
A6.12.2/04	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.2/05	Anonymous	2006	WHO/FAO JOINT EXPERT COMMITTEE ON FOOD ADDITIVES (1989) TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS Source: WHO Food Additives Series, No. 24, Geneva: World Health Organization http://www.inchem.org/documents/pims/pharm/iodine htm Report No.: Not applicable Not GLP; (published) Doc. No.: 591-008	No	N.R.
A6.12.2/06	Anonymous	2003	OCCUPATIONAL HEALTH AND FIRST AID Source: GESTIS Data Base on hazardous substances of the German institutions for statuory accident insurance and prevention (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-050	No	N.R.
A6.12.2/07	Kishiyama, J.	2005	SUMMARY OF TOXICOLOGY DATA - IODINE Source: California Environmental Protection Agency Department of Pesticide Regulation, Medical Toxicology Branch, USA Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-013	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.3/01	Matthies, W.	2006	SAFETY UPDATE REPORT - XXX, SOLUTION AS A TEAT DIP Source: ECOLAB GmbH & Co. OHG, Düsseldorf, Germany Report No.: BS0600007-139 Not GLP; (unpublished) Doc. No.: 581-012	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	ECOLAB
A6.12.4/01	Anonymous	2002	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	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.12.4/02	Domke, A. et al.	2006	USE OF MINERALS IN FOODS - TOXICOLOGICAL AND NUTRITIONAL-PHYSIOLOGICAL ASPECTS Source: BfR Wissenschaft, 2006, ISSN 1614-3795 ISBN 3-938163-11-9 (http://www.bfr.bund.de/cm/238/use_of_minerals_in_foods.pdf) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-080	No	N.R.
A6.12.4/03	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.5/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.7/01	Anonymous	2003	OCCUPATIONAL HEALTH AND FIRST AID Source: GESTIS Data Base on hazardous substances of the German institutions for statuory accident insurance and prevention (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-050	No	N.R.
A6.12.7/02	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.12.8/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.13/01	Anonymous	1998	FAO/WHO (1998) CHAPTER 16: IODINE. IN: VITAMIN AND MINERAL REQUIREMENTS IN HUMAN NUTRITION - SECOND EDITION Source: Joint FAO/WHO Expert Consultation on Human Vitamin and Mineral Requirements, 21-30 September 1998, pp. 303-317, Bangkok, Thailand Report No.: Not applicable Not GLP; (published) Doc. No.: 692-033	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.13/02	Anonymous	2002	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	No	N.R.
A6.13/03	Anonymous	1980	MINERAL TOLERANCE OF DOMESTIC ANIMALS Source: National Research Council, 1980, iii-vi and 227-235 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-020	No	N.R.
A6.13/04	Silva, C.A.M. et al.	1987	CONSEQUENCE OF EXCESS IODINE SUPPLY IN A THOROUGHBRED STUD IN SOUTHERN BRAZIL Source: J. Reprod. Fert., Suppl. 35, 1987, 529-533 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-045	No	N.R.
A6.13/05	Grimminger, S.P.	2005	ZUM IODBEDARF UND ZUR IODVERSORGUNG DER HAUS- UND NUTZTIERE UND DES MENSCHEN Source: From Website: edoc.ub.uni-muenchen.de Report No.: Not applicable Not GLP; (published) Doc. No.: 592-040	No	N.R.
A6.13/06	Johanson, K.J.	2000	IODINE IN SOIL Source: not indicated Report No.: TR-00-21 Not GLP; (unpublished) Doc. No.: 781-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.13/07	Arrington, L.R. et al.	1965	EFFECTS OF EXCESS DIETARY IODINE UPON RABBITS, HAMSTERS, RATS AND SWINE Source: J. Nutrition, Vol. 87, 1965, pp. 394-398 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-012	No	N.R.
A6.14/01	Anonymous	1998	FAO/WHO (1998) CHAPTER 16: IODINE. IN: VITAMIN AND MINERAL REQUIREMENTS IN HUMAN NUTRITION - SECOND EDITION Source: Joint FAO/WHO Expert Consultation on Human Vitamin and Mineral Requirements, 21-30 September 1998, pp. 303-317, Bangkok, Thailand Report No.: Not applicable Not GLP; (published) Doc. No.: 692-033	No	N.R.
A6.14/02	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.14/03	Anonymous	2002	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	No	N.R.
A6.14/04	Anonymous	2006	WHO/FAO JOINT EXPERT COMMITTEE ON FOOD ADDITIVES (1989) TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS Source: WHO Food Additives Series, No. 24, Geneva: World Health Organization http://www.inchem.org/documents/pims/pharm/iodine htm Report No.: Not applicable Not GLP; (published) Doc. No.: 591-008	No	N.R.
A6.14/05	Carswell, F. Kerr, M. M. Hutchison, J.H.	1970	CONGENITAL GOITRE AND HYPOTHYROIDISM PRODUCED BY MATERNAL INGESTION OF IODIDES Source: The Lancet, 1970, 1241-1243 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-042	No	N.R.
A6.14/06	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.14/07	Danziger, Y. Pertzelan, A. Mimouni, M.	1987	TRANSIENT CONGENITAL HYPOTHYROIDISM AFTER TOPICAL IODINE IN PREGNANCY AND LACTATION Source: Archives of Disease in Childhood, 1987, 62, 295-296 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-048	No	N.R.
A6.14/08	Anonymous	2001	DIETARY REFERENCE INTAKES FOR VITAMIN A, VITAMIN K, ARSENIC, BORON, CHROMIUM, COPPER, IODINE, IRON, MANGANESE, MOLYBDENUM, NICKEL, SILICON, VANADIUM AND ZINC - A REPORT OF THE PANEL OF MICRONUTRIENTS Source: Food and Nutrition Board, Institute of Medicine, National Academy Press, Washingtion, D.C., 2002 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-032	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.14/09	Kurt, T.L. et al.	1996	FATAL IATROGENIC IODINE TOXICITY IN A NINE-WEEK-OLD INFANT Source: Clinical Toxicology, 34(2), 1996, 231-234 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-044	No	N.R.
A6.14/10	Means, L.J. Rescorla, F.J. Grosfeld, J.L.	1990	IODINE TOXICITY - AN UNUSUAL CAUSE OF CARDIOVASCULAR COLLAPSE DURING ANESTHESIA IN AN INFANT WITH HIRSCHSPRUNG´S DISEASE Source: Journal of Pediatric Surgery, 25, 12, 1990, 1278-1279 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-047	No	N.R.
A6.14/11	Anonymous	2001	FAO/WHO (2001) CHAPTER 12:IODINE. IN: HUMAN VITAMIN AND MINERAL REQUIREMENTS. REPORT Source: Food and Nutrition Division, FAO Rome, , FAO/WHO 2001, Chapter 12, pp. 181-194 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-035	No	N.R.
A6.14/12	Stockton, L.K. Thomas, Jr., W.C.	1978	ABSENCE OF NEONATAL GOITER DURING MATERIAL USE OF IODINATED WATER (ABSTRACT) Source: Clinical Research, 26, 536A This study has been published as an abstract only! Report No.: Not applicable Not GLP; (published) Doc. No.: 592-069	No	N.R.
A6.14/13	Anonymous	2003	IODINE IN DRINKING-WATER - BACKGROUND DOCUMENT FOR DEVELOPMENT OF WHO GUIDELINES FOR DRINKING-WATER QUALITY Source: Guidelines for drinking-water quality, 2nd ed. Vol. 2, Health criteria and other supporting information, World Health Organization, Geneva, 1996 Report No.: WHO/SDE/WSH/03.04/46 Not GLP; (published) Doc. No.: 592-032	No	N.R.
A6.14/14	Freund, G. et al.	1966	EFFECT OF IODINATED WATER SUPPLIES ON THYROID FUNCTION Source: Not applicable Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 592-085	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.15/01	Heuwieser, W.	N.I.	INVESTIGATION OF THE EFFICACY OF DIFFERENT DIPPING PROCEDURES IN THE PROPHYLAXIS OF MASTITIS IN LACTATING DAIRY COWS - STUDY PHASE 1 - EXAMINATION OF THE SAFETY OF AN IODINE-CONTAINING DIPPING AGENT FOR PREDIPPING - INTERIM REPORT Source: University of Berlin Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 336-03024	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	ECOLAB
A6.15/02	Falkenberg, U. et al.	2002	EFFECT OF PREDIPPING WITH A IODOPHOR TEAT DISINFECTANT ON IODINE CONTENT OF MILK Source: Milchwissenschaft 57, 11/12, 2002 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-034	No	N.R.
A6.15/03	Iwarsson, K. Ekman, L.	N.I.	IODOPHOR TEAT DIPPING AND THE IODINE CONCENTRATION IN MILK Source: Nord. Vet.-Med. 1974, Vol. 26, pp. 31-38 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-002	No	N.R.
A6.15/04	Cantor,A. Most, S.	1976	MILK IODIDES - EFFECT OF IODOPHOR TEAT DIPPING AND UDDER WASHING, AND DIETARY IODIDE SUPPLEMENTATION Source: J. Milk Food Technol, Vol. 39, No. 8, 1976, 554-560 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-009	No	N.R.
A6.15/05	Terplan, G. Grove, H.H.	1979	RÜCKSTÄNDE VON DIP-PRÄPARATEN IN DER MILCH Source: Deutsche Molkerei-Zeitung (München), 1979, 362-363 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-011	No	N.R.
A6.15/06	Dunsmore, D.G. Nuzum, C. Dettmann, B.	1977	IODOPHORS AND IODINE IN DAIRY PRODUCTS - 3. TEAT DIPPING Source: Australian Journal of Dairy Technology, March 1977 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-018	No	N.R.
A6.15/07	Schumacher, E.	1975	DIE BELASTUNG DER MILCH MIT JOD UND NONXINOL BEIM ZITZENTAUCHEN MIT LORASOL® CCT Source: Milchwissenschaft, 1975, 30(6), 333-336 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-008	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A6.15/08	Galton, D.M. Petersson, L.G. Erb, H.N.	1986	MILK IODINE RESIDUES IN HERDS PRACTICING IODOPHOR PREMILKING TEAT DISINFECTION Source: J. Dairy Sci., Vol. 69, 1986, pp. 267-271 Report No.: Not applicable Not GLP; (published) Doc. No.: 692-026	No	N.R.
A6.15/09	Langman, M.	2003	SAFE UPPER LEVELS FOR VITAMINS AND MINERALS - EXPERT GROUP ON VITAMINS AND MINERALS Source: Published by Food Standards Agency, May 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.
A6.15/10	Domke, A. et al.	2006	USE OF MINERALS IN FOODS - TOXICOLOGICAL AND NUTRITIONAL-PHYSIOLOGICAL ASPECTS Source: BfR Wissenschaft, 2006, ISSN 1614-3795 ISBN 3-938163-11-9 (http://www.bfr.bund.de/cm/238/use_of_minerals_in_foods.pdf) Report No.: Not applicable Not GLP; (published) Doc. No.: 592-080	No	N.R.
A6.15/11	Anonymous	2002	EXPERT GROUP ON VITAMINS AND MINERALS - REVISED REVIEW OF IODINE Source: Not applicable Report No.: EVM/00/06.REVISEDAUG2002 Not GLP; (unpublished) Doc. No.: 681-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A6.15/12	Anonymous	2000	MAFF UK - IODINE IN MILK (SHEET 198) Source: MAFF Surveillance Information Sheet - 23 March 2000 Report No.: Sheet 198 Not GLP; (published) Doc. No.: 692-031	No	N.R.
A7.1.1.1.1/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.1.1.1.1/02	Edmonds, J.S. Morita, M.	1998	THE DETERMINATION OF IODINE SPECIES IN ENVIRONMENTAL AND BIOLOGICAL SAMPLES Source: Pure & Appl. Chem., 1998, 70(8), 1567-1584 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-003	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.1.1.1.1/03	Anonymous	1995	CD RÖMPP CHEMIE LEXIKON - IOD Source: CE Römpp Chemie Lexikon, Version 1.0, 1995 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-006	No	N.R.
A7.1.1.1.1/04	Kaplan, D.J. et al.	1999	GEOCHEMICAL DATA PACKAGE FOR THE HANFORD IMMOBILIZED LOW-ACTIVITY TANK WASTE PERFORMANCE ASSESSMENT (ILAW-PA) Source: http://www.hanford.gov/docs/gpp/fieldwork/ilaw/PNL13037.pdf Report No.: HNF-5636 Rev. 0 PNNL-13037 Not GLP; (published) Doc. No.: 792-003	No	N.R.
A7.1.1.1.1/05	Nagy, K. Körtvélyesi, T. Nagypál, I.	2003	IODINE HYDROLYSIS EQUILIBRIUM Source: Journal of Solution Chemistry, 32, 5, May 2003, 385-393 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-005	No	N.R.
A7.1.1.1.1/06	Gottardi, W.	1978	WÄSSRIGE JODLÖSUNGEN ALS DESINFEKTIONSMITTEL - ZUSAMMENSETZUNG STABILITÄT, VERGLEICH MIT CHLOR- UND BROMLÖSUNGEN Source: Zbl. Bakt. Hyg., I. Abt. Orig. B 167, 206-215, 1978 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-004	No	N.R.
A7.1.1.1.1/07	Gottardi, W.	1981	DIE BILDUNG VON JODAT ALS URSACHE DER WIRKUNGSABNAHME JODHALTIGER DESINFEKTIONSMITTEL Source: Zbl. Bakt. Hyg., I. Abt. Orig. B 172, 1981, 498-507 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-043	No	N.R.
A7.1.1.1.1/08	Gottardi, W.	1991	DISINFECTION, STERILIZATION, AND PRESERVATION - CHAPTER 8 - IODINE AND IODINE COMPOUNDS Source: Disinfection, Sterilization, and Preservation, 4, 1991, 152-165 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-044	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.1.1.1.1/09	Gottardi, W.	1998	REDOX-POTENTIOMETRIC/TITRIMETRIC ANALYSIS OF AQUEOUS IODINE SOLUTIONS Source: Fresenius J Anal Chem, 1998, 362, 263-269 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-012	No	N.R.
A7.1.1.1.1/10	Gottardi, W.	1999	IODINE AND DISINFECTION - THEORETICAL STUDY ON MODE OF ACTION, EFFICIENCY, STABILITY, AND ANALYTICAL ASPECTS IN THE AQUEOUS SYSTEM Source: Arch. Pharm. Pharm. Med. Chem. 332, 1999, 151-157 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-003	No	N.R.
A7.1.1.1.1/11	Lee, S.K. Zhai, H. Maibach, H.I.	2005	ALLERGIC CONTACT DERMATITIS FROM IODINE PREPARATIONS - A CONUNDRUM Source: Contact Dermatitis, 2005, 52, 184-187 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-046	No	N.R.
A7.1.1.1.1/12	Palmer, D.A. Ramette, R.W. Mesmer, R.E.	1984	POTENTIOMETRIC STUDIES OF THE THERMODYNAMICS OF IODINE DISPROPORTIONATION FROM 4 TO 209°C Source: Journal of Solution Chemistry, 13, 10, 1984 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-006	No	N.R.
A7.1.1.1.1/13	Köhl, W. Kirbach, I.	2007	AQUEOUS SPECIATION OF IODINE Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 181-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.1.1.1.2/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.1.1.1.2/02	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.1.1.1.2/03	Truesdale, V.W.	2007	ON THE FEASIBILITY OF SOME PHOTOCHEMICAL REACTIONS OF IODIDE IN SEAWATER Source: Marine Chemistry, 2007, 104 (3-4), 266-281 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-013	No	N.R.
A7.1.1.2.3/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.1.1.2.3/02	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.1.2.2.1/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.1.2.2.1/02	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.1.3/01	O´Connor, B.J. Mullee, D.M.	2002	IODINE - DETERMINATION OF SOIL ADSORPTION COEFFICIENT Source: Safepharm Laboratories Limited, Derby Report No.: 1580/006 GLP; (unpublished) Doc. No.: 731-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.2.1/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.2.1/02	Johanson, K.J.	2000	IODINE IN SOIL Source: not indicated Report No.: TR-00-21 Not GLP; (unpublished) Doc. No.: 781-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.2.1/03	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.2.3/01	O´Connor, B.J. Mullee, D.M.	2002	IODINE - DETERMINATION OF SOIL ADSORPTION COEFFICIENT Source: Safepharm Laboratories Limited, Derby Report No.: 1580/006 GLP; (unpublished) Doc. No.: 731-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.3.1/01	Saiz-Lopez, A. et al.	2004	ABSOLUTE ABSORPTION CROSS-SECTION AND PHOTOLYSIS RATE OF I2 Source: Atmos. Chem. Phys. Discuss., 4, 2379-2403, 2004 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-007	No	N.R.
A7.3.2/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.3.2/02	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.4.1.1/01	Laverock, M.J. Stephenson, M. Macdonald, C.R.	1995	TOXICITY OF IODINE, IODIDE, AND IODATE TO DAPHNIA MAGNA AND RAINBOW TROUT (ONCORHYNCHUS MYKISS) Source: Arch. Environ. Contam. Toxicol., Vol. 29, pp. 344-350, 1995 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-002	No	N.R.
A7.4.1.2/01	Laverock, M.J. Stephenson, M. Macdonald, C.R.	1995	TOXICITY OF IODINE, IODIDE, AND IODATE TO DAPHNIA MAGNA AND RAINBOW TROUT (ONCORHYNCHUS MYKISS) Source: Arch. Environ. Contam. Toxicol., Vol. 29, pp. 344-350, 1995 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-002	No	N.R.
A7.4.1.3/01	Mead, C. Mullee, D.M.	2002	IODINE - ALGAL INHIBITION TEST Source: Safepharm Laboratories Limited, Derby Report No.: 1580/004 GLP; (unpublished) Doc. No.: 823-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.4.1.4/01	Mead, C.	2002	IODINE - ASSESSMENT OF THE INHIBITORY EFFECT ON THE RESPIRATION OF ACTIVATED SEWAGE SLUDGE Source: Safepharm Laboratories Limited, Derby Report No.: 1580/005 GLP; (unpublished) Doc. No.: 842-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.4.2/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.4.2/02	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.5.1/01	Knoch, E.	2009	IODINE - DETERMINATION OF IODINE IN SOILS SGS Institut Fresenius GmbH, Taunusstein, Germany Report No.: IF-09/01448579 GLP, unpublished Doc. No.: 434-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.5.1.1/01	Schulz, L.	2009	IODINE - EFFECTS ON THE ACTIVITY OF SOIL MICROFLORA (NITROGEN AND CARBON TRANSFORMATION TESTS) BioChem agrar GmbH, Gerichshain, Germany Report No.: 09 10 48 024 C/N GLP, unpublished Doc. No.: 841-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.5.1.2/01	Friedrich, S.	2009	ACUTE TOXICITY OF IODINE TO THE EARTHWORM EISENIA FETIDA BioChem agrar GmbH, Gerichshain, Germany Report No.: 09 10 48 022 S GLP, unpublished Doc. No.: 833-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.5.1.3/01	Friedrich, S.	2009	EFFECTS OF IODINE ON SEEDLING EMERGENCE AND SEEDLING GROWTH OF NON-TARGET TERRESTRIAL PLANTS BioChem agrar GmbH, Gerichshain, Germany Report No.: 09 10 48 010 S GLP, unpublished Doc. No.: 851-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.5.5/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.5.5/02	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.6/01	Anonymous	2004	TOXICOLOGICAL PROFILE FOR IODINE Source: U.S. Department of Health and Human Services Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 581-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.6/02	Merke, F.	1965	DIE EISZEIT ALS PRIMORDIALE URSACHE DES ENDEMISCHEN KROPFES Source: Schweizerische Medizinische Wochenschrift, 1965, 36, 1183 - 1192 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-007	No	N.R.
A7.6/03	Johanson, K.J.	2000	IODINE IN SOIL Source: not indicated Report No.: TR-00-21 Not GLP; (unpublished) Doc. No.: 781-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A7.6/04	Anonymous	1998	CARENCE EN IODE - RAPPORT DU SECRÉTATIAT SOUMIS AU CONSEIL EXÉCUTIF POUR INFORMATION Source: Organisation Mondiale De La Sante, 1998, EB103/27, 1- 4 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-084	No	N.R.
A7.6/05	Anonymous	N.I.	IPCC/TEAP SPECIAL REPORT - SAFEGUARDING THE OZONE LAYER AND THE GLOBAL CLIMATE SYSTEM - ISSUES RELATED TO HYDROFLUORCARBONAS AND PERFLUOROCARBONS Source: WMO Report No.: Not applicable Not GLP; (published) Doc. No.: 792-008	No	N.R.
A7.6/06	Andrady, A. et. al.	2005	ENVIRONMENTAL EFFECTS OF OZONE DEPLETION AND ITS INTERACTIONS WITH CLIMATE CHANGE - PROGRESS REPORT, 2005 Source: Photochem. Photobiol. Sci., 2006, 5, 13-24 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-009	No	N.R.

Section No./ Reference No.	Author(s)	Year	Title Source (laboratory) Report No. GLP; (un)published Doc. No.	Data protection (Yes / No)	Owner
A7.6/07	Anonymous	2006	IODINE - IDLH DOCUMENTATION - CAS NO. [7553562] Source: From Website: http://www.cdc.gov/NIOSH/idlh/7553562 html Report No.: Not applicable Not GLP; (published) Doc. No.: 592-035	No	N.R.
A7.6/08	Yuita, K.	1994	OVERVIEW AND DYNAMICS OF IODINE AND BROMINE IN THE ENVIRONMENT Source: JARQ, 1994, 28, 90-99 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-010	No	N.R.
A7.6/09	Kocher, D.C.	1981	ABSTRACT - KOCHER, D.C. - 1981 Source: Abstract - Kocher, D.C. 1981 Report No.: IAEA-SM-257/56; CONF-810722-7 Not GLP; (published) Doc. No.: 792-011	No	N.R.
A7.6/10	Krone, C. Kirbach, I.	2007	EXPERT EVALUATION - OCCURRENCE, FATE AND BEHAVIOR OF STABLE IODINE 127I IN THE ENVIRONMENT INCLUDING ITS GEOCHEMICAL AND BIOCHEMICAL CIRCULATION AND POSSIBLE EFFECTS ON GLOBAL WARMING AND CONTRIBUTION TO ACID RAIN Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 781-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A8/01	Anonymous	2001	SAFETY DATA SHEET - IODINE Source: Norkem Report No.: I03 Not GLP; (unpublished) Doc. No.: 953-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A8/02	Anonymous	2006	INTERNATIONAL CHEMICAL SAFETY CARDS - IODINE - CAS NO. [7553-56-2] Source: National Institute for Occupational Safety and Health Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 950-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group
A8/03	Anonymous	2007	SAFETY DATA SHEET - IODINE Source: Cid Lines Report No.: 1 Not GLP; (unpublished) Doc. No.: 953-006	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Cid Lines
A10/01	Anonymous	2007	LITERATURE SEARCH - IODINE ELEMENTAL Source: Hazardous Substances Database Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 091-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Iodine Registration Group