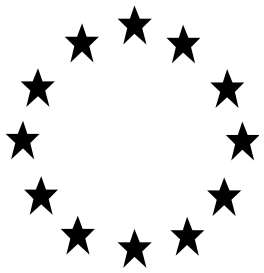
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

RISK ASSESSMENT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS

(submitted by the evaluating competent Authority)



[Betadine solution/Betadine oldat]

Product type(s) [1]

[Iodine (including polyvinylpyrrolidone iodine as included in the Union list of approved active substances]

Case Number in R4BP: [BC-CD019345-61]

Evaluating Competent Authority: [Hungary]

Date: [30/10/2018]

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1 CONCLUSION

Conclusion on physico-chemical properties
The formulation Betadine Solution is ready-to-use preparation which can be used in diluted form also.
All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable. The product is a deep brown liquid. It is not flammable, not explosive and has no oxidizing properties.
No physico-chemical hazard was identified, the product is not considered to be flammable. The physico-chemical properties of the product do not suggest any explosive, oxidising, flammable or autoflammable potential.
The accelerated and real time stability studies demonstrated that 2 years shelf life is acceptable. Analytical method for the determination of the active substance in the biocidal product was provided.

Conclusion on human health assessment
A human health risk assessment has been carried out for professional use of the product. If the professional users follow the instructions about the safe application of the product it is unlikely that the intended uses cause any unacceptable acute or chronic risk to professional users or to the patients. Bathing does not causes acute symptoms, but to avoid the potential long-term effects of iodine overdosing, wearing gloves for professional user is recommended.

Conclusion on efficacy
Betadine solution is used as a skin disinfectant prior to injection, blood sampling, punctures, biopsy, transfusion, infusion and hygienic hand disinfectant. It is also used for total or partial pre-surgery disinfection of the patient (disinfection bath). Betadine solution is bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses) and mycobactericide. Development of resistance to povidone iodine has not yet been described and is also not to be expected on account of its mechanism of action.

Conclusion on the risk assessment for the environment
The main route to the environment is via the sewer. No unacceptable risk is expected for microorganisms in the sewage treatment plant, but on the basis of the PEC/PNEC ratios, a risk is identified for aquatic and terrestrial organisms as well. However, the calculated environmental concentrations are within the typical natural background concentrations.
The calculated groundwater concentrations greatly exceed the limit of 0.1 µg/L, but this limit is granted by the Drinking Water Directive 98/83/EC and this value is for the organic pesticides described in the Directive. The calculated values are within the range of the natural background concentrations.
It is concluded that the intended uses of the product do not pose unacceptable risk to the environment.

2 ASSESSMENT REPORT

2.1 Summary of the product assessment

2.1.1 Administrative information

2.1.1.1 Identifier of the product

Identifier[1]	**Country (if relevant)**
Betadine oldat/Betadine solution	Hungary

2.1.1.2 Authorisation holder

Name and address of the authorisation holder	**Name**	Egis Gyógyszergyár Zrt./Egis Pharmaceuticals PLC
	Address	H-1106 Budapest, Keresztúri út 30-38. Hungary
Authorisation number		
Date of the authorisation		
Expiry date of the authorisation		

2.1.1.3 Manufacturer(s) of the product

Name of manufacturer	Egis Gyógyszergyár Zrt./Egis Pharmaceuticals PLC
Address of manufacturer	H-1106, Budapest, Keresztúri út 30-38., Hungary
Location of manufacturing sites	Körmendi Gyáregység, H-9900, Körmend, Mátyás király utca 65., Hungary

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

Active substance	Polyvinylpyrrolidone iodine
Name of manufacturer	Ashland Industries Europe GMBH
Address of manufacturer	Euro Haus Rheinweg 11 Switzerland-8200 Schaffhausen
Location of manufacturing sites	ISP Chemicals LLC 455 North Main street Calvert City KY, 42029

2.1.2 Product composition and formulation

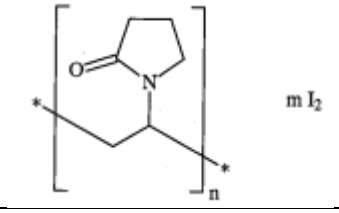
Full composition of the product is provided in a separate file: the confidential annex to PAR.

1 Please fill in here the identifying product name from R4BP.

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

Yes ☐
No ☒

2.1.2.1 Identity of the active substance

Main constituent(s)	
ISO name	Polyvinylpyrrolidone iodine
IUPAC or EC name	2-pyrrolidinone, 1-ethenyl-, homopolymer compound with iodine
EC number	607-771-8
CAS number	25655-41-8
Index number in Annex VI of CLP	
Minimum purity / content	purity of iodine content of PVP-I: 995 g/kg
Structural formula	

2.1.2.2 Candidate(s) for substitution

Not applicable.
The active substance is not candidate for substitution in accordance with Article 10 of BPR.

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

Common name	IUPAC name	Function	CAS number	EC number	Content (m/m%)
Povidone iodinated	2-pyrrolidinone, 1-ethenyl-, homopolymer compound with iodine	Active substance	25655-41-8	607-771-8	10 % active iodine content 1.2 %
		Non-active substances			ad 100%

2.1.2.4. Information on technical equivalence

Not needed. As EGIS Pharmaceuticals PLC, Hungary uses the active substance for the production whose supplier is on Article 95 list.

2.1.2.5. Information on the substance(s) of concern

Substance name	Trade name	Function of the component	CAS No	-Content m/m%
Nonoxinol 9	Arkopal N 090	Surfactant	9016-45-9	0.0971%

2.1.2.6. Type of formulation

AL and SL , can be used in undiluted and diluted form

2.1.3. Hazard and precautionary statements

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

Classification	
Hazard category	Aquatic Chronic 3
Hazard statements	H412 Harmful to aquatic life with long-lasting effects
Labelling	
Signal words	None
Pictograms	
Hazard statements	H412 Harmful to aquatic life with long-lasting effects
Precautionary statements	P102 - Keep out of reach of children. P273 Avoid release to the environment P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a doctor. P501 Dispose of contents/container in accordance with local and national regulations
Note	

2.1.4. Authorised use(s)

2.1.4.1. Use description

Table 1. Use # 1 – name of the use

Product Type	PT 1
Where relevant, an exact description of the authorised use	Please see below.
Target organism (including development stage)	Bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses), mycobactericide.
Field of use	The preparation is indicated: • as a skin disinfectant to be used prior to injection,

	blood sampling, punctures, biopsy, transfusion, infusion • for disinfection of the skin prior to surgery • for total or partial pre-surgery disinfection of the patient (disinfection bath) • hygenic hand disinfectant.
Application method(s)	The Betadine solution can be taken undiluted 1% (1:100), depending to the region we want to disinfect. Exposure is 1-2 minutes undiluted prior to injection, blood sampling or any other puncture, biopsy, transfusion or infusion or any other surgery on intact skin. For hygienic hand disinfection undiluted, exposure is 1 minute. For the pre-surgery disinfection bath a 1% solution (1:100) is used. The whole body surface should be cleaned evenly with a 1% solution of Betadine and after a 2-min exposure washed with warm water. The diluted solution should be prepared immediately prior to application and should not be stored. Betadine solution stains can be removed by washing in hot water; if the stain is severe use a solution of sodium thiosulfate. In pre-operative preparation, avoid pooling beneath the patient. Prolonged exposure to wet solution may cause irritation or rarely, severe skin reactions. Chemical burns of skin due to pooling may occur.
Application rate(s) and frequency	Several times a day. The Betadine solution can be taken undiluted or 1% (1:100), depending to the region we want to disinfect.
Category(ies) of users	Professional and non-professional.
Pack sizes and packaging material	Please see the relevant section.

2.1.4.2. Use-specific instructions for use

The Betadine solution can be taken undiluted or 1% (1:100), depending to the region we want to disinfect. Exposure is 1-2 minutes undiluted prior to injection, blood sampling or any other puncture, biopsy, transfusion or infusion, or any other surgery on intact skin. For hygienic hand disinfection undiluted, exposure time is 1 minute. For the pre-surgery disinfection bath a 1% solution (1:100) is used. The whole body surface should be cleaned evenly with a 1% solution of Betadine and after a 2-min exposure washed with warm water. The diluted solution should be prepared immediately prior to application and should not be stored. Betadine solution stains can be removed by washing in hot water; if the stain is severe use a solution of sodium thiosulfate. In pre-operative preparation, avoid pooling beneath the patient. Prolonged exposure to wet solution may cause irritation or rarely, severe skin reactions. Chemical burns of skin due to pooling may occur.

2.1.4.3. Use-specific risk mitigation measures

See General directions for use.

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

See General directions for use.

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

See General directions for use.

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

Store below 25°C, in the original packaging should be protected from light. Do not store under 0°C, keep away from frost. Shelf life:2 years

2.1.5. General directions for use

2.1.5.1. Instructions for use

The Betadine solution can be taken undiluted or diluted in water as 1% (1:100), depending to the region we want to disinfect. Exposure is 1-2 minutes undiluted prior to injection, blood sampling or any other puncture, biopsy, transfusion or infusion, hygenic hand disinfection or any other surgery on intact skin. For hygienic hand disinfection undiluted, exposure time is 1 minute. For the pre-surgery disinfection bath a 1% solution (1:100) is used. The whole body surface should be cleaned evenly with a 1% solution of Betadine and after a 2-min exposure washed with warm water. The diluted solution should be prepared immediately prior to application and should not be stored. Betadine solution stains can be removed by washing in hot water; if the stain is severe use a solution of sodium thiosulfate. In pre-operative preparation, avoid pooling beneath the patient. Prolonged exposure to wet solution may cause irritation or rarely, severe skin reactions. Chemical burns of skin due to pooling may occur.

2.1.5.2. Risk mitigation measures

-Wear eye protection -Do not use on children, pregnant or lactating women -Do not use in case of iodine sensitivity or with any condition involving thyroid

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

First aid instructions

- Skin contact: If unintended skin contact occurs remove contaminated clothing and shoes. Wash contaminated skin with soap and water. Contact poison treatment specialist if symptoms occur.
- Eye contact: Immediately flush with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses if easy to do. Continue to rinse with warm water for several minutes. Get medical attention if irritation or vision impairment occurs.
- Ingestion: Wash out mouth with water. Contact poison treatment specialist. Seek medical advice immediately if symptoms occur and/or large quantities have been ingested.
- Inhalation: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Seek medical advice immediately if symptoms occur and/or large quantities have been inhaled.
- In case of impaired consciousness place in recovery position and seek medical advice immediately. Do not give fluids or induce vomiting.
  Keep the container or label available.

Prevent substance from entering soil, sewers or living water.
In case of spill absorb the liquid in a non-flammable, inert material (sand, soil, perlite) and collect in a suitable container for disposal. Wash the effected area with water, and aerate. Wear full protective equipment.

2.1.5.4. Instructions for safe disposal of the product and its packaging

Dispose of contents and container in accordance with local and national regulations.
Do not re-use empty containers.

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

Store below 25°C, in the original packaging protected from light. Do not store under 0°C, keep away from frost. Shelf-life: 2 years.

2.1.6. Other information

Application codes

2.1.7. Packaging of the biocidal product

Type of packaging	Size/volume of the packaging	Material of the packaging	Type and material of closure(s)	Intended user (e.g. professional, non-	Compatibility of the product with the

				professional)	proposed packaging materials (Yes/No)
Green polyethylene bottle with a dropper and a white PP screw cap packed in a cardboard box	30 ml	polyethylene	Tamper-proof Plastic Screw-Polypropylene Cap Low density polyethylene dropping insert	professional/non-professional	yes
Green polyethylene bottle with a dropper and a white PP screw cap packed in a cardboard box	120 ml	polyethylene	Tamper-proof Plastic Screw-Polypropylene Cap Low density polyethylene dropping insert	professional/non-professional	yes
Green polyethylene bottle with a dropper and a white PP screw cap	1000 ml	polyethylene	Tamper-proof Plastic Screw-Polypropylene Cap Low density polyethylene dropping insert	professional/non-professional	yes

Detailed description of packaging is annexed to this document.

2.1.8. Documentation

2.1.8.1. Access to documentation

The active substance manufacturer has provided a Letter of Access for EGIS Pharmaceuticals PLC that has been included into the application. Alcoholes Montplet, registered as approved API manufacturer PVP-Iodine granted access for Ashland Industries Europe GMBH to refer and rely on its iodine dossier in order to register products. Ashland Industries Europe GMBH allowed EGIS Pharmaceuticals PLC, Hungary to refer to the Letter of Access granted by Alcoholes Montplet.

2.2. Assessment of the biocidal product

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

Table 2. Intended use # 1 – name of the use

Product Type(s)	PT1
Where relevant, an exact description of the authorised use	Please see field of use section.
Target organism (including development stage)	Bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses), mycobactericide
Field of use	The preparation is indicated: • as a skin disinfectant to be used prior to injection, blood sampling, punctures, biopsy, transfusion, infusion • for disinfection of the skin prior to surgery • for total or partial pre-surgery disinfection of the patient (disinfection bath) • hygienic hand disinfectant.
Application method(s)	The Betadine solution can be taken undiluted or diluted in water as 1% (1:100), depending to the region we want to disinfect. Exposure is 1-2 minutes undiluted prior to injection, blood sampling or any other puncture, biopsy, transfusion or infusion, hygienic hand disinfectant or any other surgery on intact skin. For hygienic hand disinfection undiluted, exposure is 1 minute. For the pre-surgery disinfection bath a 1% solution (1:100) is used. The whole body surface should be cleaned evenly with a 1% solution of Betadine and after a 2-min exposure washed with warm water. The diluted solution should be prepared immediately prior to application and should not be stored. Betadine solution stains can be removed by washing in hot water; if the stain is severe use a solution of sodium thiosulfate. In pre-operative preparation, avoid pooling beneath the patient. Prolonged exposure to wet solution may cause irritation or rarely, severe skin reactions. Chemical burns of skin due to pooling may occur.
Application rate(s) and frequency	Several times a day. The Betadine solution can be taken undiluted or diluted in water as 1% (1:100), depending to the region we want to disinfect.
Category(ies) of user(s)	Professional and non-professional.
Pack sizes and packaging material	30 ml, 120 ml, 1000 ml

2.2.2. Physical, chemical and technical properties

Property	**Guideline and Method**	**Purity of the test substance (% (w/w)**	**Results**	**Reference**
Appearance Physical state at 20C and 101.3 kPa Colour Odour [2]	ICH Q6A guideline Egis method		Solution with a deep brown colour and the odour of iodine, free from suspended particles or sedimentation	in house observation
Acidity /alkalinity(pH)[2]	ICH Q6A guideline Ph. Eur. 2.2.3 method		pH value 5,48 at 25°C Since the pH value of the biocidal product is between 4 and 10 the acidity or alkalinity does not need to be tested.	
Density	Ph. Eur. 2.2.5		1.02 - 1.04 g/cm^3	
Storage stability test – **accelerated storage** Storage stability test – **long term storage at ambient temperature**	Q1A(R2),Q1 E guidelines	30 ml., 120 ml and 1000 ml HDPE flasks were tested Batch number BOL080516 for tested in accelerated intermediate and long-term stability test	Samples were kept at 54°C/50%RH, at 40°C/75%RH, at 30°C/65%RH, at 25°C/60%RH and at different time points appearance, colour, odour, density, dynamic viscosity, pH and iodine, iodine content microbiological quality were tested. Data of 2 weeks, 3, 6, 12, 18 and 24 months show 2 years of shelf life is acceptable.	EGIS Zrt. Stability test Report Code: 0A-004-0034-10-1M
Storage stability test – **low temperature**			no test was performed which	

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
stability test for liquids			is acceptable if the following is on the label: Do not store under 0°C, keep away from frost.	
Effects on content of the active substance and technical characteristics of the biocidal product - **light**	Guidance on the BPR, Volume 1, Part A Egis method		The results comply with the requirements. See attachment (stability data)	
Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity**	Q1A(R2),Q1 E guidelines		See attachment (stability data)	
Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material**	Guidance on the BPR, Volume 1, Part A Leaching test		IR spectra of packaging materials are identical with that of the IR spectra of references at initial and after 8 weeks. See details in attachment.	
Wettability			Not applicable	
Suspensibility, spontaneity and dispersion stability			Not applicable	
Wet sieve analysis and dry sieve test			Not applicable	
Emulsifiability, re-emulsifiability and emulsion stability			Not applicable	
Disintegration time			Not applicable	
Particle size distribution, content of dust/fines, attrition, friability			Not applicable	
Persistent foaming			Not applicable	
Flowability/Pourability/Dustability			Not applicable	
Burning rate — smoke generators			Not applicable	
Burning			Not applicable	

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
completeness — smoke generators				
Composition of smoke — smoke generators			Not applicable	
Spraying pattern — aerosols			Not applicable	
Physical compatibility			Not applicable	
Chemical compatibility			Not applicable	
Degree of dissolution and dilution stability			Not applicable	
Surface tension	Guidance on the BPR, Volume 1, Part A		40.88 – 42.11 mN/m	See attached test report.
Dynamic Viscosity	ICH Q6A guideline Ph. Eur. 2.2.9 method		6.0 – 10.0 mPas	

Conclusion on the physical, chemical and technical properties of the product
Based on the available data, the product is appropriate for the intended use. Tests were performed according to Ph. Eur. methods, in-house methods, and ICH guidelines which are publicly available. The physical, chemical and technical properties of the product are deemed to be acceptable. Storage stability studies (accelerated, intermediate and long term) show that 24 months shelf life is acceptable. There are no observations of degradation of the packaging.

2.2.3. Physical hazards and respective characteristics

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
Explosives			not applicable	
Flammable gases			Not applicable	
Flammable aerosols			Not applicable	
Oxidising gases			Not applicable	
Gases under pressure			Not applicable	
Flammable liquids			None of its ingredients is	

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			classified as flammable, so flammable properties can be excluded. Flash point does not need to be tested.	
Flammable solids			Not applicable	
Self-reactive substances and mixtures			Not applicable	
Pyrophoric liquids			Not applicable	
Pyrophoric solids			Not applicable	
Self-heating substances and mixtures			Not applicable	
Substances and mixtures which in contact with water emit flammable gases			Not applicable	
Oxidising liquids	Guidance on the BPR, Volume 1, Part A See method in attached technological declaration!		Waived on the basis of the classifications of the ingredients. Active substance has slightly oxidising character.	See attached technological declaration!
Oxidising solids			not relevant	
Organic peroxides			not relevant	
Corrosive to metals	Guidance on the BPR, Volume 1, Part A See method in attachment!		Slightly corrosive for Al, Cu (incl. bronze), Zn, Sn, Pb, Ag and its alloys. The product is not classified as mixture having Met. Corr. hazard.	See details in attachment!
Auto-ignition temperatures of products (liquids and gases)			Based on the physico-chemical data and classification of of the	

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			ingredients (see SDSs) the product is not ignitable.	
Relative self-ignition temperature for solids	Not applicable		Not applicable	
Dust explosion hazard	Not applicable		Not applicable	

Conclusion on the physical hazards and respective characteristics of the product
Concerning the above-mentioned points, the product is not concluded to represent any physical hazard. It is not flammable, explosive and is not classified as oxidizing liquid.

2.2.4. Methods for detection and identification

	Analytical methods for the analysis of the product as such including the active substance, impurities and residues								
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Method/System precision**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
						Range	Mean	RSD		
active (available) iodine	titrimetric determination with sodium thiosulfate using starch indicator	3-3 paralel between a.s content 80-120 %	R^2 NLT 0.995	RSD NMT 1.0%		not necessary				Egis method
total -iodine and iodide	complex titration reduction of all iodine to iodide and determination of it using Jacob Volhard back titration	3-3 paralel between a.s. content 80-120 %	R^2 NLT 0.995	RSD NMT 1.0%						Egis method

NMT: not more than, NLT: not less than
From the percentage of total iodine substract the percentage of available (active) iodine as determined to obtain the percentage of iodide .

Conclusion on the methods for detection and identification of the product
The analytical method for the determination of active iodine by titration is applicable and acceptable for the determination active substance in the Betadin solution. Referenced Ph. Eur. methods and detailed description of EGIS methods are annexed to this document.

Conclusion on the methods for detection and identification of residues of active substance for monitoring
Analytical methods were provided and validated at EU level during the approval of active substance for the determination of iodine residue in soil, water, air and milk. Analytical method in biological matrices are not required as active substance is not toxic.

2.2.5. Efficacy against target organisms

2.2.5.1. Function and field of use

The preparation is indicated:

- as a skin disinfectant to be used prior to injection, blood sampling, punctures, biopsy, transfusion, infusion
- for disinfection of the skin prior to surgery
- for total or partial pre-surgery disinfection of the patient (disinfection bath)
- hygienic hand disinfectant.

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

Bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses), mycobactericide

2.2.5.3. Effects on target organisms, including unacceptable suffering

The microbicidal activity of povidone iodine covers a broad spectrum of human pathogens such as bacteria, viruses, fungi, mycobacteria.
The broad spectrum of activity of PVP iodine may be explained by its mechanism of action; free iodine is known to react with oxidiziable amino acids in microbial enzymes and proteins thereby causing their inactivation.

2.2.5.4. Mode of action, including time delay

Mechanism of action: free iodine is known to react with oxidizable amino acids in microbial enzymes and proteins thereby causing their inactivation.
The fact that PVP iodine shows microbicidal action despite the low free availability of iodine can be explained by the high rate of release from the depot of PVP iodine being within the millisecond range.
As a result of the low concentration of free iodine the concentration of hypoiodous acid being formed by disproportioning of iodine is also extremely low. (Hypohalogenous acids evoke dermal damage when applied locally.)
The iodine released from the PVP iodine complex shows the known reaction with amino acids such as histidine and tyrosine thus causing destruction of the structure (secondary, tertiary) of membranes, organelles and cytoplasmic components of microorganisms.

2.2.5.5. Efficacy data

According to the results of the appropriate EN tests listed below the Betadine solution has bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses) and mycobactericide effect.

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
Bactericide effect	Bactericide effect of Betadine solution	Betadine solution	*Staphylococcus aureus* ATCC 6538 *Pseudomonas aeruginosa* ATCC 15442 *Escherichia coli* ATCC 10536 *Enterococcus hirae* ATCC 10541 *MRSA* 1* *MRSA* 2* *MRSA* 3* * isolated from hospital	MSZ EN 1276:2010	1 % of Betadile solution, 0,3 g/l bovine albumin 1 min, 2 min room temperature	The Betadin solution was effective after 1 and 2 minutes under test conditions for all tested strains of bacteria.	Országos Epidemiológiai Központ: Test Report {MSZ EN 1276:2010}
Fungicide effect	Fungicide effect of Betadine solution	Betadine solution	*Candida albicans* ATCC 10231 *Aspergillus brasiliensis* ATCC 16404	MSZ EN 1650:2008+A1	1 % of Betadine solution 0,3 g/l bovine albumin 1 min, 2 min room temperature	The Betadin solution was effective after 1 and 2 minutes under test conditions for all tested strains of fungy.	Országos Epidemiológiai Központ: Test Report {fungicide hatás értékelése}
Mycobactericide effect	Mycobactericide effect of Betadine solution	Betadine solution	*Mycobacterium terrae* ATCC 15755 *Mycobacterium aciusm* ATCC 15769	MSZ EN 14348:2005	1 % of Betadine solution 3 g/l bovine albumin 1 min, 2 min room temperature	The Betadin solution was effective after 1 and 2 minutes under test conditions for all tested strains of mycobacteria.	Emberi Erőforrások Minisztériuma: Test Report
Virucide effect	Virucide effect of Betadine solution	Betadine solution	Poliovirus 1 Murine Norovirus Adenovirus 5	MSZ EN 14476:2013+A1	1 % of Betadine solution 0,3 g/l bovine albumin 2 min room temperature	The Betadin solution was effective against Adenovirus 5 and Norovirus, was not effective against Poliovirus 1.	Országos Epidemiológiai Központ: Test Report {Virucid hatékonyság vizsgálat}
Investigation on disinfectant	disinfectant effect	Betadine solution	Escherichia coli K12 NCTC 10538	MSZ EN 1500:2013	3 ml of Betadine solution, 1 min.,	The Betadin solution was effective under test conditions.	Országos Közegészségügyi

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
effect of the skin	of the skin				room temperature		Intézet: Test Report
Investigation of bacteriostatic effect	bacteriostatic effect of Betadine solution	Betadine solution	Staphylococcus aureus Escherichia coli Salmonella typhi Proteus vulgaris Pseudomonas aeruginosa	serial dilution technique	72 hour incubation time	The bacteriostatic effect of Betadine solution produced by Egis and Betadine solution produced by Mundipharma are identical against 4 bacteria. The only difference was found in the growth inhibition of Staphylococcus aureus. In case of Egis product 1.56 % solution was necessary while in the case of Mundipharma product a 0.7812% solution was already sufficient to inhibit the growth of S. aureus.	Márta Milassin: Comparative bacteriological investigation of Betadine antiseptic liquid soap and solution
Investigation of bactericide effect	bactericide effect of Betadine solution	Betadine solution	Staphylococcus aureus Escherichia coli Salmonella typhi Proteus vulgaris Pseudomonas		72 hour incubation time	Betadine solution prepared by Egis and Betadine solution prepared by Mundipharma are identical for all test strained examined.	Márta Milassin: Comparative bacteriological investigation of Betadine antiseptic liquid soap and solution
Investigation on disinfectant effect of the skin	disinfectant effect of the skin	Betadine solution	E.coli	hands was infected with 0.1 ml of E.coli culture the infected part	bouillon medium the plates were incubated for 24 or 48 hours	It can be concluded that both products have excellent disinfectant effects on the skin, as the number of re-cultured E.coli	Márta Milassin: Comparative bacteriological investigation of Betadine

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
				of the skin was wiped with a special tissuepaper soaked with 3 ml of the disinfectant		colonies was in the range of 0-10 for 100% of the hands examined.	antiseptic liquid soap and solution
Examination of skin disinfectant effect of Betadine solution	disinfection of the skin	Betadine solution	Coagulase negative Staphylococci Corynebacterium xerosis Bacillus genus	sample collection - with a tampon soaked in bouillonfrom regions most often used for injections disinfection from these areas again sample collection		68 CFU (colony forming unit) could be demonstrated on average before disinfection After washing the skin with Betadine solution a total 14 CFU-s were identified.	T. Major SR, M.Major, C. Bognár, Á. Herendi, M. Németh, B. Bánkúti : Clinico-Bacterological Examination of Betadine skin Disinfectant Fluid and Liquid Soap in Hospitalized Patients and Hospital Employees
Examination of Betadine solution	cleaning the surgical site, for disinfection of the mucous membran	Betadine solution		cleaning the surgical site lavage the abdominal cavity		The authors diluted the original 10% PVP-iodine solution by adding physiological saline to achieve	András Erös M.D., János Kiss M.D. and Endre Szirányi M.D.: Study on the effect of Betadine®

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
	e of the operated intestine, and to lavage of the infected abdomina l cavity					a 1:50 dilution. They lavaged the abdominal cavity with 1000 ml of this diluted solution.	surgical scrub and Betadine® solution for surgery patients
Betadine solution was used before skin suture and dressing.	preoperative skin disinfection	Betadine solution		Betadine solution was used for skin disinfection before operation. After drying, using several gauze sheets, the skin of the surgical site was rubbed with Betadine, and after drying this treatment was repeated twice	thioglicolate (TG) and meatbouillon containing medium incubating for 24 hours at 37 degrees temperature	During bacteriological examination after the skin disinfection in 25 septic and 21 non-septic operations and in 4 lumbar punctures, neither aerobic, nor anaerobic pathogens were isolated. After aseptic operations, micrococcus was found in three cases.	Rózsa Báthy M.D., Ivana Stöger M.D., Zsuzsanna Szabó M.D,and József Soós M.D.: PREOPERATION SKIN DISINFECTION WITH BETADINE SOLUTION Dél-Pest Hospital Clinic
The authors examined the in vitro effect of various disinfectants.	disinfection	Betadine solution Desmanol Dodesept	1.20 MRSA isolates *2.Pseudomonas aeruginosa* /5 isolated strains/, *Escherichia coli* /5 isolated strains/, *Enterococcus faecalis* /1 strain/,	suspension cultures	After three minutes, the antibacterial effect of the disinfectant was inactivated by adding 0.1 ml	Betadine completely blocked the growth of all 20 MRSA isolates at all concentrations. We obtained similar results for all other strains studied.	Domestic Operations, Products Department: The role of Betadine in fighting methicillin

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
			Enterococcus faecalis– vancomycin resistant /1 strain/, *Staphylococcus aureus (non MRSA)* /2 strains/, *Staphylococcus epidermidis* /1 strain/, *Staphylococcus epidermidis* – methicillin resistant /1 strain/)		neutralising agent (0.5% sodium thyoglicolate for Betadine®, and a solution containing 5% Tween 80 and 0.5% lecithin for Desmanol® and Dodesept®). After this we placed a 0.1 ml sample with a pipette on the surface of blood agar and dispersed it evenly. After incubating the samples for 24 hours at 37 °C the colonies were counted.	Betadine blocked all bacteria studied in all concentrations	resistant Staphylococcus aureus
Chlorhexidine gluconate (CHG) and povidone iodine (PI), alone and combined, were evaluated against bacteria listed in test organisms	efficacy against bacteria	Polyvinylpyrr olidone iodine (PI) 10%	Staphylococcus aureus (methicillinsusceptible S aureus [MSSA] and methicillinresistant S aureus [MRSA), Staphylococcus	checkerboard microbroth dilution techniques Fractional bactericidal concentration indexes (FBCls) were	Tissue plugs from freshly excised porcine vaginal mucosa were infected with S aureus (MSSA), treated for 2 hours with CHG 3%, PI 5%,	In broth, CHG demonstrated dosedependent bactericidal activity, whereas PI activity was all-or-none. All isolates studied were similarly susceptible to CHG (MBCs: 0.0078%± 0.0019%. 0.0069% ±	Michele J. Anderson, PhD,a Mary E. Horn, BS,a Ying-Chi Lin, PhD,a Patrick]. Parks, MD, PhD,a.b

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
column.			epidermidis (MRSE), Acinetobacter baumannii, Pseudomonas aeruginosa, and Escherichia coli	calculated to determine CHG and PI compatibility.	or CHG 3% and PI 5% combined and then viable bacteria on the tissue plugs enumerated.	0.0026%. 0.0024% ±0.0005%, 0.0024% ± 0.0005%, 0.0059% ± 0.0% and 0.0029% ± 0.0%, respectively). The MBCs (minimum bacterial concentration) of PI were identical (0.625%) for all isolates. Overall, FBCI (fractional bactericidal concentration index) calculations showed indifference. Treatment of MSSAinfected porcine tissue for 2 hours demonstrated that the CHG-PI combination was superior to either antiseptic alone.	and Mamie L. Peterson, PharmD, PhDa: Efficacy of concurrent application of chlorhexidine gluconate and povidone iodineagainst six nosocomial pathogens
Prophylaxis of newborns against ophthalmia neonatorum	efficacy against bacteria strains	povidone iodine solutions (Betadine, Purdue Frederick, Norwalk, Connecticut)	four strains of Neisseria gonorrhoeae, a clinical isolate of Chlamydia trachomatis, and one strain of herpes simplex virus type II	The strains were taken from chocolate agar plates and suspended in normal saline at a concentration of approximately 10^8 organisms per	three different concentrations of povidone-iodine (5%, 1 %, and 0.1 %)	The challenge inoculum of Neisseria gonorrhoeae and herpes simplex virus type II were completely sterilized by all three solutions. The chlamydia titer was reduced by two log units at the 5% and 1 % concentrations, but not the 0.1% concentration.	William J. Benevento, B.A., Patrick Murray, Ph.D., Charles A. Reed, A.B., and Jay S. Pepose, M.D.: The Sensitivity of Neisseria gonorrhoeae, Chlamydia trachoma tis, and

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
				millilitre by optical density.			Herpes Simplex Type II to Disinfection With Povidone-Iodine
10 formulations as mycobactericidal agents in Mycobacterium tuberculosiscontaminated suspensions and stainless steel surfaces (carrier test) were investigated with sputum as the organic load	efficacy against Mycobacteria	povidone iodine solution	Mycobacterium tuberculosis Mycobacterium smegmatis	Disinfectant tests were carried out in the wells of a 24-well plastic cell culture plate	Disinfectant efficacy tests were carried out with M. tuberculosis in suspension (suspension test) and dried on stainless steel surfaces (carrier test). Povidone iodine (1.0% titratable I2) contact time of 1 min was selected for the testing of all disinfectants	Povidone-iodine was not as efficacious when the test organism was dried on a surface as it was in suspension, and its activity was further reduced in the presence of sputum. In the suspension test, the povidone-iodine solution was more effective than the lower-concentration iodophore, producing at least a 5-log10 reduction in CFU (maximum level of detection). However, the test organism was resistant to its action in the carrier test in the presence of sputum.	M. BEST,I S. A. SATTAR, V. S. SPRINGTHORPE, AND M. E. KENNEDy: Efficacies of Selected Disinfectants against Mycobacterium tuberculosis
The inactivation of MRSA, MSSA, VRE and VSE is tested.	efficacy against bacteria	0.5% aqueous chlorhexidine gluconate 10% povidone iodine aqueous	methicillin-resistant Staphylococcus aureus (MRSA) methicillin-sensitive Staphylococcus aureus (MSSA) vancomycin-resistant enterococcus (VRE) vancomycin-sensitive	European surface test method	10% povidone iodine	Povidone iodine was equally active against resistant and sensitive strains of both species with microbicide effects (ME), i.e. the $\log_{10}$ concentration of micro-organisms compared with controls	C. Block, E. Robenshtok,A. Simhan and M. Shapiro: Evaluation of chlorhexidine and povidone iodine activity against

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		solution	Enterococcus faecalis (VSE)			treated with distilled water, after 1.5 min of 3.14 and 3.49 for VRE and VSE respectively, and 3.47 and 3.78 for MRSA and MSSA.	methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus faecalis using a surface test.
The effectiveness of handcleansing agents (plain liquid soap, 70% ethyl alcohol, 10% povidone-iodine, and 4% chlorhexidine gluconate) for removing a hospital strain of Acinetobacter baumannii from artificially contaminated hands of 5 volunteers was studied.	efficacy against bacteria	10% povidoneiodine	Acinetobacter baumannii	Latin square statistical design with two 5 x 4 randomized blocks, and the results were estimated by ANOVA	10% povidoneiodine Five millilitres of povidone iodine was carefully poured into the hands previously moistened in sterile distilled water, and rubbed palm to palm (50 to 60 times), including fingertips for 30 seconds, and the hands were then dried in air for 30 seconds. Next, the hands were rinsed with sterile distilled water for 15 seconds and softly dried with 2 sterile paper	In the first block, all products tested were effective, almost completely removing the microbial population of .A baumannii artificially applied to the hands. In the second block, the use of handc1eansing agents resulted in 91.36% (4% chlorhexidine), 92.33% (liquid soap), 98.49% (10% povidoneiodine), and 98.93% (70% ethyl alcohol) reduction in counts of A baumannii cells applied to the fingertips. The ethyl alcohol and povidone iodine had significantly higher removal rates than plain soap and chlorhexidine. (P< .05).	Celso Luiz Cardoso, PhD Heloise Henriques Pereira Juliana Campos Zequimb Marcio Guilhermetti: Effectiveness of handcleansing agents for removing Acinetobacter baumannii strain from contaminated hands

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
					towels for 15 seconds.		
in vitro effectiveness of PVP iodine and chlorhexidine(CXD) was tested	efficacy against bacteria	PVP iodine solution	Acanthamoeba polyphaga Acanthamoeba castellanii Acanthamoeba mauritaniensis VEPV-1 Acanthamoeba mauritaniensis VEPV-2, Acanthamoeba sp. strain ANPV-t, and Acanthamoeba sp. strain GEPV-1.	Experiments were performed according to the method of Kilvington et al. with modifications	0.5 to 2.5%	The results showed that PVP-I solution from 0.5 to 2.5% has a better antiamoebic activity both on trophic and cystic stages of Acanthamoeba spp. than does CXD.	Simonetia Gati,Claudia Cevin, Antonella Bruno,Gabriella Penso, Paolo Rama,And Massimo Scaglia:In Vitro Effectiveness Of Povidone-Iodine On Acanthamoeba Isolates From Human Cornea
In vitro study was undertaken to determine the sporicidal efficiency of povidone iod ine, an iodineliberating complex, and to evaluate such sporicidal efficiency with that of other commonly used skin antiseptics.	efficacy against spores	Povidone iodine Solution containing 1% available iodine Iodine Tincture, U. S. P. containing 2 % free iodine, 2.4 %	Bacillus subtilis, Clostridium perfingens Clostridium tetanii	5 ml of povidone iodine was added to each of the test bacteria culture	Transplants of one loopful (4 mm.) and 0.1 ml separately were made at intervals of 5, 10, 15, 30, 45 and 60 minutes and every half hour thereafter for 4 hours, then every hour 10 hours had elapsed and the final transplant at	All of the antiseptic solutions tested except the Povidone-iodine Solution and the Iodine Tincture did not kill any of the test bacteria within 24 hours either at 20°C or at 37°C.	Louis Gershenfeld: POVIDONE.IODINE AS A SPORICIDE

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		sodium iodide, and 47% alcohol.			the end of 24 hours. All transplants were incubated at 37°C for one week and examined daily during this period		
The in vitro antiviral activity of 2 % PVP-I solution and 0.5% PVP-I scrub were investigated.	efficacy against viruses	2% PVP-I solution 0.5% PVP-I scrub 2 % PVP-I solution for animals	avian influenza A (highly pathogenic avian influenza virus, H5N1) 3 low pathogenic avian influenza A viruses: A/whistling swan/Shimane/499/83 8 (H5N3) A/whistling swan/Shimane/42/80 (H7N7) A/duck/Hokkaido/26/ 99 (H9N2)	embryonated hen's egg	2% PVP-I solution 0.5% PVP-I scrub 10 sec	Viral infectious titers were reduced to levels below the detection limits by incubation for only 10 s with the PVP-I products used in this study.	Hiroshi Ito, Toshihiro Ito, Muneo Hikida, Junko Yashiro, Akira Otsuka, Hiroshi Kida, Koichi Otsuki: Outbreak of highly pathogenic avian influenza in Japan and anti-influenza virus activity of povidoneiodine products (2006)
The in vitro virucidal efficacy of povidoneiodine products against swine influenza viruses (H1N1, H3N2 and H1N2) was	virucidal efficacy of povidoneiodine	PVP-I solution, PVPI gargle PVP-I scrub and PVP-I palm	swine influenza viruses (H1N1, H3N2 and H1N2)		10 sec	The in vitro virucidal efficacy of povidoneiodine products against swine influenza viruses (H1N1, H3N2 and H1N2) was investigated. The viral infectious titers were reduced below detection	Ito H.,Hikida M.,Yashiro J.,Kida H.,Ito T.: Virucidal efficacy of povidone-iodine products against swine

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
investigated.						limit by incubation with povidone-iodine products used in this study (PVP-I solution, PVP-I gargle, PVP-I scrub and PVP-I palm) for only 10 seconds.	influenza viruses (2009)
To study the bacterial activity of 5% povidoneiodine, 10% povidone iodine and several other disinfectants.	efficacy against nosocomial pathogens	5% povidoneiodine, 10% povidone iodine	Methicillin resistant Staphylococcus aureus (MRSA) Multi drug resistant (MDR) Pseudomonas aeruginosa Acinetobacter baumannii Escherichia coliextended spectrum beta lactamase producers (ESBL) Klebsiella pneumoniae (ESBL)	suspension test	The pathogen was exposed to 5% povidoneiodine, 10% povidone iodine 15, 30, 60, 120 and 240 seconds at room temperature.	Povidone iodine (10%) and 60% ethyl alcohol were found to be effective against 20 bacterial strains.	Jayakumar S et al: The in vitro efficacy testing of skin disinfectants against nosocomial pathogens
The authors investigated the ability of various concentrations of povidone iodine to inactivate Human Immunodeficiency Virus (HIV) in vitro.	efficacy in vitro against HIV virus	Commercially available Betadine solution and Betadine Surgical Scrub.	Human Immunodeficiency Virus (HIV)	virus inactivation assay	HIV was infected in H9 cell lines, these cells were grown in faecal calf serum. HIV was exposed to varying concentrations of povidone iodine solutions for 5 seconds to 10 minutes	In these studies the authors found that povidone iodine is a highly effective disinfectant for HIV in readily achievable concentrations. The concentrations of virus utilized in this study are well above those likely to be encountered in body fluids.	Amy G. Durno Joan C. Kaplan Robert T. Schooley: INACTIVATION OF HUMAN IMMUNE DEFICIENCY VIRUS BY POVIDONE IODINE

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
efficacy of several povidone-iodine (PVP-I) products, and a number of other chemical agents and various physical conditions were evaluated for their ability to inactivate the severe acute respiratory syndrome coronavirus (SARS-CoV).	efficacy against severe acute respiratory syndrome coronavirus	povidone iodine solution, scrub, gargle	severe acute respiratory syndrome coronavirus (SARS-CoV)	the virus was propagated in Vero E6 cells inactivation of infectivity of SARSCoV infected Vero E6 cells by chemical reagents Physical Inactimtion of SA RS-CoV	Fixation of SARS-CoVinfected Vero E6 cells with a fixative including formalin, glutaraldehyde, methanol and acetone for 5 min or longer eliminated all infectivity. Heating the virus at 56°C for 60 min or longer reduced the infectivity of the virus from 2.6 x 10^7 to undetectable levels. Irradiation with ultraviolet light at 134 µW/cm^2 for 15 min reduced the infectivity from 3.8 x 10^7 to 180 $TCID_{50}$/ml; however, prolonged irradiation (60 min) failed to	Treatment of SARS-CoV with PVP-I products for 2 min reduced the virus infectivity from 1.17 x10^6 $TCID_{50}$/ml to below the detectable level.	Hiroaki Kariwa, Nobuhiro Fujii, Ikuo Takashima: Inactivation of SARS Coronavirus by Means of Povidone-Iodine, Physical Conditions and Chemical Reagents

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
					eliminate the remaining virus, leaving 18.8 $TCID_{50}$/ml.		
Patients requiring an epidural catheter for postoperative analgesia were randomly assigned to receive skin preparation with 0.5% chlorhexidine ethanol (CE group) or 10% povidoneiodine (PI group) before catheter insertion.	skin preparation before epidural catheter	10% povidoneiodine solution	cutaneous antisepsis before epidural catheter	cutaneous antisepsis; after two days the catheter was removed and the insertion site was analysed by the doctor who was blind to the antiseptic solution used. Before and after insertion of the epidural catheter, the palm sides of gloves were contacted with agar medium cultured, and the number of bacteria was counted after 48 h of	Using surgical aseptic techniques, catheters were inserted into either the lumbar or the thoracic epidural space. Gloves used at catheter insertion, swabs of insertion site skin and the catheter tip at catheter removal were qualitatively cultured.	The effect of 0.5% chlorhexidine ethanol is not different from that of 10% povidone-iodine in reducing catheter colonization associated with short-term epidural catheter placement.	Haruyuki Kasudaa,Hirokazu Fukuda, Hideaki Togashi, Kunihisa Hotta, Yoshikazu Hirai, Mutsumu Hayashi: Skin Disinfection before Epidural Catheterization: Comparative Study of Povidone-Iodine versus Chlorhexidine Ethanol

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
				incubation at 37° C.			
Inactivation of a range of viruses. such as adeno-. mumps, rota-. polio- (types I and 3), coxsackie-, rhino-, herpes simplex, rubella, measles, influenza and human immunodeficiency viruses, by povidone- iodine (PVP- I) and other commercially available antiseptics was studied in accordance with the standardized protocol in vitro.	efficacy against viruses	PVP-I solution, PVPI gargle, PVPI cream, chlorhexidine gluconate, alkyldiaminoe thyl -glycine hydrochloride, benzalkonium ch loride (BAC) and benzethonium chloride (BEC) were used	adeno-. mumps, rota-. polio- (types I and 3), coxsackie-, rhino-, herpes simplex, rubella, measles, influenza and human immunodeficiency viruses	Virus suspension in phosphatebuffered saline was mixed with an equal volume of PVP-I solution of a designated concentration and incubated at 25 °C for a designated time length. At the end of treatment 2 vol of 0.1 N$Na_2S_2O_3$ were added and the mixture was diluted with MEM (Eagle's essential medium) and inoculated onto the cell cultures for	please see article	PVP- I was effective against all the virus species tested. PVP-I drug products which were examined in these experiments, inactivated all the viruses within a short period of time. PVP·1 had a wider virucidal spectrum, covering both enveloped and non-enveloped viruses than the other commercially available antiseptics	R. Kawana,T Kitamura,O. Nakagomi, Matsumoto M. Arita,N. Yoshihara K. Yanagi,A. Yamada 0. Morita,Y. Yoshida Y. Furuya,S. Chiba: Inactivation of Human Viruses by Povidone-Iodine in Comparison with Other Antiseptics

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
				the plaque or $TClD_{50}$ assay of residual virus			
the virucidal efficacy of nine hand sanitisers were investigated	hand disinfection	10% povidoneiodine solution	feline Calicivirus	fingerpad method of Sattar and Ansari with minor modifications	10% povidoneiodine	Antiseptics containing 10% povidone-iodine (equivalent to 1% available iodine) reduced virus titre by a log_{10} reduction factor of 2.67 within 30 s contact time. This viral reduction rate was higher than that achieved with any of the alcohol-based 5aniti5ers, non-alcoholic sanitisers or antimicrobial soaps.	S.L.S. Lages, M.A. Ramakrishnan, S.M. Goyal: In-vivo efficacy of hand sanitisers against feline calicivirus: a surrogate for norovirus
Virucidal activity of four antiseptics were tested	Efficacy against virus	10% povidoneiodine solution (diluted), NaOCl, 10% Benzethonium chloride solution (BEC), 20% chlorhexidine	Murine norovirus virus (MNV) (strain MT30-2)	Plaque assay, RT-PCR	PVP-I 0.2% and 1%, NaOCl 0.1% and 0.2%, BEC 0.1%, CHG 0.5% virus titer was determined with plaque assay after adding the antiseptic agents. Quantitative RTPCR was also used for determining the efficacy of povidone-iodine.	Both 0.2% and 1% PVP-I reduced the titer by 4 log_{10} within 15 s. PVP-I and NaOCl, even at low concentrations efficiently and rapidly inactivated MNV. The other two antiseptics BEC and CHG appeared to be ineffective against MNV.	Matsuhira T, Kaji C, Murakami S, Maebashi K, Oka T, Takeda N, Katayama K. Evaluation of four antiseptics using a novel murine norovirus.

Experimental data on the efficacy of the biocidal product against target organism(s)							
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		gluconate (CHG)					
Assessing efficacy of PVP-I and dexomethasone	Efficacy against bacteria, fungi, and Acanthamoeba clinical isolates	0.4% Povidoneiodine -0.1% dexamethason e suspension	MRSA, P. aeruginosa, Serratia marcescens, C. albicans, Fusarium solani, Acanthamoeba castellanii	organisms were inoculated into PVP-IDexamethasone suspension in a microtiter plate, then aliquots were streaked onto sheep blood agar plate and agar-agar	100 ml of 10_4 CFU/mL of ocular isolates of organisms were inoculated into 100 µL of 0.4% PVP-0.1% Dexamethasone suspension in a 96-well microtiter plate incubated at room temperature. Organism viability was assessed 15, 30, 60 s by removing 10µL aliquots and streaking onto a 5.0% sheep blood agar plate (fungi and bacteria) and agar-agar (Acanthamoeba) using a 0.001 calibrated loop. The plates were then incubated at 35ºC and monitored for up	99.9 % of MRSA, P. aeruginosa, S. marcescens and C. albicans were killed after a 15 sec inoculation and F solani after 60 seconds. Acanthamoeba castellanii cyst viability was not inhibited by exposure to PVP-I and dexamethasone suspension. Organism growth was achieved on all control broth.	99.9 % of MRSA, P. aeruginosa, S. marcescens and C. albicans were killed after a 15 sec inoculation and F solani after 60 seconds. Acanthamoeba castellanii cyst viability was not inhibited by exposure to PVP-I and dexamethasone suspension. Organism growth was achieved on all control broth.

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
					to 7 days. Isolates were inoculated into 200 µL of trypticase soy broth as controls. Number of colonies was counted and compared with controls.		
Review; Avian Influenza, disinfectants efficacy against Influenza A virus	Influenza A susceptibility	Disinfectants like sodium hypochlorite, 60-95% ethanol, quaternary ammonium compounds, aldehydes, phenols, acids, povidoneiodine and other agents.	Influenza			Influenza A viruses are susceptible to povidoneiodine and other agents.	Fowl Plague, Grippe Aviare. Avian Influenza
Review of different studies, 1.Activity	Bactericidal, virucidal, activity,	1.Povidone iodine solution	1.10 genotipically different MRSA and 5 E. faecium	1. Different exposure times and different	1. Without protein load, optimal bactericidal	Iodine and Consequences for New Application Areas	

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
against MRSA 2. Tolerability of nasal ciliated epithelium 3. Tolerability of PVP-I on the synovial membrane and articular cartilage after experimental Intra-articular application (review of various studies) 4.Virucidal and chlamydicidal activity	tolerability	2.Povidone iodine solution 3.Povidone iodine solution 4.Povidone iodine solution	2. ciliated cells from concha nasalis inferior (10 healthy volunteers) 4.Herpes simplex, Coxsackie virus, Adenovirus, Rhinovirus, Influenza A, Chlamydia	concentrations, with and without protein load 2. freshly taken vital ciliated cells were incubated under physiological conditions, ciliary frequency was measured before and after the exposure to different concentrations of Betaisodona solution for 5 mins 3.application on cartilage in vitro, local tolerance test in vivo 4. different cell cultures for different viruses	effect against MRSA was achieved within 30 seconds of exposure and in dilutions up to 1% of the original Betaisodona solution. Against E. faecium, 1- 10% of the original solution was most effective in short exposure times 30 second or 1 minute. 2. 50% and 25% solution completely inhibited the activity of the cilia, but without structural damage. 12.5% solution did not inhibit the ciliated cells. 3. Kallenberger decribed inhibitory effects of PVP-I on foetal rat		

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
					cartilage in vitro and assessed PVP-I products not suitable for intra-articular application. In an in vivo local tolerance test on chinchilla rabbits PVP-I showed advantages over gentamicin. 4. PVP-I is highly effective against Herpes simplex. Coxsackie was rather resistant. Adenovirus type 8 and rhinovirus and influenza A was sensitive to PVP-I. Activity against Chlamydial activity was excellent.		
Bactericidal activity of povidone-iodine against	Bactericidal activity	Povidoneiodine solution	Mycobacterium (18 strains, 3 standards and 15 clinical isolates)	suspension test	18 strains of Mycobacterium were cultured, suspended,	Three standard strains were completely inhibited by 0.1% PVP-I within 30 seconds. 15 clinical	T Rikimaru, M kondo, S Kondo, K Oizumi. Bactericidal

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
Mycobacterium was assessed					bacteria were exposed to different concentrations of PVP-I; 01 or 0.02% with 2% human serum for various incubation periods from 30 to 120 seconds. PVP-I was inactivated by 0.5% sodium thiosulfate	isolates were almost killed by 0.1% commercially available PVP-I solution within 60 seconds. Commercially available PVP-I product appeared to be useful against Mycobacterium.	Activities of Povidone-Iodine against Mycobacterium (1997)
Antiseptic activity against Mycobacteria in vitro.	Bactericidal activity	10% Povidoneiodine solution PVPI (S), 10% PVP-I solution from povidone iodine (PVP-I C), chlorhexidine gluconate (CHG), 10% alkylamino	Mycobacteriua (M. avium, M. kansasii, M. tuberculosis)	suspension test	PVP-I (C) concentrations 0.02 and 0.1% with exposure times of 30, 60 and seconds. PVP-I (S) 0.0.2%, 0.05%,0.1% and 0.2% with exposure times of 15,30 and 60 seconds. CHG 0.5% tested with exposure times 10, 60,120 min. Benzalkonium chloride 0.1%	The effects of different antiseptics on mycobacteria (Mycobacterium avium, M. kansasii and M. tuberculosis) were examined. At concentrations of 0.05%, povidone-iodine (PVP-I) killed 99% or more of all strains tested within 15 seconds, while 0.5% chlorhexidine gluconate and 0.1% benzalkonium chloride showed no bactericidal activity against mycobacteria. M. kansasii and M. tuberculosis were killed	T Rikimaru, M Kondo, S Kondo, K Oizumi. Efficacy of common antiseptics against mycobacteria (2000)

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		ethyl glycine hydrochloride (AEG). 10% benzalkonium chloride, saponated cresol, 20% glutaraldehyde			tested with exposure times 10, 60,120 min. AEG 0.1%, 0.2%, 0.5% with exposure times 30, 60, 120 min. Cresol 0.5%, 1%, 3.0% with exposure times 30,60,120,180 s. Glutaraldehyde 0.5%, 2.0% for 1,5,10,30 min.	after exposure to cresol for 60 seconds at concentrations of 1.0%, but M. avium was unaffected even after 60 seconds. While M. kansasii and M. tuberculosis were killed by treatment with 2.0% glutaraldehyde for 5 minutes, M. avium was highly resistant to this agent.	
Determining useful antiseptics against Mycobacterium tuberculosis.	Antiseptics	10% Povidone iodine solution, cresol, 10% alkyldiaminoe thyl glycine hydrochloride (AEG), 20% glutaraldehyde	Mycobacterium tuberculosis(13 clinically isolated and 1 standard)	Suspension test	PVP-I 0.01%,0.05%(15, 30,60,120,180 second exposure time), 0.1%, 0.2%(15,30,60,120 s) 0.02%, cresol 0.5%,1.0%,3.0% (30,60,120,180,300 s), AEG 0.1%, 0.2%(30,60,120, 180 s), glutaraldehyde 0.5%(1,3,5,10,15,30, 60 min), 2.0% (1,3,5,10 min)	PVP-I At 0.2%, more than 99.9% of bacteria kill was achieved within 60 seconds. At 0.1 and 0.2%, PVP-I killed all bacteria within 120 sec. Cresol: the activity varied according to strain. At 1%, 60 seconds needed for the satisfactory effect. AEG: at all concentrations AEG killed more than 99% of bacilli within 30 minutes. glutaraldehyde: 0.5% for 30 min needed to kill most bacteria PVP-I and cresol possess strong sterilising activity against MDR-TB even in	T Rikimaru, M Kondo, K kajimura, K Hashimoto, K Oyamada, S Miyazaki, K Sagawa, H Aizawa, K Oizumi. Efficacy of common antiseptics against multidrug-resistant Mycobacterium tuberculosis (2002 a)

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
						with 2% serum.	
Antiseptic activity against Mycobacterium tuberculosis	Antiseptics	10% Povidone iodine solution, cresol, 10% alkyldiaminoe thyl glycine hydrochloride (AEG), 20% glutaraldehyde	Mycobacterium tuberculosis (17 clinical isolates, and 4 standard)	Suspension test	PVP-I: 0.2% (15,30,60, 120 s) Cresol 1% (30,60,120,180 s) Glutaraldehyde 2.0% (1,3,5,10 min) AEG 0.2% (30,60,120 min)	PVP-I at 0.2% conc. killed 99.9% or of all strains tested within 30 s. All of the strains tested with PVP-I were killed almost completely within 60 s. Cresol: at 1 % almost 99.9% or more of all strains were killed after 60 second of exposure. AEG: 0.2% achieved a 99.9% kill after 60 min. Glutarldehyde: 2.0% after 5 min exposure caused a 99.9% kill.	T Rikimaru, M Kondo, K Kajimura, K Hashimoto, K Oyamada, K Sagawa, S Tanoue, K Oizumi. Bactericidal Activities od commonly used antiseptics against Multidrug-resistant Mycobacterium tuberculosis (2002 b)
Suprathelantiseptic matrix model for local antiseptic treatment	Antiseptics	Acetic acid 3%, povidoneiodine solution 11%, polyhexadine 0.04%, phenoxyethanol 2%/octenidine dihydrochloride 0.1%,	E.coli, P vulgaris, P aeruginosa, A baumannii, E faecalis, S epidermidis, S aureus, MRSA, Bhaemolytic streptococcus group A and B	Suprathelantiseptic matrix soaked with antiseptic agent, then placed on agar-agar plates.	Suprathel was soaked in each tested antiseptic agents for 10 minutes. acetic acid 3%, povidone-iodine 11%, polyhexadine 0.04%, phenoxyethanol 2%/octenidine dihydrochloride 0.1%, mafenide acetate 5% chlorhexidine gluconate 1.5/cetrimid	After 20 min contact time with Suprathel-antiseptic matrix there were detectable CFU only with mafenide acetate and the control group.	Ryssel H, Andreas Radu C, Germann G, Kloeters O, Riedel K, Otte M, Kremer T. Suprathel-antiseptic matrix: in vitro model for local antiseptic treatment?

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		mafenide acetate 5% chlorhexidine gluconate 1.5/cetrimid 15%			15%. Antiseptic soaked suprathel sheets were placed onto agar plates with the tested bacteria. Incubation time was 20 min then the sheets were removed.		
Disinfection efficacy of Poviodne-iodine	Disinfection	PVP-I aqueous solution, PVPI surgical scrub	Non-spore forming bacteria, spore forming bacteria (Clostridia), Fungal hyphae, Fungal spores, Trichomonas vaginalis		please see article	PVP-I has a rapid killing action on vegetative cells of various bacteria and fungi in vitro. (Most of the organisms are killed within 1 min). Smooth surfaces (glass, metal) are also rapidly disinfected. Action on spores is weaker. (For fungal spore 1 ½ hour, for Clostridia and other bacilli 17 hour survival time).	Saggers B.A., Stewart G.T. Polyvinyl-pyrrolidoneiodine: an assessment of antibacterial activity.
Virucidal efficacy of disinfectants	Antiseptics	Ethanol, Isopropanol, Benzalkonium chloride, Iodophor, Sodium hypochlorite,	Coronaviruses and parvoviruses: Mouse hepatitis virus (MHV), Canine coronavirus (CCV), Kilham rat virus (KRV), Canine parvovirus (CPV)	suspension test, plaque assay, heat inactivation	The diluted disinfectants were mixed with an equal volume of stock virus and incubated for 10 minutes.	3 groups were formed. First group (iodophor, sodium hypochlorite, sodium chlorite, formaldehyde) killed both corona- and parvoviruses. Second group (ethanol, isopropanol, benzalkonium chloride and cresol soap) had	Saknimit M, Inatsuki I, Sugiyama Y, Yagami K. Virucidal efficacy of physico-chemical treatments against coronaviruses and parvoviruses of

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		Sodium chlorite, Cresol soap, Formaldehyde , Chlorhexidine digluconate				efficiency against corona but not parvoviruses. Third group had nearly no efficacy against either virus (chlorhexidine digluconate).	laboratory animals.
Virucidal efficacy	Antiseptics	Povidoneiodine solution, Chlorhexidine digluconate	Vaccinia virus, Bovine viral diarrhoea virus (BVDV), Poliovirus, Adenovirus, Polyomavirus SV40	quantitative suspension test	Betaisodona 80% exposure time 0.5,1,3,5,15,30,60 min.(with and without serum) Betaseptic 80% exposure time 0.5,1,3,5,15,30 min.(with and without serum)	Betaisodona solution showed virucidal efficacy against vaccinia virus, BVDV, Polyomavirus SV40 within 0.5 min and adenovirus type 5 within 3-5 min (with and without organic load). Betaseptic inactivated significantly all model viruses for virucidal testing including poliovirus type 1 within 5 min (with or without organic load).	Sauerbrei A, P Wutzler. Virucidal efficacy of povidone-iodine-containing disinfectants (2010)
Virucidal efficacy	Antiseptics	Liposomal povidone-iodine, povidoneiodine solution, peracetic acid (PAA),	Human Adenovirus subgenera C and D	Suspension test, nested PCR	PVP-I 0.125%, 0.5%, 2.5%(60 min exposure time), PAA 0.1%, 0.2%(60 min), 0.5%, FA 0.7%	PVP-I 0.125% killed most of the serotypes within 60 minutes. PCR did not reveal genomic destruction in most serotypes. PAA 0.5% did not inactivate the hexon gene of adenovirus types 22 and 44. Hexon gene of	Sauerbrei A, K Sehr, U Eichhorn, K Reimer, P Wutzler. Inactivation of human adenovirus genome by different groups of

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		formaldehyde(FA)				adenovirus type 22 was not altered by 0.7% formaldehyde.	disinfectants.(2004)
Virucidal activity	Antiseptics	povidoneiodine (type of product is not specified)	Influenza A	fluroescenceand chromogenicbased plaque inhibition assay, sialidase inhibiton assay, receptor binding inhibition and hemagglutinin inhibition assay		1.56 mg/ml PVP-I inhibited infections in MDCK (Madin-Darby canine kidney) cells of human and avian influenza A viruses, including H1N1, H3N2, H5N3 and H9N2 from 23.0-97.5%. PVP-I affected viral hemagglutinin rather than host-specific sialic acid receptors.	Sriwilaijaroen N, Wilairat P, Hiramatsu H, Takahashi T, Suzuki T, Ito M, Ito Y, Tashiro M, Suzuki Y. Mechanisms of the action of povidone-iodine against human and avian influenza A viruses: its effects on hemagglutination and sialidase activities
Bactericidal activity	Antiseptics	Glutaraldehyde, povidoneiodine (Betadine), nitrous acid (type of product is not specified)	Bacillus subtilis spores	suspension test, phrase contrast microscope		Glutaraldehyde or an iodine-based disinfectant (Betadine) did not cause detectable mutagenesis, and spores (termed alphabeta-) lacking the major DNA-protective alpha/beta-type, small, acid-soluble proteins (SASP) exhibited similar sensitivity to these agents. A recA mutation did not	Tennen R, Setlow B, Davis KL, Loshon CA, Setlow P.: Mechanisms of killing of spores of Bacillus subtilis by iodine, glutaraldehyde and nitrous acid.

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
						sensitize wild-type or alpha-beta- spores to Betadine or glutaraldehyde, nor did spore treatment with these agents result in significant expression of a recA-lacZ fusion when the treated spores germinated. Spore glutaraldehyde sensitivity was increased dramatically by removal of much spore coat protein, but this treatment had no effect on Betadine sensitivity. In contrast, nitrous acid treatment of wild-type and alpha-betaspores caused significant mutagenesis, with alphabeta- spores being much more sensitive to this agent. A recA mutation further sensitized both wild-type and alpha-betaspores to nitrous acid, and there was significant expression of a recA-lacZ fusion when nitrous acid treated spores germinated.	
Disinfection	Antiseptics and antimicrobias	Various Disinfectants and				Povidone iodine has a broad spectrum of germicidal activity and is effective against most	CT Spann, SC Taylor, JM Weinberg. Topical Antimicrobial

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
		antimicrobials povidone iodine (type of product is not specified)				bacteria, some bacterial spores, viruses, fungi and M. tuberculosis. Iodophors exert their antibacterial effects through a mechanism of cell wall penetration and oxidation and the release of free iodine.	Agents in dermatology
Bactericidal activity	Antiseptics	10% povidoneiodine solution (Betadine), 4% PVP-I scrub	504 multi resistant bacterial strains isolated from hospital acquired infections. S aureus, coagulase negative Staphylococci, Enterococci. E. coli, E aerogenes, K pneumoniae, S marcescens, P mirabilis, P aeruginosa, B cepacia, S maltophilia, Acinetobacter	micromethod	PVP-I solution diluted 1:2-1:80, over 1-5 min exposure time, PVP-I scrub diluted 1:2-1:48, over 1-5 min exposure	After 1 min exposure, 89.3% of the strains were susceptible to the PVP-I dermic solution (1:10 dilution). PVP-I scrub preparation 99% of the strains were sensitive at dilution 1:2 after 1 min, and 98.4% at 1:3.	O Traoré, S Fournet Fayard, H Laveran. An in vitro evaluation of the activity of povidone-iodine against nosocomial bacterial strains.
Preoperative povidone-iodine showers	Antiseptics	10% povidoneiodine (liquid detergent based)		Patients allocated to the povidoneiodine group took a shower with	Patients older than 18 years scheduled for elective and clean plastic surgery procedures on	Staphylococcal skin colonization was significantly lower in the povidone-iodine group ($p < 0.001$). No microorganism growth was observed on 33	Veiga DF, Damasceno CA, Veiga Filho J, Silva RV Jr., Cordeiro DL, Vieira AM, Andrade CH,

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
				liquid detergentbased povidoneiodine 10% 2 hours before surgery.	the thorax or abdomen were assigned randomly to the povidone-iodine group (n = 57) or to a control group (n = 57). Patients allocated to the povidoneiodine group took a shower with liquid detergent-based povidone-iodine 10% 2 hours before surgery. Quantitative skin cultures were obtained just before the preoperative scrub in the operating room. Samples were plated on hypertonic mannitol agar, blood agar, Sabouraud agar with chloramphenicol, and eosinmethylene	percent of the post shower skin cultures from patients in the povidone-iodine shower group compared with 0 percent of the cultures from patients in the control group. Colonies of fungi and enterobacteria were recovered in small amounts in both groups, and povidone-iodine showers did not significantly reduce skin colonization by these microorganisms.	Ferreira LM. Influence of povidoneiodine preoperative showers on skin colonization in elective plastic surgery procedures.

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
					blue agar. Samples were collected and processed, and results were assessed by blinded investigators.		
Virucidal activity and cytotoxicity	Antiseptics	Povidoneiodine solution (10 % Betaisodona), liposomal Povidoneiodine 5% formulation	Influenza A, Herpes Simplex virus type 1, Human Adenovirus type 8, human Rhinovirus type 14	XTT tetrazolium reduction assay EZ4U, lactate dehydrogenase assay, DNA fragmentation assay, TUNEL assay	PVP-I 10% Betaisodona solution diluted 1:1000 (0.009%),1:80(0.11%), 1:40(0.23%), 1:20 (0.45%) exposure time 0.5, 1, 1.5, 2, 5, 15, 30 min. Liposomal PVP-I 5% dilutions: 1:500(0.009%), 1:40 (0.11%), 1:20 (0.23%), 1:10 (0.45%) exposure times 0.5,1,1.5,2,5,15,30 min.	As to the virucidal activity against influenza A virus, herpes simplex virus type 1, adenovirus type 8 and human rhinovirus type 14, the liposomal formulation of PVP-I proved to be approximately as active as the aqueous one. Half maximum cytotoxic PVP-I concentrations were 0.01-0.07% for aqueous PVP-I and 0.03-0.27% for the liposomal PVP-I formulation.	P Wutzler, A Sauerbrei, R Klöcking, B Brögmann, K reamer. Virucidal activity and cytotoxicity of the liposomal formulation of povidone iodine.

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Conclusion on the efficacy of the product
Betadine solution is used as a skin disinfectant prior to injection, blood sampling, punctures, biopsy, transfusion, infusion and hygienic hand disinfectant. It is also used for total orpartial pre-surgery disinfection of the patient (disinfection bath). Betadine solution is bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses) and mycobactericide. Development of resistance to povidone iodine has not yet been described and is also not to be expected on account of its mechanism of action.

2.2.5.6. Occurrence of resistance and resistance management

According to Expert opinion_1997:
The formation of resistance of microorganisms has not yet been observed,and it is not anticipated. This phenomenon is due to the principle of the universal non-specific effect of iodine as oxidation material. It has been shown that in contrast to the other antiseptic ingredients (like chlorohexidingluconate and benzalconiumchloride) at altogether 353 strains of 9 species - all of which were clinically relevant and highly resistant pathogens - no resistance to Polyvidon-iodine could be established (SHIRAISHI and NAKAGAWA 1993)

HINGST etal. (1995, Attachment No.71) studied the epidemiology of microbial biocide resistance of the relevant bacteria strains (like pseudomonads, enterobacteria, E. coli. etc.) under the influence of Polyvidon-iodine preparation (in this case Braunol 2000®, company Braun was used). Neither formation of resistance nor an increased absolute level of resistance could be observed.

Recently some communications were published reporting on contaminations with supposedly 'resistant' bacteria strains in PVP-iodine products; they eventually stem from the same product manufactured in the USA.
According to the literature at expert's disposal (including international computer data banks) up to now there is no evidence of the existence of really primarily- resistant strains of bacteria. The lack of sensitivity with respect to Polyvidon- iodine preparations are due to a special structure, metabolism or special decomposition mechanism which has not yet been recorded. Various strains or types of pathogens possess eventually various sensitivity to the nonspecific effect of the liberated molecular iodine, being manifested in the longer efficiency period or in the higher ingredient concentration. Besides, the quality of Polyvidon-iodine preparation as well as the appropriate handling of the preparation is eventually of definite
importance.

The research group of ANDERSON and PANLILIO 1991,1992) has reported contaminations in Polyvidon-iodine preparations with pseudomonads (Pseudomonas cepacia and Pseudomonas aeruginosa). These authors have found, that the usual Polyvidon-iodine preparations normally kill pseudomonads very quickly at a free concentration of iodine of ^ 1 ppm. The American preparations affected with contamination contain an unusually low concentration of the free iodine (from 0.2 to 0.46 ppm). The special conditions of production (PVC-tubes and container) were advantageous for spiking it with pathogens and as a consequence, for formation of a thick mucous layer (Glykokalix). This way pathogens have mechanically protected themselves from the free iodine being already present in a concentration that is too low. In the subsequent laboratory experiments all of the pathogens always proved to be sensitive to PVP-iodine. The research group itself have emphasized that the pharmaceutical formulation is of great importance for the unlimited and secure efficacy of PVP-iodine preparations.

SASATSU and co-workers,1993 have published results concerning the various sensitivity of

methycillin-resistant Stapphylococcus aureus (MRSA) strains regarding the various antiseptic substances. These pathogens required longer efficiency periods, partially even longer than 4.5 minutes in the case of PVP-iodine (at concentrations < 0.8 per cent), too. However, it should be taken into consideration, that in the study an aqueous solution of a raw PVP-iodine material was utilized, and not a standardized PVP-iodine medicine. Data concerning the free iodine content in this preparation were not obtained.

LACEY and CATTO 1993 compared the sensitivity of 40 isolated MRSA clinical samples with methycillin sensitive Stapphylococcus aureus strains to PVP-iodine solution (it was not a ready preparation). The authors did not record any difference between the sensitivity of methicillinresistant and -sensitive pathogens. Even in higher dilution, the bactericidal effect of PVPiodine to the Staphyllococus germs could be registered with a period of efficiency of 10 seconds. The highest bactericidal effectivness was achieved at a 1 minute period of efficiency. In the further experiments the group was engaged with possible selection of resistant pathogens. For this purpose the authors isolated germs which survived a 10 second period of efficiency. Then the germs were cultivated repeatedly, supposing that Staphylococcus germs possessing higher level of resistance were selected. However, the authors did not manage to do that. The cultivated 'survivor' germs possessed the same sensitivity; the lowest bactericidal concentration of PVP-iodine did not increase. The authors concluded that the observed variability to PVP-iodine was not a primary resistance or a formation of resistance, but a possible aggregation of bacteria cells. As a consequence, a prevented penetration of PVP-iodine has taken place.
Besides the widely investigated resistance of bacteria, also a growing number of studies were published in the recent years dealing with the appearance and the theoretical possibility of formation of disinfection materials and the antiseptic resistance.

LYON et al. 1987 describe a resistance mechanism against antiseptic substances (quaternary amines, acriflavin,ethydiumbromide, cadmium). Due to an aimed refluxsystem a decreased concentration of agents was present in the internal space of the cells in bacteria. This mechanism can only function if the target of microbial substances are present exclusively in the internal space of cells. However, for iodine this is not the case.

KAULFERS,1995 reports a resistance to mercury. This occurs as a consequence of the deactivation of active mercury ions in the cell by means of exclusion of the poisoned moiety. Although in certain occasions the formation of a mucosity or capsulation of pathogens causes increase of the-minimal inhibition concentration (MHK) values, however, this is not a stable property and is also not a real resistance phenomenon.

Exactly this case was reported by BROWN et al. in1995.
These authors concluded that increased contact periods with iodine were required for mucus covered bacterial colonies in order to achieve the peculiar cells of bacteria. A real resistance of bacteria to iodine can hardly be formed, or can not be formed at all since molecular iodine universally attacks the cell wall, cytoplasm membranes and intracellular structures - i.e. upon the building units, like enzymes. Consequently, in expert’s opinion, the declaration of the manufacturer in the information material is correct considering the present state of science. They state that 'for PVP-iodine there is no danger of specific primary resistance, as well as of formation of secondary resistance, during prolonged application'.
However, in individual cases (a special pathogen) one should decide if it is practical and effective to apply PVP-iodine under the given clinical circumstances. Particularly, e.g. in the case of an unusually long efficiency period, the application should be pointed out, and should not be propagated. This case corresponds to the statement present in the information material: 'Spores and certain virus-species, in general, are inactivated in an appropriate extent only after a longer efficiency period.'

Pub Med was searched to see if there is a change since 1997.
PubMed search has been conducted with following key words: povidone iodine resistance, PVP-I. (Limitation: humans)
Povidone iodine search gave 172 matches.
Most of the articles were not relevant. 3 articles were related in deed to povidone iodine resistance:
In one article 50 blood donors were evaluated in Brazil. On the first arm, 10% povidoneiodine/ two-stage technique was used. On the opposite arm, 0.5% chlorhexidine digluconate alcohol solution/one-stage technique was used. The authors found that microbial reduction was significantly higher for 10% povidone-iodine technique (98.57-98.87%) when compared with 0.5% chlorhexidine technique (94.38-95.06%). The species Leuconostoc mesenteroides and Staphylococcus hominis showed resistance to both disinfection techniques.(Celere et al.)

In second article 2632 patients were evaluated during 36 months in South-Africa. Patient with burns were evaluated especially those who had Pseudomonas aeruginosa wound infection. (34 patient) All isolates were sensitive to chlorhexidine, whereas 92.5% were resistant to povidone-iodine.(Coetzee et al.)

In France an in vitro evaluation was made of the activity of povidone iodine against nosocomial bacterial strains. When the micro method was carried out at 20 degrees C, 10.7% (54/504) of the strains were resistant to the PVP-I skin disinfectant (dilution 1:10) and 1.6% (8/504) were resistant to the handwashing formulations (dilution 1:3) after 1 min exposure. By increasing the temperature to 32 degrees C, the resistance rate to the skin disinfectant fell to 1.9% (10/504).(Traoré et al.)
Until 2000 in the medical databases there were no reports on povidone-iodine resistance, recently only 3 relevant articles can be found which are related to povidone iodine containing solutions.

2.2.5.7. Known limitations

The only limitation with povidone iodine is the slight discoloration on application. According to the Company Core Data Sheet the following contraindications are listed:

Contraindications
· Patients with known hypersensitivity to iodine or povidone
· Hyperthyroidism
· Other acute thyroid diseases

Special precautions for this product
For formulations to be used in surgical procedures.
In pre-operative preparation, avoid pooling beneath the patient. Prolonged exposure to wet solution may cause irritation or rarely, severe skin reactions. Chemical burns of skin due to pooling may occur. In instances of skin irritation, contact dermatitis or hypersensitivity, discontinue use. Do not heat prior to application.

For all povidone iodine containing products
Patients with goitre, thyroid nodules, or other non-acute thyroid diseases are at risk of developing thyroid hyperfunction (hyperthyroidism) from the administration of large amounts of iodine. In this patient population, povidone-iodine solution should not be applied for an extended period of time and to large areas of the skin unless strictly indicated. Even after the end of the treatment one should look for the early symptoms of possible hyperthyroidism and if necessary the thyroid function should be monitored. It should not be used prior to or after radioiodine scintigraphy or radioiodine treatment of

thyroid carcinoma.
Newborns and small infants are at increased risk of developing hypothyroidism from the administration of large amounts of iodine. Because of the permeable nature of their skin and their increased sensitivity to iodine, the use of povidone-iodine should be kept to the absolute minimum in newborns and small infants. A check of the child's thyroid function (e.g. T4 levels and TSH levels) may be necessary. Any oral ingestion of povidone-iodine by the infant must be avoided.

2.2.5.8. Evaluation of the label claims

Povidone ioded has bactericide (including MRSA), fungicide, selective virucide (Norovirus, Adenovirus, enveloped viruses) and mycobactericide effects as it is supported in the efficacy studies.
Thanks to these effects povidone iodine containing Betadine solution is indicated:
• as a skin disinfectant to be used prior to injection, blood sampling, punctures, biopsy, transfusion, infusion
• for disinfection of the skin prior to surgery
• for total or partial pre-surgery disinfection of the patient (disinfection bath)
• hygienic hand disinfectant.

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

2.2.6. Risk assessment for human health

No new studies were submitted to assess the toxic properties of Betadine solution. All of its components are classified according to Regulation 1272/2008/EC, therefore the product is classified according to principles laid down in that Regulation.

2.2.6.1. Assessment of effects on Human Health

Skin corrosion and irritation

Conclusion used in Risk Assessment – Skin corrosion and irritation	
Value/conclusion	Not irritating to the skin
Justification for the value/conclusion	Based on intrinsic properties of individual components of the biocidal product.
Classification of the product according to CLP and DSD	No classification required.

Data waiving	
Information requirement	Annex III of BPR, point 8.1 "Skin corrosion or skin irritation"
Justification	Studies on potential skin corrosive or skin irritating properties of the product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012), section 8.1 "Skin corrosion or skin irritation": "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to

	the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition of the product is known. For each components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by skin irritation to the extent which would require classification of the mixture, the product is not need to be classified.

Eye irritation

There is no experimental data available regarding eye irritation effect of Betadine solution.

Conclusion used in Risk Assessment – Eye irritation	
Value/conclusion	Causes serious eye damage
Justification for the value/conclusion	Based on intrinsic properties of individual components of the biocidal product.
Classification of the product according to CLP and DSD	According to the CLP the product has Eye Damage 1. Hazard Class and Category Code because of the active substance. The relevant Hazard Statement Code is H318.

Data waiving	
Information requirement	Annex III of BPR, point 8.2 "Eye irritation"
Justification	Studies on potential eye damaging or eye irritating properties of the product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012), section 8.2 "Eye irritation": "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition of the product is known. For each components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, the biocidal product is need to be classified with respect to local effects on the eyes. It causes eye damage because of the active substance.

Respiratory tract irritation

There is no data available on respiratory irritation effect either of povidone iodine or Betadine Antiseptic Solution in experimental animals.

Conclusion used in the Risk Assessment – Respiratory tract irritation	
Value/conclusion	Based on intrinsic properties of individual components of the biocidal product is not irritating to the respiratory tract.
Justification for the value/conclusion	Based on intrinsic properties of individual components of the biocidal product.
Classification of the product according to CLP and DSD	No classification required.

Data waiving	
Information requirement	Up to May 2018, there are currently no standard tests and no OECD TG available for respiratory irritation and there is no testing requirement for respiratory irritation under the Biocides Regulation. Consequently respiratory irritation is not included in the testing strategies suggested in this Guidance. There are no testing requirements for respiratory irritation under the BPR.
Justification	Studies on potential respiratory tract irritation properties of the biocidal product are not required. Up to May 2018, there are no testing requirements for respiratory irritation under the BPR. Nevertheless, Annex I, chapter 3.8.3.4.5 of Regulation (EC) No. 1272/2008 (CLP) allows for extrapolation of the toxicity of a mixture that contains substances classified with respect to specific target organ toxicity after single exposure category 3 (STOT SE, Cat. 3; H335) based on valid data on all components in the mixtures classified with STOT SE, Cat. 3; H335. The exact composition of the product is known. For each of the individual components in the products, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by respiratory tract irritation the product is not need to be classified.

Skin sensitization

Conclusion used in Risk Assessment – Skin sensitisation	
Value/conclusion	Not sensitising to skin.
Justification for the value/conclusion	Based on intrinsic properties of individual components of the biocidal product.

Classification of the product according to CLP and DSD	No classification required.

Data waiving	
Information requirement	Annex III of BPR, point 8.3 "Skin sensitisation"
Justification	Studies on potential skin sensitisation properties of the biocidal product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012), section 8.3 "Skin sensitisation" : "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition of the product is known. For each of the individual components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by skin sensitisation the product is not need to be classified.

Respiratory sensitization (ADS)

There are only limited data available regarding acute toxicity of povidone iodine or Betadine Antiseptic Solution in experimental animals. Lack of animal data is justifiable with data from human studies.

Conclusion used in Risk Assessment – Respiratory sensitisation	
Value/conclusion	Not sensitising to respiratory tract.
Justification for the value/conclusion	Based on intrinsic properties of individual components of the biocidal product.
Classification of the product according to CLP and DSD	No classification required.

Data waiving	
Information requirement	Annex III of BPR, point 8.4 "Respriatory sensitisation" (ADS)
Justification	Studies on potential respiratory sensitisation properties of the biocidal product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012) section 8.4 "Respiratory sensitisation": "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in

	Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition of the biocidal product is known. For each of the individual components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by respiratory sensitisation the product is not need to be classified.

Acute toxicity

Acute toxicity by oral route

Value used in the Risk Assessment – Acute oral toxicity	
Value	Not acutely toxic via the oral route.
Justification for the selected value	Based on intrinsic properties of individual components of the biocidal product
Classification of the product according to CLP and DSD	No classification required.

Data waiving	
Information requirement	Annex III of BPR, point 8.5 "Acute toxicity"
Justification	Studies on the potential acute oral toxicity of the biocidal product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012), section 8.5 "Acute toxicity": "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition is known. For each of the individual components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by acute oral toxicity the product is not need to be classified.

Acute toxicity by inhalation

There is no data available regarding acute inhalation toxicity of povidone iodine or Betadine Antiseptic Solution in experimental animals.

Value used in the Risk Assessment – Acute inhalation toxicity	
Value	Not acutely toxic via the inhalation route.
Justification for the selected value	Based on intrinsic properties of individual components of the biocidal product
Classification of the product according to CLP and DSD	No classification required.

Data waiving	
Information requirement	Annex III of BPR, point 8.5 "Acute toxicity"
Justification	Studies on the potential acute oral toxicity of the biocidal product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012), section 8.5 "Acute toxicity": "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition is known. For each of the individual components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by acute inhalation toxicity the product is not need to be classified.

Acute toxicity by dermal route

Value used in the Risk Assessment – Acute dermal toxicity	
Value	Not acutely toxic via the dermal route.
Justification for the selected value	Based on intrinsic properties of individual components of the biocidal product.
Classification of the product according to CLP and DSD	No classification required.

Data waiving

Information requirement	Annex III of BPR, point 8.5 "Acute toxicity"
Justification	Studies on the potential acute oral toxicity of the biocidal product are not required. According to Annex III, Title 1 of the BPR (Regulation (EU) 528/2012), section 8.5 "Acute toxicity": "testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected." The exact composition is known. For each of the individual components in the product, valid data on the intrinsic properties are available through state-of-the-art safety data sheets. There is no indication of synergistic effects between any of the components. Consequently, classification of the mixtures can be made according to the rules laid down in Regulation (EC) No 1272/2008 (CLP) and testing of the components and/or of the biocidal product itself is not required. According to the CLP principles, as no component of Betadine solution is classified by acute dermal toxicity the product is not need to be classified.

Information on dermal absorption

Value(s) used in the Risk Assessment – Dermal absorption	
Substance	Iodine PT-2
Value(s)*	12 % in case of the all dilutions of the Betadine solution.
Justification for the selected value(s)	According to the CAR of the active substance the dermal absorption value is 12%.

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

In case of the Betadine solution none of the components are substance of concern.

Available toxicological data relating to a mixture

In case of the Betadine solution none of the components are substance of concern.

2.2.6.2. Exposure assessment

Identification of main paths of human exposure towards active substance(s) and substances of concern from its use in biocidal product

Summary table: relevant paths of human exposure		
Exposure	**Primary (direct) exposure**	**Secondary (indirect) exposure**

path	Industrial use	Professional use	Non-professional use	Industrial use	Professional use	General public	Via food
Inhalation	N/A	Yes	Yes	N/A	No	No	No
Dermal	N/A	Yes	Yes	N/A	No	No	No
Oral	N/A	No	No	N/A	No	No	No

The main path of exposure to Betadine solution is via skin contact. The disinfection solution is a rinse-off products that allow only for a short (about 2 min.) contact time. Iodine as a 1.2% aqueous solution as in the biocidal product is only semi-volatile. The generation of an inhalable mist during bathing 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.

Betadine solution is a concentrate, for some applications it must be diluted in a 1:100 ratio before use. The empty bottles are discarded, and the diluted solution is rinsed off from the body of the patient into the canalisation system; therefore no further human exposure is expected.

List of scenarios

Summary table: scenarios			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	Mixing & loading	Manual dilution of the concentrate – primary	professionals
2.	Bathing – professionals	Disinfecting bathing prior surgeries – primary	professionals
3.	Bathing – non-professionals	Disinfecting bathing prior surgeries – primary (patient's exposure)	non-professionals
4.	Hand disinfection	Hygienic hand disinfection - primary	professionals

Industrial exposure

Industrial use is not supported.

Professional exposure

Scenario 1 Mixing & loading

Before the disinfecting bath the product must be diluted with water to make a working solution. As the packaging is a bottle with volume of 0.03-1 L, *Mixing & loading Model 2* from *Biocides Human health Exposure Methodology* was selected. Inhalation exposure in this scenario is deemed negligible. Default number of operations is 4 (see Recommendation no. 9 of the BPC *Ad hoc Working Group on Human Exposure: Hand*

disinfection in hospitals) and as the working solution must be prepared fresh, prior application, number of mixing & loading steps is also 4.

Description of Scenario 1		
The user will pour approximately 30 ml of concentrate into a vessel with water, then mix it carefully. The professional health worker can be expected to wear dispensable rubber gloves during the operation.		
	Parameters	Value
Tier 1	Number of events	4/day
	Concentration of a.s.	1.2%
	Hand exposure	3.2 mg event
	Dermal absorption	12%
	Body weight	60 kg
Tier 2	Protection factor of gloves	90%

Calculations for Scenario 1

Summary table: estimated exposure from professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** mg/kg bw	**Estimated dermal uptake** mg/kg bw	**Estimated oral uptake**	**Estimated total uptake** mg/kg bw
Scenario 1	Tier 1	N/A	0.00031	N/A	0.00031
Scenario 1	Tier 2	N/A	0.000031	N/A	0.000031

Scenario 2 Disinfecting bath-professional

There is no suitable model for giving a disinfecting bath. As a worst case, it is assumed that a full liquid film covers the nurse's hands (film thickness is 0.1 mm, surface of hands 820 cm^2, see Recommendation no. 14 of the BPC *Ad hoc Working Group on Human Exposure: Default human factor values for use in exposure assessments for biocidal products*). Number of applications is 4 (see Scenario 1).

Inhalation exposure is possible, as the iodine continuously evaporates from the body of the patient. It is calculated with ConsExpo, as advised in Recommendation 9 (see Appendix 3.2).

Description of Scenario 2		
Using a sponge or a cloth the nurse evenly smears the working solution on the body of the patient, leaves it on for 2 minutes, then rinses it off.		
	Parameters	Value
Tier 1	Number of events	4/day

	Concentration of a.s.	0.012%
	Amount of solution on hands	8.2 g/event
	Dermal absorption	12%
	Body weight	60 kg
Tier 2	Protection factor of gloves	90%

Calculations for Scenario 2

Summary table: estimated exposure from professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** mg/kg bw	**Estimated dermal uptake** mg/kg bw	**Estimated oral uptake**	**Estimated total uptake** mg/kg bw
Scenario 1	Tier 1	0.00000373	0.0079	N/A	0.0079
Scenario 1	Tier 2	0.00000373	0.00079	N/A	0.00079

Combined scenarios

Summary table: combined systemic exposure from professional uses					
Scenarios combined	**Tier/PPE**	**Estimated inhalation uptake** mg/kg bw	**Estimated dermal uptake** mg/kg bw	**Estimated oral uptake** mg/kg bw	**Estimated total uptake** mg/kg bw
Scenarios 1+2	Tier 1	0.00000373	0.00821	N/A	0.00821
Scenarios 1+2	Tier 2	0.00000373	0.000821	N/A	0.000825

Scenario 4 Hand disinfection

For hand disinfection the neat product is used. The product is rubbed to the skin of the hand, left on it for 1 minute then washed off. Default number of operations for professional workers is 10 (see Recommendation no. 9 of the BPC *Ad hoc Working Group on Human Exposure: Hand disinfection in hospitals*.

Description of Scenario 4		
According to the Recommendation, the amount of product used for disinfection of both hands is 3 g. Inhalation exposure is deemed negligible for this use.		
	Parameters	Value
Tier 1	Number of events	10/day

	Concentration of a.s.	1.2%
	Hand exposure	3 g
	Retention	1%
	Dermal absorption	12%
	Body weight	60 kg

Calculations for Scenario 4

Summary table: estimated exposure from professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** mg/kg bw	**Estimated dermal uptake** mg/kg bw	**Estimated oral uptake**	**Estimated total uptake** mg/kg bw
Scenario 4	Tier 1	N/A	0.00031	N/A	0.0072

Non-professional exposure

Scenario 3 Disinfecting bath-non-professional

The surface of the patient is covered with the disinfecting solution (surface area 16600 cm^2), left on for 2 minutes, the rinsed off. It produces a 0.1 mm thick liquid film on the skin. According to Recommendation 9 after rinsing 1% remains on the skin, which is available for absorption.

Inhalation exposure is calculated as in Scenario 2 but with only one event instead of four. Only Tier 1 calculation is performed, as PPE can not be worn.

Description of Scenario 3		
	Parameters	Value
Tier 1	Number of uses	1/day
	Amount of solution on the skin	166 g
	Concentration of a.s.	0.012%
	Retention	1%
	Dermal absorption	12%
	Body weight	60 kg

Calculations for Scenario 3

Summary table: estimated exposure from professional uses

Exposure scenario	Tier/PPE	Estimated inhalation uptake mg/kg bw	Estimated dermal uptake mg/kg bw	Estimated oral uptake	Estimated total uptake mg/kg bw
Scenario 2	Tier 1	0.000000932	0.0004	N/A	0.00018

Exposure of the general public

The general public is not exposed to the product.

Dietary exposure

The active substance from the product does not enter the food chain.

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

Betadine splution is produced in industrial environment with automated equipment, the personnel is properly trained about the hazards of the product and its components and wear suitable personal protective equipment.

Summary of exposure assessment

Scenarios and values to be used in risk assessment			
Scenario number	**Exposed group (e.g. professionals, non-professionals, bystanders)**	**Tier/PPE**	**Estimated total uptake**
1.	professionals	Tier 1	0.00031
1	professionals	Tier 2	0.000031
2.	professionals	Tier 1	0.0079
2.	professionals	Tier 2	0.00079
3.	non-professionals	Tier 1	0.00018
4.	professionals	Tier 1	0.0072

2.2.6.3. Risk characterisation for human health

Reference values to be used in Risk Characterisation

Reference	Study	NOAEL (LOAEL)	AF	Correction for oral absorption	Value
AELshort-term	Upper intake level deduced by Scientific committee on food	600 µg/d	-	-	0.01 mg/kg bw/d
AELmedium-term					
AELlong-term					
AEC			-	-	1 mg/m^3

					(0.1 ppm)
ARfD	n.a.	-	-	-	-
ADI	n.a.	-	-	-	-

Maximum residue limits or equivalent

MRLs or other relevant reference values	Reference	Relevant commodities	Value
AEL = UL (Upper Intake Level)	Iodine CAR	food	Europe: 600 µg/day for adult (0.01 mg/kg bw/d.), 200 µg/day for infant, toddler and child (1-3 years old), 250 µg/day for child of 4-6 years old[8]. USA: 1200 µg/day, 0.02 mg/kg bw/d.
ARfD	Iodine CAR	-	Not applicable. Substance is not acute toxic or harmful.
Drinking water limit	Iodine CAR	water	No drinking water limit is established. 30 µg/L is a threshold proposed and calculated is based on 10% Upper Intake Level and a daily intake of 2 L drinking water
MRL	Competent Authorities meetings of 17 March and 17 May 2017	Food of animal origin	No MRL required.

The Scientific Committee on Food (SCF) based the iodine tolerable upper intake (UL) on studies of short term duration and in a small number of subjects (n=10-32). For iodine intakes about 1700-1800 µg/day, the studies showed an increased serum thyroid-stimulating hormone (TSH) and thyrotropin-releasing hormone (TRH), but these changes were considered marginal and not associated with any clinical adverse effects. The results were supported by a five years study where, for approximately similar iodine intakes, no clinical thyroid pathology occurred. An uncertainty factor of 3 was selected to derive the UL for adults. The ULs for toddlers and children were derived by adjustment of the adult UL on the basis of metabolic weight, since there is no evidence of increased susceptibility in children. The SCF adopted the value of 600 µg/day as a UL for adults including pregnant and lactating women (2002). The UL for toddlers was set at 200 µg/day.
Nevertheless, in the iodine CAR, it is reported that a healthy adult can tolerate iodine intake of more than 1000 µg/day without any adverse effects.
As indicated by the SCF, the tolerable upper intake levels ULs are not a safety threshold. Indeed, the SCF indicated that the UL "may be exceeded for short periods without appreciable risk to the health of the individuals concerned".

Furthermore, besides the exposure due to the disinfection procedure the user is also exposed to dietary source of iodine. An assessment for dietary exposure is included. User is exposed to iodine through background in tap water, milk (due to natural sources and feed supplementation) and by other dietary sources.

Risk for industrial users

Industrial use is not supported.

Risk for professional users

Systemic effects

Task/ Scenario	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 1	Tier 1	0.01	0.00031	3.1	yes
Scenario 1	Tier 2	0.01	0.000031	0.31	yes
Scenario 2	Tier 1	0.01	0.0079	79	yes
Scenario 2	Tier 2	0.01	0.00079	7.9	yes
Scenario 4	Tier 1	0.01	0.0072	72	yes

Combined scenarios

Scenarios combined	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 1+2	Tier 1	0.01	0.00821	82.1	yes
Scenario 1+2	Tier 2	0.01	0.000825	8.25	yes

Local effects

Betadine solution is not irritating or sensitizing to the skin and eyes, therefore local effects are not expected.

Conclusion
The risk for professionakl users from the application of Betadine solution is within acceptable levels with or without using PPE.

Risk for non-professional users

Systemic effects

Task/ Scenario	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 3	Tier 1	0.01	0.00018	1.8	yes

Local effects

Patients will be exposed to the diluted solution only, which lacks any irritating properties.

Conclusion

The risk for non-professionakl users from the use of Betadine solution is within acceptable levels.

Risk for the general public

General public is not affected.

Risk for consumers via residues in food

Iodine is a biological active substance it is needed for the proper functioning of thyroid. Its main source is drinking water and food.

The iodine concentration of water is highly variable (e.g. from 2–140 µg/L in tap water in Denmark; from 0.2–15.5 µg/L (median 2.6 µg/L) and decreasing from north to south in 26 regions of Germany). In Hungary it varies between 30 and 1200 µg/L. Where the intake is lower than the optimal, sodium iodide, sodium iodate, potassium iodide and potassium iodate may be added to foods and food supplements.

The iodine content of foods is highly variable between food categories as well as within each category. The richest sources are marine products (such as fish, shellfish, molluscs, seaweed), eggs and milk, as well as their derivatives and iodised salt. Iodine content of milk and eggs is influenced by feeding and hygienic practices. According to WHO/UNICEF iodine fortification of salt has been implemented in 40 European countries, being mandatory in 13 countries, voluntary in 16 and not regulated in the remaining countries; the amount of iodine added varies from 10–75 mg/kg salt with a majority of values in the range 15–30 mg/kg. The iodine content of certain foods for healthy people is regulated, for example of infant and follow-on formulae.

According to the EFSA's paper: *Scientific Opinion on Dietary Reference Values for iodine* consuming amount of 70 µg iodine per day (0.00112 mg/kg bw/day) is necessary to avoid signs of goitre. Taking into consideration the dose coming from the worst case of disinfecting bath, the final dose is still acceptable.

0.00112 + 0.00821 = 0,00933 (**93.3%** of UL)

However, the recommended intake is 200 µg iodine per day (0.00333 mg/kg bw/day). In case the professional workers receive a proper amount of iodine with their food and do not use PPE during disinfection, the total dose exceeds the upper intake level.

0.00333 + 0.00821 = 0.01154 (**115,4%** of UL)Therefore the workers should be warned to use gloves during the disinfecting bath or wash their hands after the procedure.

In case of hygienic hand disinfection no PPE can be worn and the exposure also exceeds the UL:

0.00333 + 0.0072 = 0.01053 (**105,3%** of UL)

It should be noted that in the calculation of the hand disinfection exposure it was assumed that all residues on the skin would be absorbed and the consequent hand washes would not remove the iodine from the earlier disifection, which is not realistic. The actual exposure would be lower. In addition as it was shown above, exceeding the upper intake

level most probably would not harm the health of the user, therefore the risk in this case is deemed acceptable.

Risk assessment for the environment

Effects assessment on the environment

The stable isotope of iodine, ^{127}I, is a naturally occurring, ubiquitous constituent of the earth's crust and the least abundant of the halogen elements. In the course of the development of the earth, iodine has been leached from the surface soil by snow, rain, and glaciations and carried into the sea. This process has been associated with a constant decrease of iodine background levels in soil and a constant increase of its concentration in sea water, which now ranges between 45 and 60 µg iodine/L. Background concentrations of iodine in soil vary between 0.5 and 20 mg iodine/kg whereas concentrations between 0.5 and 380 ppm are found in bedrock, with maximum values in sedimentary bedrock. The background values in rain water (0.1 to 20 µg iodine/L) are comparable to those of surface water.

The table below provides an overview on environmental background levels of iodine.

Background levels of iodine from natural sources in different environmental compartments

Compartment	**Iodine background level**
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
Surface freshwater	0.5 - 20 µg/L
Marine water	45 - 60 µg/L
Rain water	0.1-15 µg/L
Freshwater sediment	Typically: 6 mg/kg
Marine sediment	Typically: 3-400 mg/kg
Air	Atmosphere: 10-20 ng/m^3 Atmospheric concentration: over land 2-14 ng/m^3; over ocean 17-52 ng/m^3 Marine air contains: 100 µg/l (may refer to local inhalable air)

The results of the toxicity tests on organisms in the aquatic compartment (fish, aquatic invertebrates, algae) are presented in Table 3 (ECHA, 2013; U.S. EPA, 2006b). They indicate that iodine is acutely toxic to aquatic species. Daphnia magna showed the highest sensitivity (EC_{50} 0.315 mg/L iodine in a study using PVP iodine).

Toxicity of iodine, iodide and iodate for aquatic species

Species	**Test**	**L/EC_{50} (mg/L) Iodine**	**L/EC_{50} (mg/L) Iodide**	**L/EC_{50} (mg/L) Iodate**
Oncorhynchus mykiss	Acute toxicity, 96 h, LC_{50}	1.67	3780	220
Lepomis	Acute toxicity, 96 h,	0.61		

macrochirus	LC_{50}			
Daphnia magna	Acute toxicity, 48 h, LC_{50}/Immobilization, EC_{50}, 48 h	0.315*, 0.59	0.83	58.5
Desmodesmus subspicatus	Growth inhibition, 72 h, ErC_{50}	1.3		
Activated sewage sludge micro-organisms	Respiration inhibition, 3 h, EC_{50}	290		

*The study has been conducted using PVP iodine.

Results of acute terrestrial toxicity tests on earthworms, plants and soil micro-organisms are available (Table 4; ECHA, 2013). Out of 6 tested plant species, *Avena sativa* and *Allium cepa* were the species with the highest and lowest sensitivity to iodine in terms of seedling emergence and growth (21-day EC_{50} 13.4 mg/kg dwt and 26.7 mg/kg dwt, respectively).

Table 4: Toxicity of iodine for terrestrial species

Species	**Test**	**L/EC_{50} (mg/kg dwt) Iodine**
Eisenia fetida	Acute test, 14 d LC_{50}	1000
Avena sativa	Seedling emergence and growth, 21 d, EC_{50}	13.4
Allium cepa	Seedling emergence and growth, 21 d, EC_{50}	26.7
Soil microorganisms	Respiration inhibition, 28 d, EC_{50}	148.7
Soil microorganisms	Nitrate formation, 28 d, EC_{50}	82.6

The PNEC values are summerised below.

Compartment	**iodine species**	**PNEC value**
STP	iodine (I_2)	2.9 mg/L
surface water	iodine (I_2)	0.00032 mg/L
	iodate (IO_3^-)	0.0585 mg/L
	iodide (I^-)	0.00083 mg/L
freshwater sediment	-	not used (I_2: 0.016 mg/kg, IO_3^-: 2.84 mg/kg and I^-: 0.04 mg/kg)
Seawater	iodine (I_2)	0.000059 mg/L
	iodine (I_2 in product)	0.000032 mg/L
	iodate (IO_3^-)	0.00585 mg/L

	iodide (I^-)	0.000083 mg/L
marine sediment	-	not used
terrestrial	iodine (I2)	0.0118 mg/kg_{wwt}
	iodate (IO3-)	0.304 mg/kg_{wwt}
	iodide (I-)	0.0043 mg/kg_{wwt}

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

The product contains 10% PVP-Iodine as an active substance. There is one non-active component that could be ecotoxicologically relevant, which is the ethoxylated Nonylphenol (CAS no.: 9016-45-9). It is classified as Aquatic Chronic 2. However, the concentration of this constituent is under 0.1% in the product.

Further Ecotoxicological studies

Data waiving	
Information requirement	No additional data are required
Justification	There are valid data available on each of the relevant components and synergistic effects are not expected.

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

Data waiving	
Information requirement	No additional data are required
Justification	No additional test on other target organisms is needed.

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

Data waiving	
Information requirement	No additional data are required
Justification	The product is not in the form of bait or granules

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

Data waiving	
Information requirement	No additional data are required
Justification	The product is not in the form of bait or granules

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

Not relevant.

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

The product is predominantly applied indoors, mainly in hospitals and other public health institutions although other fields of use are also possible to a negligible extent. The main emission pathway to the emvironment is considered via STP.
See Fate and distribution in exposed environmental compartments for further details.

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

Conclusion used in Risk Assessment – Further studies on fate and behaviour in the environment	
Value/conclusion	
Justification for the value/conclusion	
Data waiving	
Information requirement	No additional data are required
Justification	No additional studies on fate and behaviour are needed

Leaching behaviour (ADS)

Not relevant.

Testing for distribution and dissipation in soil (ADS)

Data waiving	
Information requirement	No additional data are required
Justification	No additional test on distribution in soil is needed

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

Data waiving	
Information requirement	No additional data are required
Justification	No additional test on distribution in water is needed

Testing for distribution and dissipation in air (ADS)

Data waiving	
Information requirement	No additional data are required

Justification	No additional data on distribution in air are needed

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

Not relevant.

Acute aquatic toxicity

Data waiving	
Information requirement	No additional data are required
Justification	No additional test on aquatic toxicity is needed

Chronic aquatic toxicity

Data waiving	
Information requirement	No additional data are required
Justification	No additional test on aquatic toxicity is needed

Aquatic bioconcentration

Data waiving	
Information requirement	No additional data are required
Justification	No additional test on bioconcentration is needed

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

Not relevant.

Exposure assessment

General information

Assessed PT	PT 1
Assessed scenarios	Scenario 1: Skin disinfection by professionals in the health care sector
ESD(s) used	Environmental Emission Scenarios for biocides used as human hygiene biocidal products, January 2004
Approach	Scenario 1: Average consumption
Distribution in the	Calculated based on ECHA Guidance on the BPR, Vol IV Part

environment	B+C, October 2017. STP simulation is based on the CAR
Groundwater simulation	Not performed.
Confidential Annexes	NO
Life cycle steps assessed	Scenario n: Production: No Formulation No Use: Yes Service life: No
Remarks	

The Betadine solution product is intended to be used typically in hospitals and other health care institutes by professionals as a skin and hand disinfectant.

The detailed description of the intended uses are as follows:

- skin disinfectant, prior to injection, blood sampling, punctures, biopsy, transfusion, infusion
- skin disinfection, prior to surgery
- aseptic treatment of wounds
- treatment of bacterial and fungal diseases
- total or partial pre-surgery disinfection of the patient
- hygienic hand disinfectant

Some of these uses ("aseptic treatment of wounds" and "treatment of bacterial and fungal diseases") do not fall within the scope of the BPR. Therefore, they have not been taken into account during risk assessment.
The "hygienic hand disinfectant" use as liquid soap disinfectant is covered by the recommended scenario in the ESD for skin and hand application in hospitals based on the average consumption (Table 4.5), modified by the WG-V-2014 agreement on the consumption of active ingredient per bed (QsustbedN and QsustbedS for nursing staff and surgical staff, respectively) calculation.
It is considered that the "total or partial pre-surgery disinfection of the patient" and "skin disinfection, prior to surgery" uses are also partially covered by the previously mentioned scenario even if it is not used by the surgical staff, but it is used on the patients (see below for details).
The remaining skin disinfectant uses, such as the applications in the course of "prior to injection, blood sampling, punctures, biopsy, transfusion, infusion" are also included in the scenario for skin and hand application in hospitals.
The emissions from private uses are not taken into account, because those uses are not intended for biocidal purposes but primarily for medicinal ones.

Emission estimation

Scenario 1 – Skin disinfection by professionals in the health care sector

The used amount is 3 g/application in case of using it undiluted as a hygienic hand disinfectant. When it is used prior to surgery on patients, the applied amount for the

whole body (16600 cm^2) can be derived from the 3 g of application on hands (820 cm^2) and then it is 0.61 g product/event (61 g of the 1% solution). In addition, the operative site on the patient is treated just before the operation in the operating room. It is assumed that the surface is 10% of the whole body (1 mg product/cm^2) and the number of treatments is as much as the surgical hand scrubs as a worst case. Although there are no harmonised scenarios and default values for these kind of applications, it is the opinion of the HU CA that these parameters are safe enough especially with regard to the number of treatments, because more hand scrubs are performed for a surgical operation.
The product, depending on the different disinfection uses, is rinsed off or remains on the skin or clothing for a period of time. Since the emission to air is not considered to be relevant as iodide and iodate are assumed not to be volatile as stated in the CAR, the fraction released to the wastewater is set to 1 as a default.
The release to wastewater is calculated based on the ESD PT1 hospital scenario supplemented with the TAB agreement (v1.3; WG-V-2014) on the calculation of the consumption of active ingredient per bed.

Input parameters for calculating the local emission			
Input	**Value**	**Unit**	**Remarks**
Scenario: Skin disinfection by professionals in the health care sector			
Number of beds in model hospital	400	-	D
Fraction released to wastewater	1	-	D
Efficient dose rate of the hand disinfectant - for nursing staff - for patients	 0.003 0.0166+ 0.00061	kg/event	S, see above
Number of hospital personal per bed	1.5	FTE/bed	D
Fraction of active substance in the hand disinfectant	0.0012	-	S, 10% PVP-Iodine
Number of disinfection events/FTE/day	10	1/FTE*d	D
Consumption of active ingredient per bed - for nursing staff - for patients	 5.4E-05 3.1E-05	kg/bed*d	TAB v1.3; ENV34

Calculations for Scenario 1

Resulting local emission to relevant environmental compartments		
Compartment	**Local emission ($Elocal_{compartment}$) [kg/d]**	**Remarks**

Resulting local emission to relevant environmental compartments		
Compartment	**Local emission ($Elocal_{compartment}$) [kg/d]**	**Remarks**
Elocalwater	0.034	

Fate and distribution in exposed environmental compartments

The detailed fate and behaviour of the active substance can be found in the CAR of Iodine (including PVP-iodine).
Iodine and iodine compounds are ubiquitously distributed and there is a natural cycle of iodine species in the environment. Environmental background values as presented in the table above (in section 2.2.8.1 Effects assessment on the environment) are likely to be encountered for soil, water and air.
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 and iodate. In surface waters, the proportion of iodide to iodate will vary depending on the microbial activity and the release of iodine species from terrestrial sources.

Identification of relevant receiving compartments based on the exposure pathway									
	Fresh-water	Freshwater sediment	Sea-water	Seawater sediment	STP	Air	Soil	Ground-water	Other
Scenario 1	yes	yes	n.r.	n.r.	yes	no	yes	yes	no

nput parameters (only set values) for calculating the fate and distribution in the environment			
Input	Value	Unit	Remarks
Molecular weight	253.81	g/mol	I_2
Log Octanol/water partition coefficient	not relevant	Log 10	
Organic carbon/water partition coefficient (Koc)	165.8	l/kg	not used
solid-water partition coefficient in suspended matter	220	cm^3/g	CAR
solid-water partition coefficient in soil	5.8	cm^3/g	CAR
Biodegradability	not applicable		
soil-water partitioning coefficient	8.9		
suspended matter-water partitioning coefficient	55.9		

first order rate constant for removal from top agricultural soil	2.7E-04	1/d	

Calculated fate and distribution in the STP *[if STP is a relevant compartment]*			
Compartment	Percentage [%]		Remarks
	Scenario 1	Scenario n	
Air	0		not calculated, see the CAR for details
Water	80%		
Sludge	20%		
Degraded in STP	0		

Calculated PEC values

Summary table on calculated PEC values								
	PEC_{STP}	**PEC_{water}**	**PEC_{sed}**	**$PEC_{seawater}$**	**PEC_{seased}**	**PEC_{soil}**	**PEC_{GW}[1]**	**PEC_{air}**
	[mg/L]	[mg/L]	[mg/kg_{wwt}]	[mg/l]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[µg/l]	[mg/m^3]
Iodine	0.0136	0.0014	0.066	n.r	n.r.	0.082	15.38	n.r.
Iodide	0.0136	0.0014	0.066	n.r	n.r.	0.012	2.15	n.r.
Iodate	0.019	0.0019	0.09	n.r	n.r.	0.11	21.3	n.r.

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

Primary and secondary poisoning

Primary poisoning

It is not expected.

Secondary poisoning

According to the CAR, iodine has a low potential for bioconcentration and bioaccumulation. 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.

Risk characterisation

The Tables that show the PEC values contain results calculated not only for Iodine, but also for Iodide and Iodate. If an unacceptable risk is determined based on the PEC/PNEC ratios, then the given PECs are compared to the natural background level.

Atmosphere

Conclusion: 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. Consequently, air is not an environmental compartment of concern and the potential effect on the ozone layer could be considered as negligible.

Sewage treatment plant (STP)

Summary table on calculated PEC/PNEC values	
	$PEC/PNEC_{STP}$
Iodine	0.005
Iodide	n.a.
Iodate	n.a.

Conclusion: Although there are no PNEC values for the STP microorganisms with regard to the Iodide and Iodate, but since these species are less toxic for aquatic organisms than Iodine, based on the PEC/PNEC values determined for it, Iodine and its dominant species do not pose unacceptable risk to microorganism in the STP.

Aquatic compartment

Summary table on calculated PEC/PNEC values				
	$PEC/PNEC_{water}$	**$PEC/PNEC_{sed}$**	**$PEC/PNEC_{seawater}$**	**$PEC/PNEC_{seased}$**
Iodine	4.23	4.23		
Iodide	1.63	1.63		
Iodate	0.03	0.03		

Conclusion: The PEC/PNEC ratios indicate unacceptable risk, but the calculated 1.4 µg/L value for PECwater is within the 0.5-20 µg/L natural background concentration. The PEC/PNEC values for sediment are derived by EPM method, this is why they are same as the ratios for water and the predicted environmental concentration for sediment is well below the 6 mg/kg typical natural background concentration.

Terrestrial compartment

Calculated PEC/PNEC values	
	$PEC/PNEC_{soil}$
Iodine	6.96
Iodide	2.68
Iodate	0.37

Conclusion: The PEC/PNEC ratios indicate unacceptable risk, but the calculated 0.082 mg/kg value for PECsoil is below the lower limit of the typical natural background concentration for soil (0.5-20 mg/kg).

Groundwater

The calculated PEC values for groundwater exceed the limit value of 0.1 µg/L, but they are within the range of the natural background concentration of 1-70 µg/L. Therefore, the risk is considered acceptable.

Primary and secondary poisoning

Primary poisoning

Not relevant

Secondary poisoning

Conclusion: Iodine has a low potential for bio-concentration and bioaccumulation. 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.

Mixture toxicity

The product contains only one active substance and there is not any relevant substance in it beside the active substance.

Aggregated exposure (combined for relevant emmission sources)

Conclusion: Aggregated exposure assessment has not been performed because no guidance is currently available.

Overall conclusion on the risk assessment for the environment of the product
The main route to the environment is via the sewer. No unacceptable risk is expected for microorganisms in the sewage treatment plant, but on the basis of the PEC/PNEC ratios, a risk is identified for aquatic and terrestrial organisms as well. However, the calculated environmental concentrations are within the typical natural background concentrations. The calculated groundwater concentrations greatly exceed the limit of 0.1 µg/L, but this limit is granted by the Drinking Water Directive 98/83/EC and this value is for the organic pesticides described in the Directive. The calculated values are within the range of the natural background concentrations. It is concluded that the intended uses of the product do not pose unacceptable risk to the environment.

Measures to protect man, animals and the environment

Please see summary of the product assessment.

2.2.10. Assessment of a combination of biocidal products

The product is not intended to be authorised for the use with other biocidal products. Comparative assessment is not relevant.

3. ANNEXES

3.1. List of studies for the biocidal product

References for Risk Assessment:

ATSDR (U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry), 2004. Toxicological profile for iodine

Below H, Behrens-Baumann W, Bernhardt C, Völzke H, Kramer A, Rudolph P (2006) Systemic iodine absorption after preoperative antisepsis using povidone-iodine in cataract surgery – An Open Controlled Study. Dermatology 212, 41-46. DOI:10.1159/000089198

ECHA (2013) Assessment Report for Iodine according to Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

ECHA (2014) Recommendation no. 1 of the BPC Ad hoc Working Group on Human Exposure: Hand disinfection - PT 1 harmonisation of exposure determinants for professional users

ECHA (2015a) Biocides Human Health Exposure Methodology. First Edition, October 2015

ECHA (2015b) Guidance on the Biocidal Products Regulation: Volume III Human Health - Part B Risk Assessment, Version 2.0, October 2015

ECHA (2015c) Guidance on the Biocidal Products Regulation: Volume IV Environment - Part B Risk Assessment (active substances), Version 1.0, April 2015

ECHA (2015d) Recommendation no. 6 of the BPC Ad hoc Working Group on Human Exposure. Methods and models to assess exposure to biocidal products in different product types

ECHA (2016) Draft Guidance on the Biocidal Products Regulation, Volume V, Guidance on Disinfection By-Products, Version 1.0

EFSA NDA Panel (European Food Safety Authority, Panel on Dietetic Products Nutrition and Allergies), 2014. Scientific Opinion on Dietary Reference Values for iodine. EFSA Journal 12, 3660, 57 pp. doi:10.2903/j.efsa.2014.3660

Erdoğan MF, Tatar FA, Unlütürk U, Cin N, Uysal AR (2013) The effect of scrubbing hands with iodine-containing solutions on urinary iodine concentrations of the operating room staff. Thyroid 23,342-345. doi: 10.1089/thy.2012.0325.

European Commission, Directorate-General for the Environment / Dutch National Institute for Public Health and the Environment, RIVM. (2004) Environmental Emission Scenarios, Biocides: PT 1 – Human hygiene biocidal products

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2011. Evaluation of certain contaminants in food. 72nd report of the Joint

FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series 959, 115 pp.

Görtz G, Reimer K, Neef H (1996) Entwicklung, Eigenschaften und Bedeutung von PVP-Iod. In: Hierholzer C (Ed.) Topische Infektionstherapie und Prophylaxe: aktueller Stellenwert von PVP Iod. Thieme, Stuttgart, New York
Harrison J (1963) The fate of radioiodine applied to human skin. Health Phys 9, 993-1000

Hansch C, Leo A, Hoekman D (1995) Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society, p. 3

IOM (Institute of Medicine), 2001. Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academies Press, Washington DC, USA, 797 pp.

Laurberg P, Cerqueira C, Ovesen L, Rasmussen LB, Perrild H, Andersen S, Pedersen IB, Carle A (2010) Iodine intake as a determinant of thyroid disorders in populations. Best Pract Res Clin Endocrinol Metab 24, 13-27

Lavell KJ, Daedens DJ, Kleit SA et al. (1974) Iodine absorption in burn patients treated topically with povidone-iodine. Clin Pharmacol Ther 17,355-362

Lividas DP, Piperingos GD, Sfontouris J, Koutras DA (1978) Lack of Influence of Povidone-Iodine on Tests of Thyroid Function. J Int Med Res 6, 406

Michalaki M, Pylioti A, Loutas V, Mamali I, Markou KB (2013) Absence of differences in urinary iodine excretion and thyroid function tests in operating room staff members using or not using iodine-containing antiseptic solutions. Thyroid 23, 1659-1660. doi: 10.1089/thy.2013.0218. Epub 2013 Aug 1.

Mitchell IM, Pollock JC, Jamieson MP et al. (1991) Transcutaneous iodine absorption in infants undergoing cardiac operation. Ann Thorac Surg 52, 1138-1140

Nesvadbova M, Crosera M, Maina G, Larese Filon F (2015) Povidone iodine skin absorption: an ex-vivo study. Toxicol Lett 235, 155-160. doi: 10.1016/j.toxlet.2015.04.004. Epub 2015 Apr 6

Ph. Eur. (European Pharmacopoeia, ver. 7.0), 2010. Monograph 1142

SFC (Scientific Committee on Food), 2002. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine. 15 pp.

Teng W, Shan Z, Teng X, Guan H, Li Y, Teng D, Jin Y, Yu X, Fan C, Chong W, Yang F, Dai H, Yu Y, Li J, Chen Y, Zhao D, Shi X, Hu F, Mao J, Gu X, Yang R, Tong Y, Wang W, Gao T, Li C (2006) Effect of iodine intake on thyroid diseases in China. N Engl J Med 354, 2783-2793

U.S. EPA (United States Environmental Protection Agency), 2006a. Reregistration Eligibility Decision for iodine and iodophor complexes

U.S. EPA (United States Environmental Protection Agency), 2006b. Iodine and Iodophor Complexes: Revised Antimicrobials Division's Review of the Disciplinary Sciences for Issuance of the Reregistration Eligibility Decision (RED) Document. Reregistration Case No.: 3080

Van der Poel P, Bakker J (2002) Emission Scenario Document for Biocides: Emission Scenarios for all 23 product types of EU Directive 98/8/EEC. RIVM report 601 450 009

WHO IPCS (World Health Organization, International Programme on Chemical Safety), 2009. Concise International Chemical Assessment Document 72, Iodine and inorganic iodides: Human health aspects

References for efficacy section

Anderson, M.J., Horn, M.E., Lin, Y.-C., Parks, P.J., and Peterson, M.L. (2010). Efficacy of concurrent application of chlorhexidine gluconate and povidone iodine against six nosocomial pathogens. Am. J. Infect. Control 38, 826–831.

Rózsa Báthy M.D., Ivana Stöger M.D., Zsuzsanna Szabó M.D. and József Soós: Pre-operation skin disinfection with Betadine solution

Benevento, W.J., Murray, P., Reed, C.A., and Pepose, J.S. (1990). The sensitivity of Neisseria gonorrhoeae, Chlamydia trachomatis, and herpes simplex type II to disinfection with povidone-iodine. Am. J. Ophthalmol. 109, 329–333.

Best, M., Sattar, S., Springthorpe, V.S., Kennedy, M.E. Efficacies of selected disinfectants against Mycobacterium tuberculosis. J. Clin. Microbiol. October 1990 vol. 28 no. 10 2234-2239

Block, C., Robenshtok, E., Simhon, A., and Shapiro, M. (2000). Evaluation of chlorhexidine and povidone iodine activity against methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus faecalis using a surface test. J. Hosp. Infect. 46, 147–152.

Istvánné Bohn, Miklós Füzi M.D. – ÁNTSZ (National Public Health and Medical Officer Service) Institution in Budapest; György Premecz Ph.D. – EGIS, Directorate of Domestic Operations Commerce, Products Department: The role of Betadine in fighting methicillin resistant Staphylococcus aureus

Cardoso, C.L., Pereira, H.H., Zequim, J.C., and Guilhermetti, M. (1999). Effectiveness of hand-cleansing agents for removing Acinetobacter baumannii strain from contaminated hands. Am. J. Infect. Control 27, 327–331.

András Erös M.D., János Kiss M.D. and Endre Szirányi M.D.: Study on the effect of Betadine surgical scrub and Betadine solution for surgical patients

Gatti S, Cevini C, Bruno A, Penso G, Rama P, Scaglia M. In vitro effectiveness of povidoneiodine on Acanthamoeba isolates from human cornea. Antimicrob Agents Chemother. 1998 Sep; 42(9):2232-4.

Gershenfeld L. Povidone-iodine as a sporicide Am J Pharm 1962; 134: 78-81.

Ito, H., Ito, T., Hikida, M., Yashiro, J., Otsuka, A., Kida, H., and Otsuki, K. (2006). Outbreak of highly pathogenic avian influenza in Japan and anti-influenza virus activity of povidone-iodine products. Dermatol. Basel Switz. 212 Suppl 1, 115–118.

Ito, H, Hikida, M, Yashiro, J, Kida, H, and Ito, T (2009). Virucidal efficacy of povidone-iodine products against swine influenza viruses. 日本化学療法学会雑誌Jpn. J. Chemother. 57, 508–510.

Jayakumar, S., Kanagavalli, M., Shameem Banu, A.S., Renu, M., Kalyani, M., and Binesh,L.Y. (2011). The in vitro efficacy testing of skin disinfectants against nosocomial pathogens. JCDR 231–235.

Kaplan, J.C., Crawford, D.C., Durno, A.G., and Schooley, R.T. (1987). Inactivation of human immunodeficiency virus by Betadine. Infect. Control 8, 412–414.

Kariwa, H., Fujii, N., and Takashima, I. (2004). Inactivation of SARS coronavirus by means of povidone-iodine, physical conditions, and chemical reagents. Jpn. J. Vet. Res. 52, 105–112.

Kasuda, H., Fukuda, H., Togashi, H., Hotta, K., Hirai, Y., and Hayashi, M. (2002). Skin disinfection before epidural catheterization: comparative study of povidone-iodine versus chlorhexidine ethanol. Dermatol. Basel Switz. 204 Suppl 1, 42–46.

Kawana, R., Kitamura, T., Nakagomi, O., Matsumoto, I., Arita, M., Yoshihara, N., Yanagi, K.,Yamada, A., Morita, O., Yoshida, Y., et al. (1997). Inactivation of human viruses by povidone-iodine in comparison with other antiseptics. Dermatol. Basel Switz. 195 Suppl 2, 29–35.

Matsuhira, T., Kaji, C., Murakami, S., Maebashi, K., Oka, T., Takeda, N., and Katayama, K.(2012). Evaluation of four antiseptics using a novel murine norovirus. Exp. Anim. 61, 35–40.

Major SR, M.Major, C.Bognár, Á. Herendi, M.Németh, B. Bánkúti :Clinico- Bacterological Examination of Betadine skin Disinfectant Fluid and Liquid Soap in Hospitalized Patients and Hospital Employees

Márta Milassin: Comparative bacteriological investigation of Betadine antiseptic liquid soap and solution

Pelletier JS, Miller D, Liang B, Capriotti JA. In vitro efficacy of a povidone-iodine 0.4% and dexamethasone 0.1% suspension against ocular pathogens. J Cataract Refract Surg. 2011 Apr; 37 (4):763-6.

Plague, F., and Aviaire, G. (2009). Avian Influenza.

Reimer, K., Wichelhaus, T.A., Schafer, V., Rudolph, P., Kramer, A., Wutzler, P., Ganzer, D.,and Fleischer, W. (2002). Antimicrobial effectiveness of povidone-iodine and consequences for new application areas. Dermatol. Basel Switz. 204 Suppl 1, 114–120.

Rikimaru, T., Kondo, M., Kondo, S., and Oizumi, K. (1997). Bactericidal activities of povidone-iodine against Mycobacterium. Dermatol. Basel Switz. 195 Suppl 2, 104–106.

Rikimaru, T., Kondo, M., Kondo, S., and Oizumi, K. (2000). Efficacy of common antiseptics against mycobacteria. Int. J. Tuberc. Lung Dis. Off. J. Int. Union Tuberc. Lung Dis. 4, 570–576.

Rikimaru, T., Kondo, M., Kajimura, K., Hashimoto, K., Oyamada, K., Miyazaki, S., Sagawa,K., Aizawa, H., and Oizumi, K. (2002a). Efficacy of common antiseptics against multidrugresistant Mycobacterium tuberculosis. Int. J. Tuberc. Lung Dis. 6, 763–770.

Rikimaru, T., Kondo, M., Kajimura, K., Hashimoto, K., Oyamada, K., Sagawa, K., Tanoue, S., and Oizumi, K. (2002b). Bactericidal activities of commonly used antiseptics against

multidrug-resistant mycobacterium tuberculosis. Dermatol. Basel Switz. 204 Suppl 1, 15–20.

Ryssel, H., Andreas Radu, C., Germann, G., Kloeters, O., Riedel, K., Otte, M., and Kremer,T. (2011). Suprathel-antiseptic matrix: in vitro model for local antiseptic treatment? Adv. Skin Wound Care 24, 64–67.

Saggers, B.A., and Stewart, G.T. (1964). POLYVINYL-PYRROLIDONE-IODINE: AN ASSESSMENT OF ANTIBACTERIAL ACTIVITY. J. Hyg. (Lond.) 62, 509–518.

Saknimit, M., Inatsuki, I., Sugiyama, Y., and Yagami, K. (1988). Virucidal efficacy of physicochemical treatments against coronaviruses and parvoviruses of laboratory animals. Jikken Dobutsu 37, 341–345.

Sauerbrei, A., and Wutzler, P. (2010). Virucidal efficacy of povidone-iodine-containing disinfectants. Lett. Appl. Microbiol. 51, 158–163.

Sauerbrei, A., Sehr, K., Eichhorn, U., Reimer, K., and Wutzler, P. (2004). Inactivation of human adenovirus genome by different groups of disinfectants. J. Hosp. Infect. 57, 67–72.

Sriwilaijaroen, N., Wilairat, P., Hiramatsu, H., Takahashi, T., Suzuki, T., Ito, M., Ito, Y.,Tashiro, M., and Suzuki, Y. (2009). Mechanisms of the action of povidone-iodine against human and avian influenza A viruses: its effects on hemagglutination and sialidase activities.Virol. J. 6, 124.

Tennen R, Setlow B, Davis KL, Loshon CA, Setlow P. Mechanisms of killing of spores of Bacillus subtilis by iodine, glutaraldehyde and nitrous acid. J Appl Microbiol. 2000 Aug; 89(2):330-8.

Thornton Spann, C., Taylor, S.C., and Weinberg, J.M. (2004). Topical antimicrobial agents in dermatology. Dis. Mon. 50, 407–421.

Traore, O., S.Fournet Fayard, and H. Laveran, An In-Vitro Evaluation Of The Activity Of Povidone-Iodine Against Nosocomial Bacterial Strains, Journal of Hospital Infection, 34 (1996), 217-222.

Veiga, D.F., Damasceno, C.A., Veiga Filho, J., Silva Jr, R.V., Cordeiro, D.L., Vieira, A.M.,Andrade, C.H., Ferreira, L.M., and others (2008). Influence of povidone-iodine preoperative showers on skin colonization in elective plastic surgery procedures. Plast. Reconstr. Surg. 121, 115–118.

Wutzler, P., Sauerbrei, A., Klocking, R., Brogmann, B., and Reimer, K. (2002). Virucidal activity and cytotoxicity of the liposomal formulation of povidone-iodine. Antiviral Res. 54, 89–97.

References for resistance section:

Shiraishi T, Nakagawa Y: Review of disinfectant susceptibility of bacteria isolated in hospital to commonly used disinfectants; Postgrad Med J 69 (Suppl.3) S70-S77

Hingst et al: Untersuchungen zur Epidemiologie mikrobieller Biozidresistenzen. Zbl Hyg 197 (1995) 232-251

Celere MS, Ferreira O, Ubiali EM, Julião FC, Fernandes AF, de Andrade D, Segura-Muñoz SI.: Antimicrobial activity of two techniques for arm skin disinfection of blood donors in Brazil. Transfus Med. 2012 Apr; 22(2):116-21. doi: 10.1111/j.1365-3148.2012.01132.x. Epub 2012 Jan 27.

Coetzee E, Rode H, Kahn D.: Pseudomonas aeruginosa burn wound infection in a dedicated paediatric burns unit., S Afr J Surg. 2013 May 3;51(2):50-3. doi: 10.7196/sajs.1134.

Traoré O, Fayard SF, Laveran H.: An in-vitro evaluation of the activity of povidone-iodine against nosocomial bacterial strains; J Hosp Infect. 1996 Nov; 34 (3):217-22.

Lacey RW, Catto A.: Action of povidone-iodine against methicillin-sensitive and -resistant cultures of Staphylococcus aureus; Postgrad Med J. 1993; 69 Suppl 3:S78-83.

Medical Expertise to Efficacy of Betaisodona Solution of the Mundipharma GmBH, Limburg Germany, 1997

Expert reports:

Medical Expertise to Efficacy of Betaisodona Solution of the Mundipharma GMBH, Limburg Germany, 1997

Expert Report on the clinical documentation for Betaisodona solution, 2003

Betadine clinical overview, 2015

Betadine solution-literature references for expert report 2003

3.2. Output tables from exposure assessment tools

Inhalation exposure of professionals:

ConsExpo 4.1 report

file name:
Report date: 2018.07.30.

Product

Compound

Compound name :	Iodine	
CAS number :		
molecular weight	254	g/mol
vapour pressure	40,7	Pascal
KOW		linear

General Exposure Data

exposure frequency	4	1/day
body weight	60	kilogram

Inhalation model: Exposure to vapour : evaporation

weight fraction compound	0,012	%
exposure duration	10	minute
room volume	80	m3

ventilation rate	1,5	1/hr
applied amount	166	gram
release area	1,66E4	cm2
application duration	2	minute
mol weight matrix	18	g/mol
mass transfer rate	0,207	m/min

Uptake model: Fraction

uptake fraction	100	%
inhalation rate	32,9	m3/day

Output

Inhalation (point estimates)

inhalation mean event concentration :	0,000245	mg/m3
inhalation mean concentration on day of exposure:	6,79E-6	mg/m3
inhalation air concentration year average :	6,79E-6	mg/m3/day
inhalation acute (internal) dose :	9,32E-7	mg/kg
inhalation chronic (internal) dose :	3,73E-6	mg/kg/day

Integrated (point estimates)

total external dose:	9,32E-7	mg/kg
total acute dose (internal):	9,32E-7	mg/kg
total chronic dose (internal):	3,73E-6	mg/kg/day