Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*

3.6.2 Other limiting factors

[redacted]

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing

[redacted]

4.2 Intended actual scale of biocide application

[redacted]

4.3 Relevance compared to field conditions

[redacted]

4.3.1 Application method

[redacted]

4.3.2 Test organism

[redacted]

4.3.3 Observed effect

[redacted]

4.4 Relevance for read-across

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*

[redacted]

5.2 Reliability

[redacted]

5.3 Assessment of efficacy, data analysis and interpretation

[redacted]

5.4 Conclusion

Iodine has innate efficacy against bacteria, amoebae and viruses in water.

5.5 Proposed efficacy specification

[redacted]

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Comments	[redacted]
Summary and conclusion	[redacted]

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Doc. No.: 381-017

Title:	BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD
Author(s):	Fotheringham, V.J.C.
Report date:	Apr/2007

SCC Project No.:	854-005
Name of database:	Iodine

EVANS VANODINE
INTERNATIONAL PLC
Global Hygiene Solutions

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW

Prepared by Valerie J C Fotheringham
Chief Microbiologist, Evans Vanodine International plc

FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD

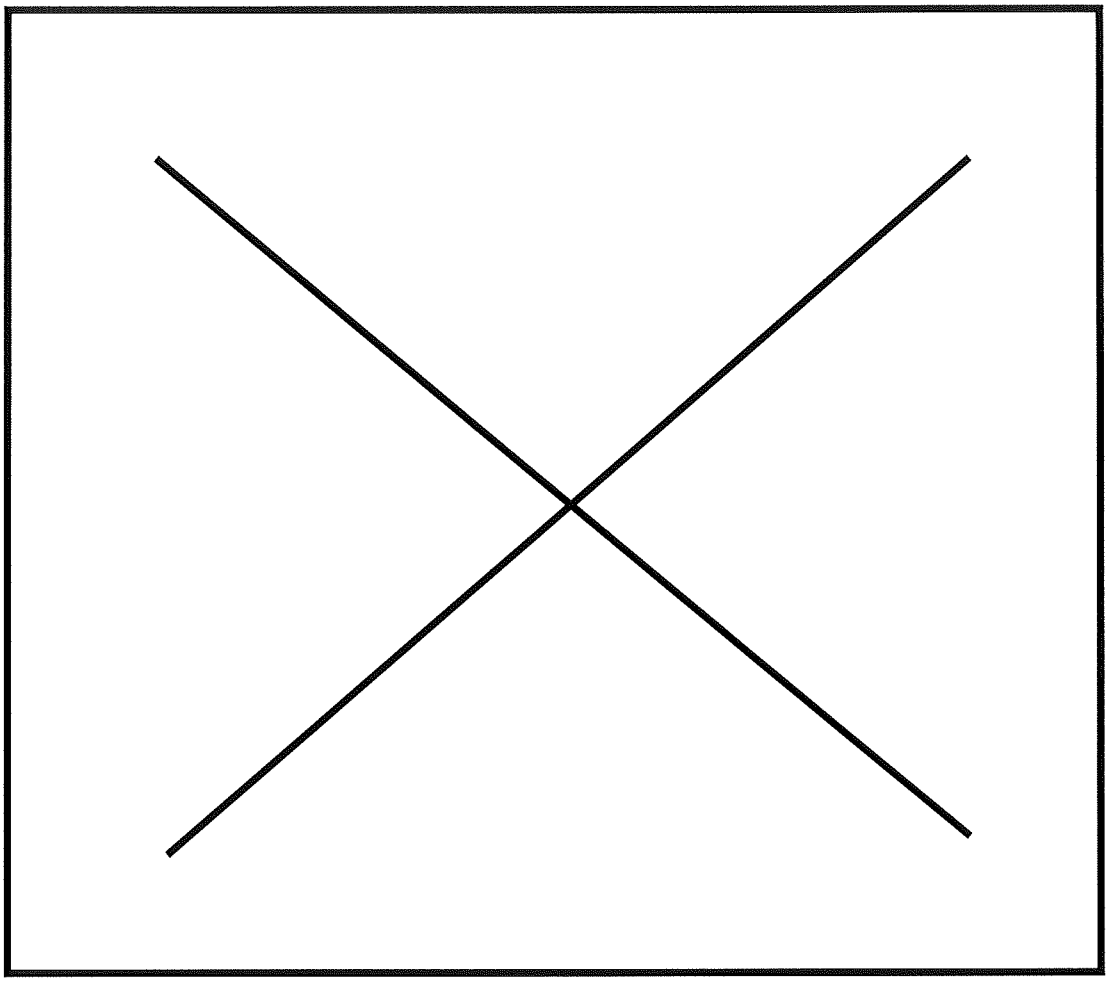
APRIL 2007

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CONTENTS

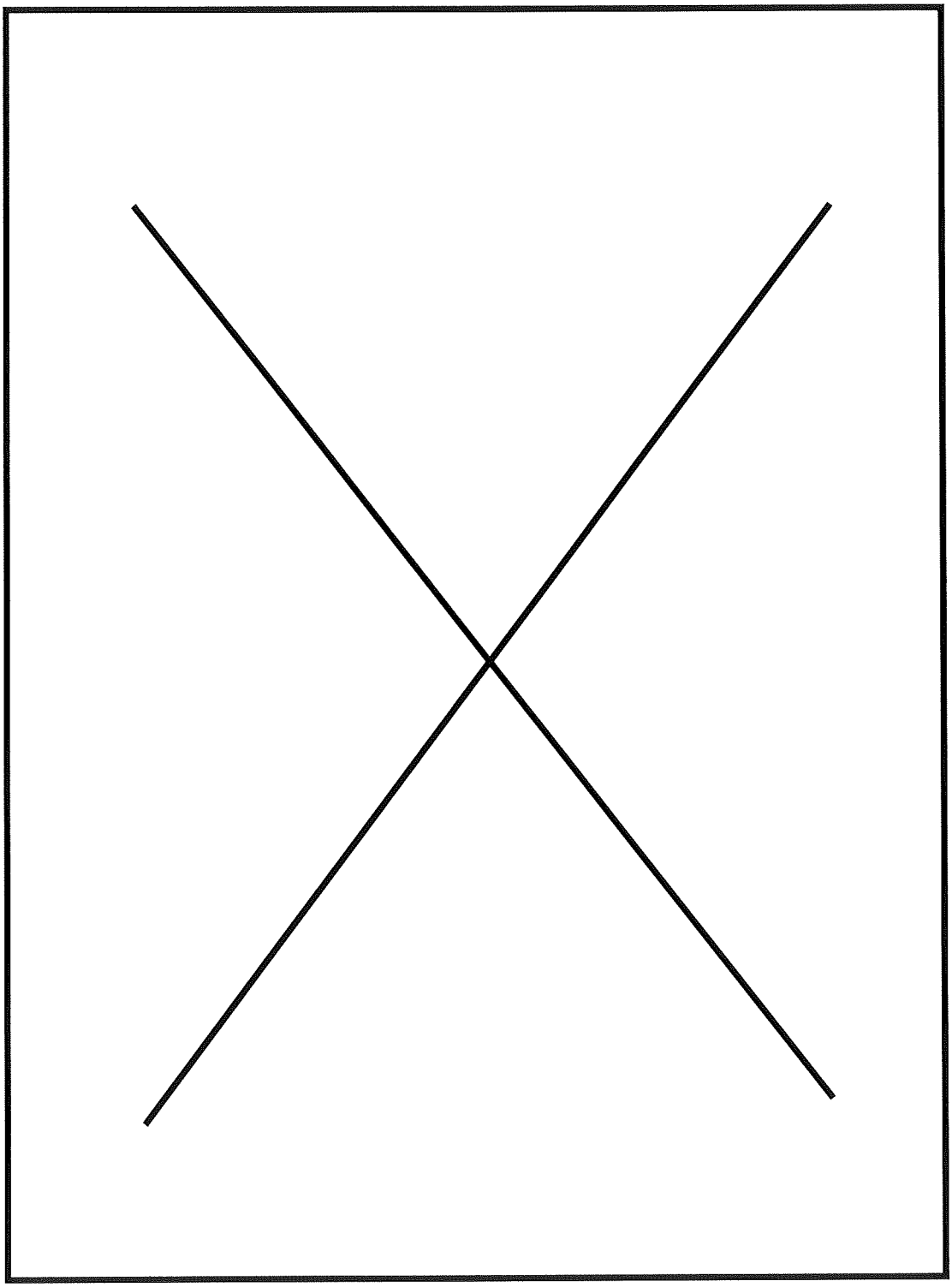
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

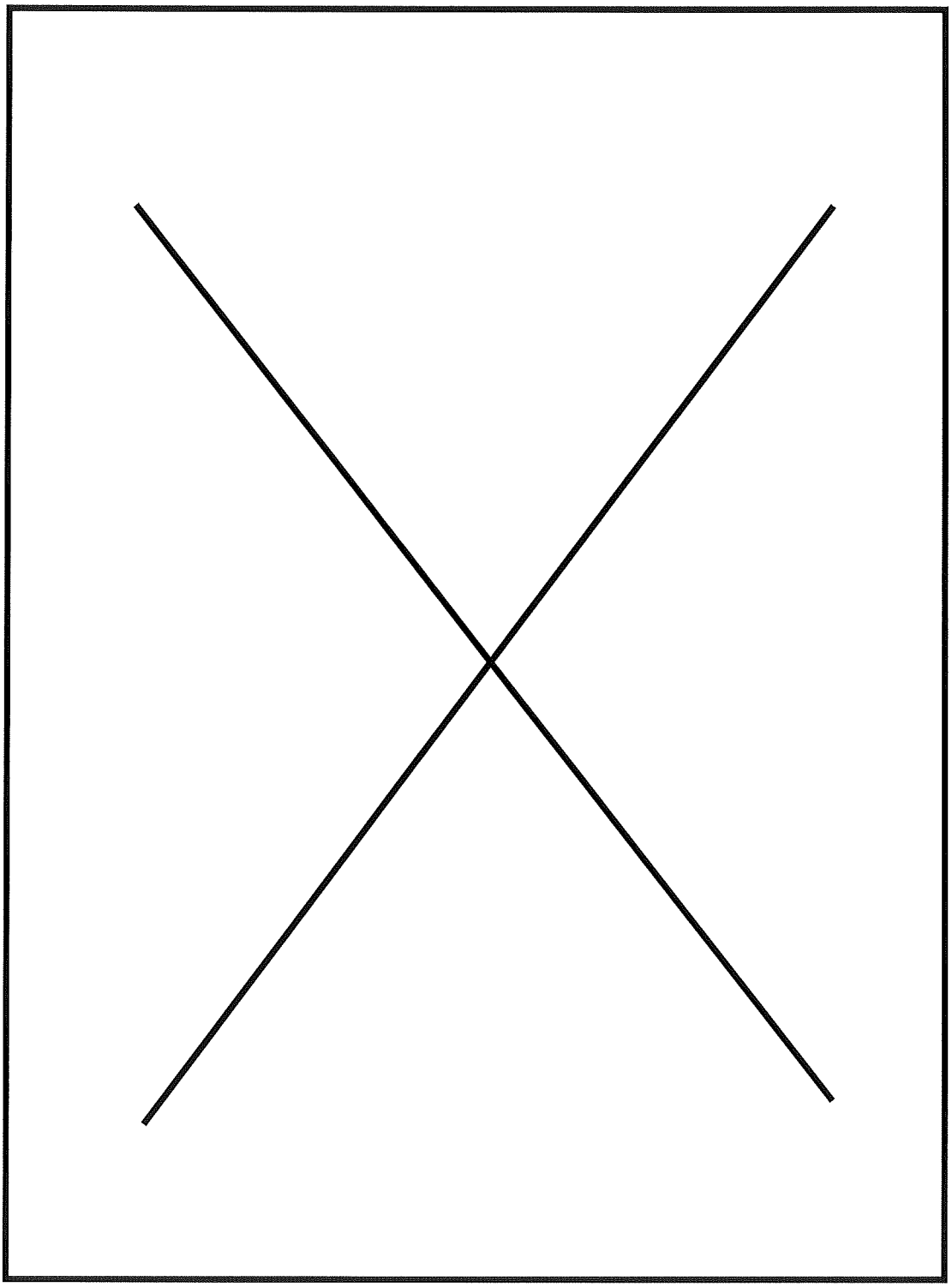
A REVIEW



EVANS VANODINE INTERNATIONAL PLC

Page 4 of 16

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW



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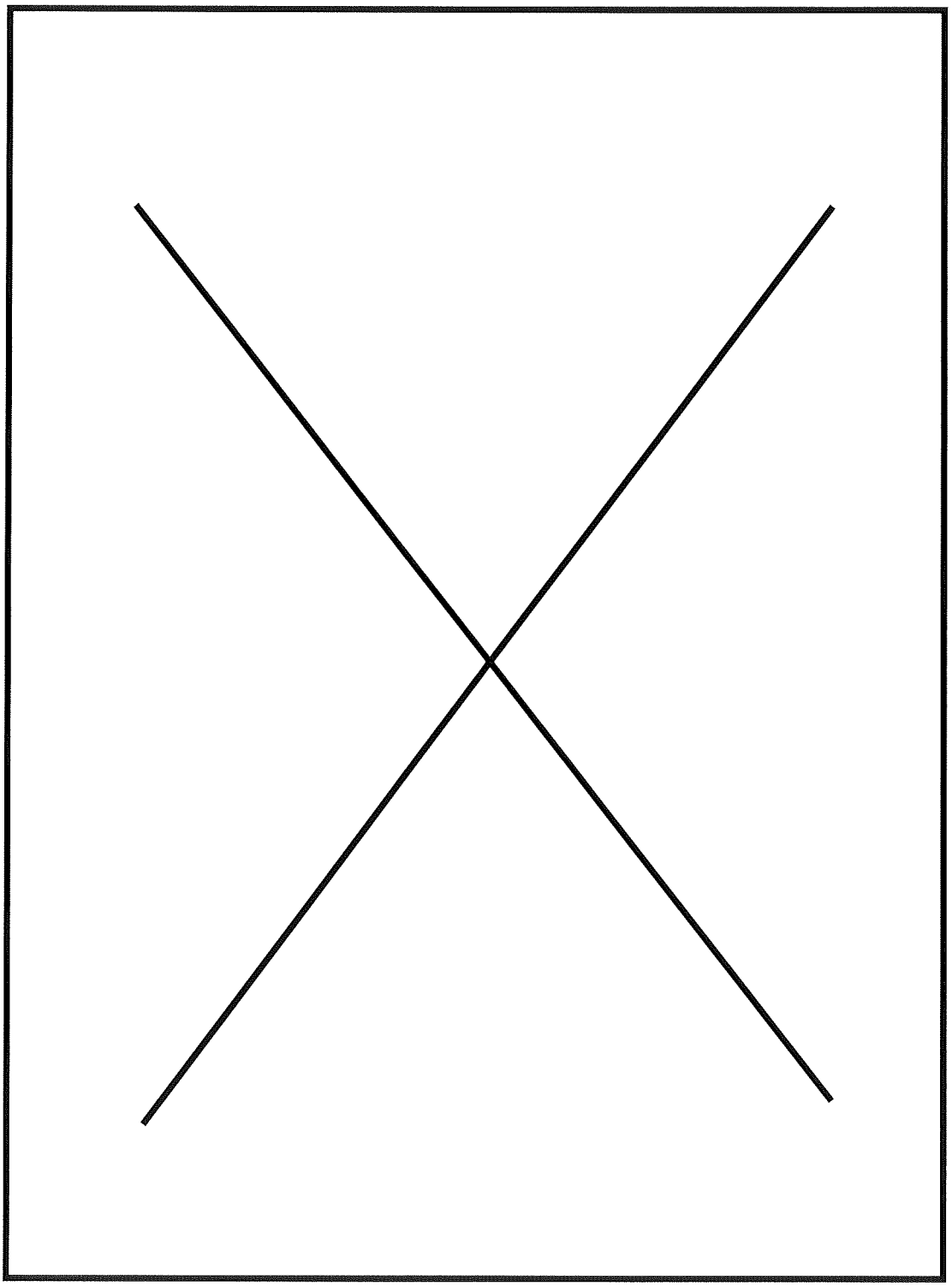
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

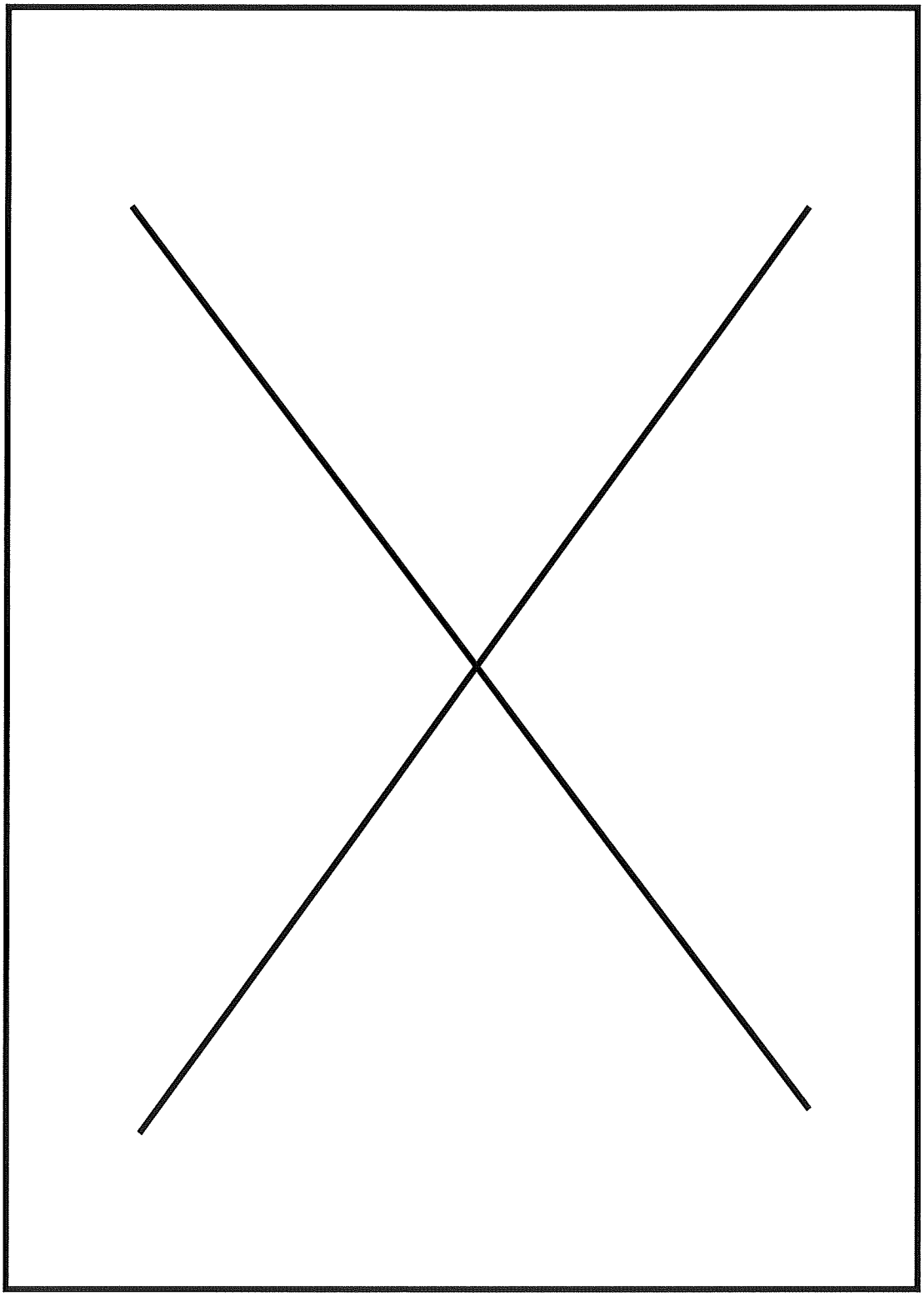


EVANS VANODINE INTERNATIONAL PLC

Page 6 of 16

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

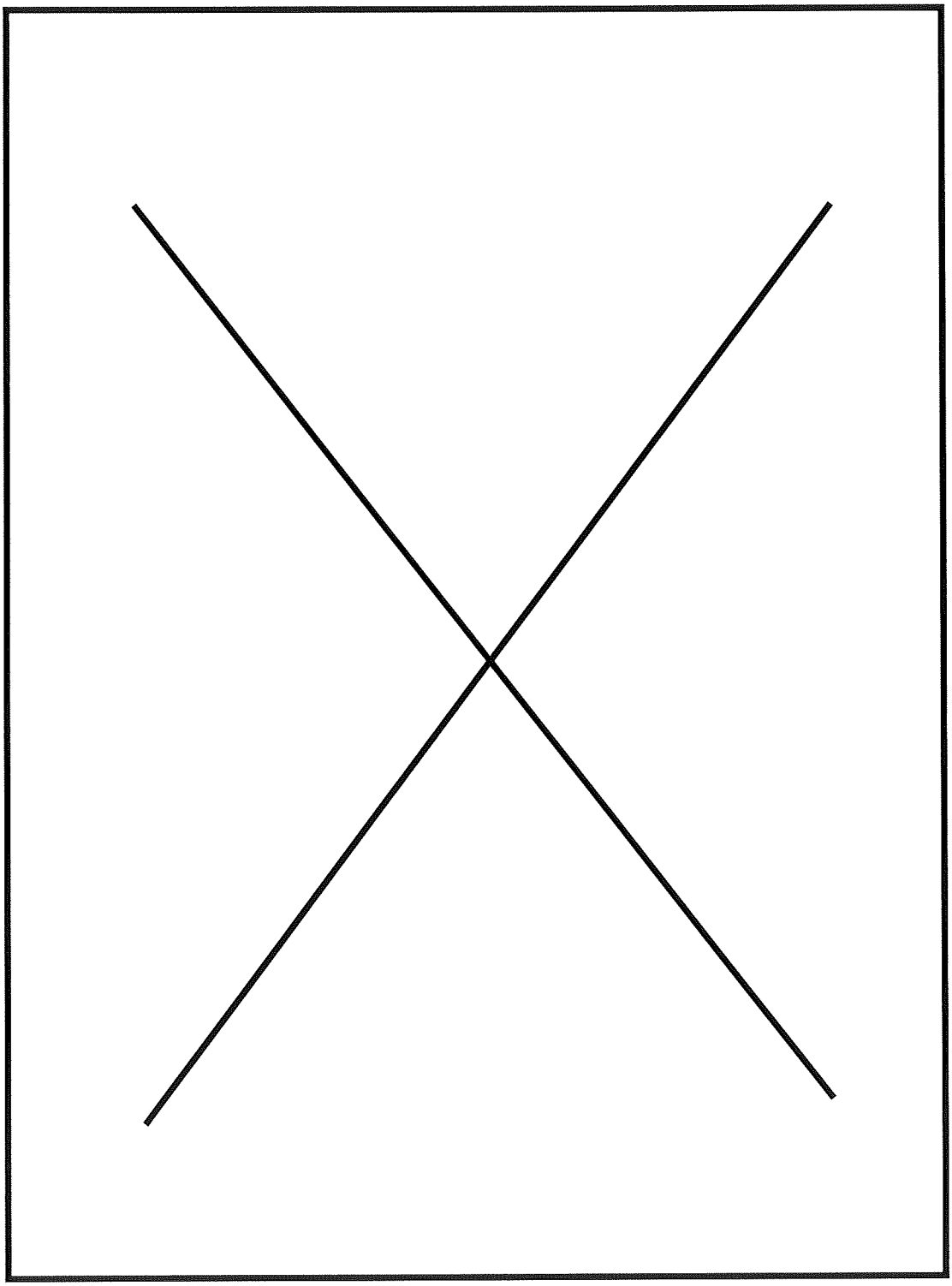


EVANS VANODINE INTERNATIONAL PLC

Page 7 of 16

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

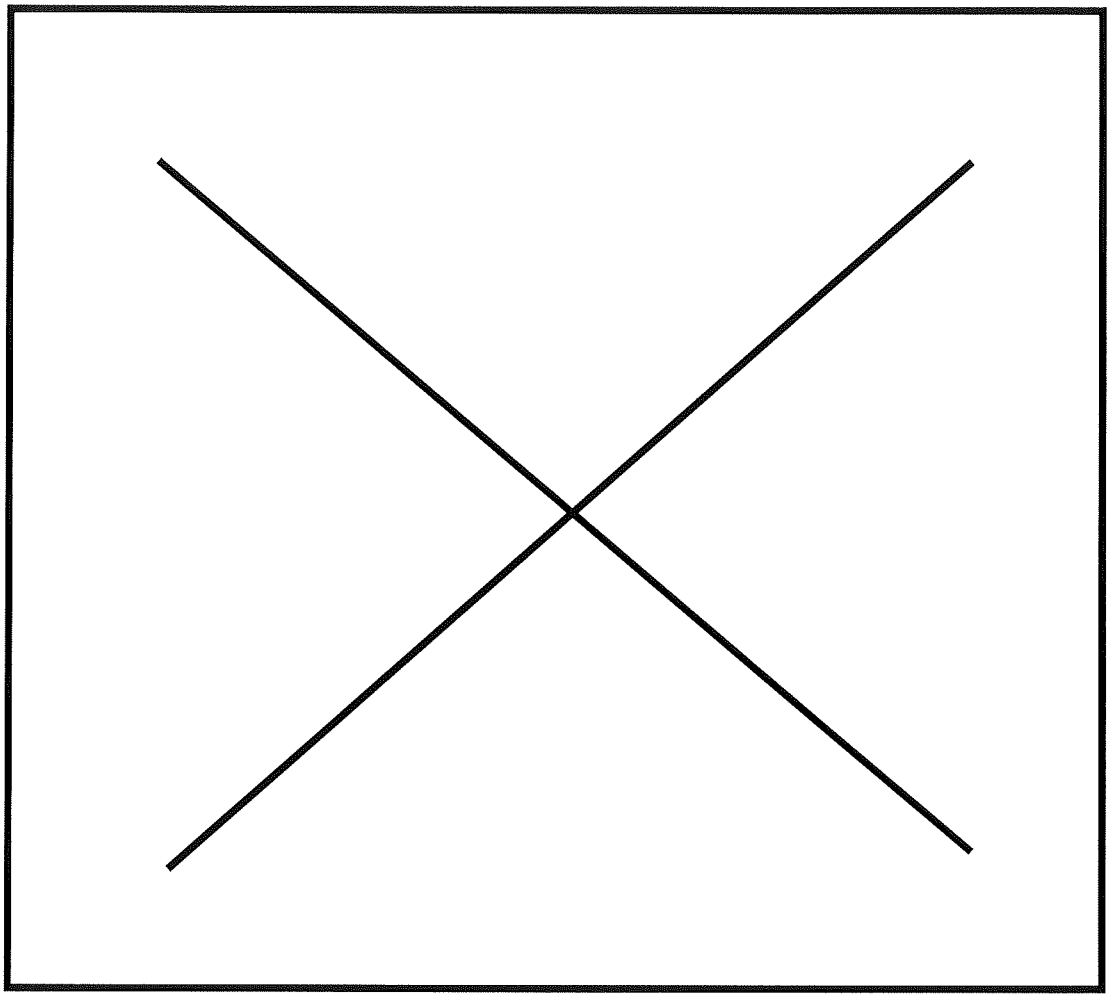


EVANS VANODINE INTERNATIONAL PLC

Page 8 of 16

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



Valerie J C Fotheringham B.Sc., C.Biol, M.I.Biol.
Chief Microbiologist

DATE: 30 April 2007.

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 1: PASS DILUTIONS FOR IODOPHOR SURFACE DISINFECTANT* AGAINST A RANGE OF MICRO-ORGANISMS

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BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 2: PASS DILUTIONS FOR IODOPHOR TEAT DISINFECTANT*** AGAINST A RANGE OF BACTERIA

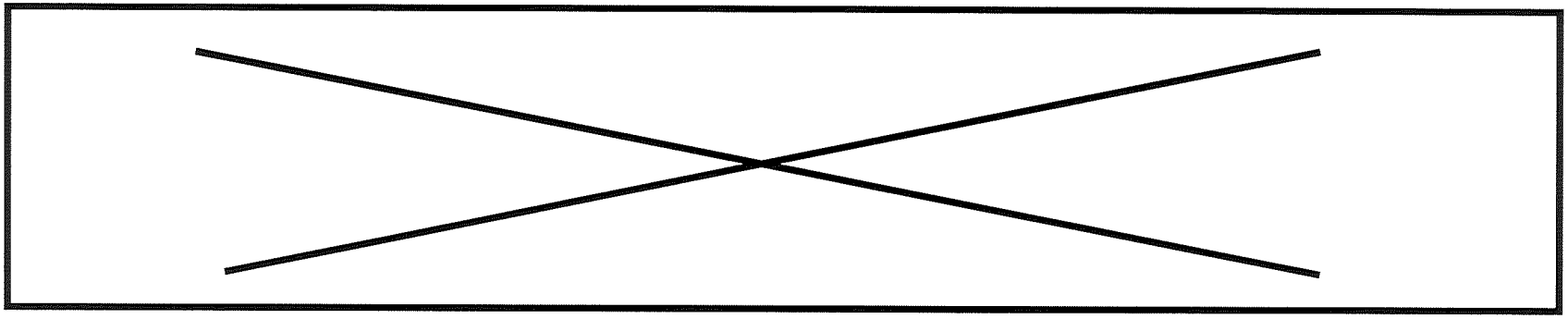
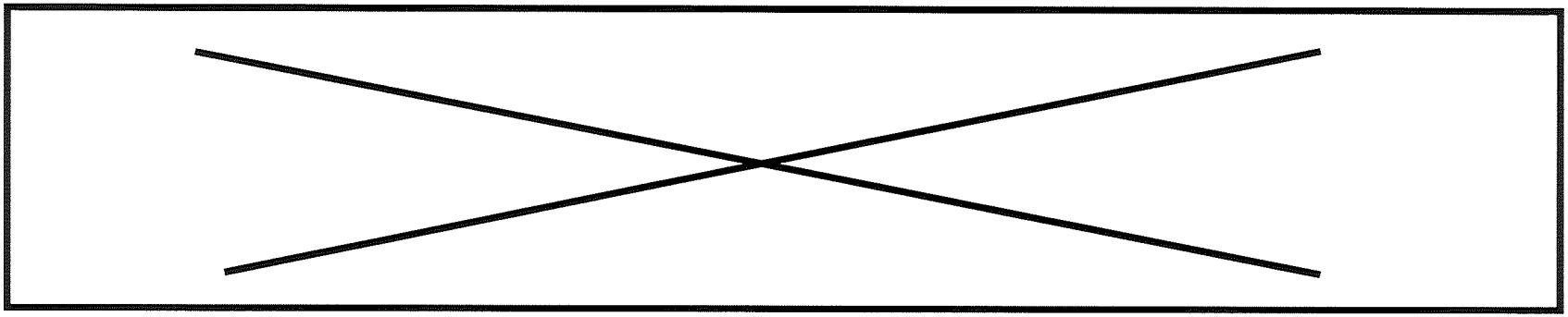


TABLE 3: PASS DILUTIONS FOR QUATERNARY AMMONIUM COMPOUND DISINFECTANT# AGAINST A RANGE OF BACTERIA



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

CHART 1: RELEVANCE OF REFERENCES SITED FOR IODINE RESISTANCE

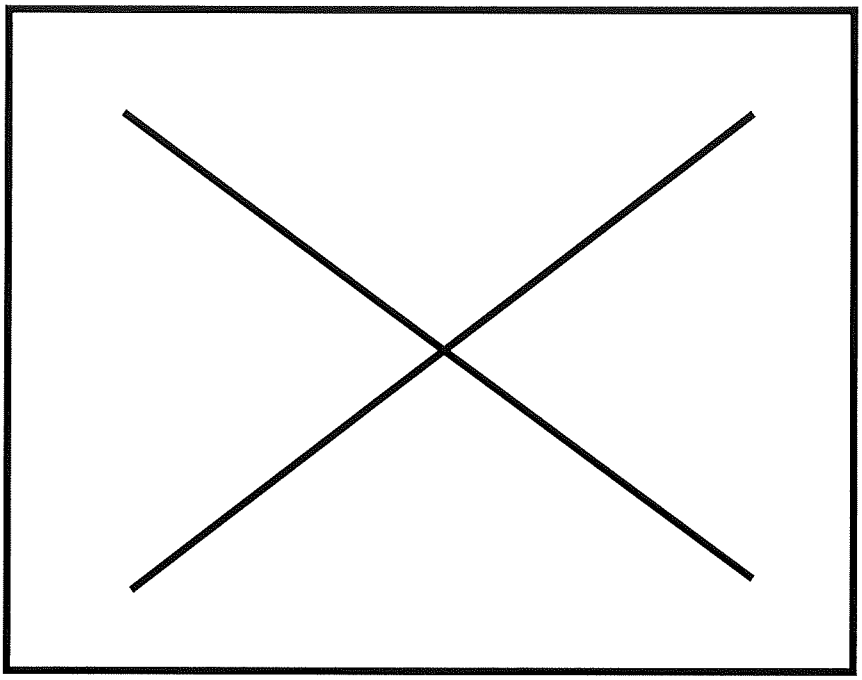
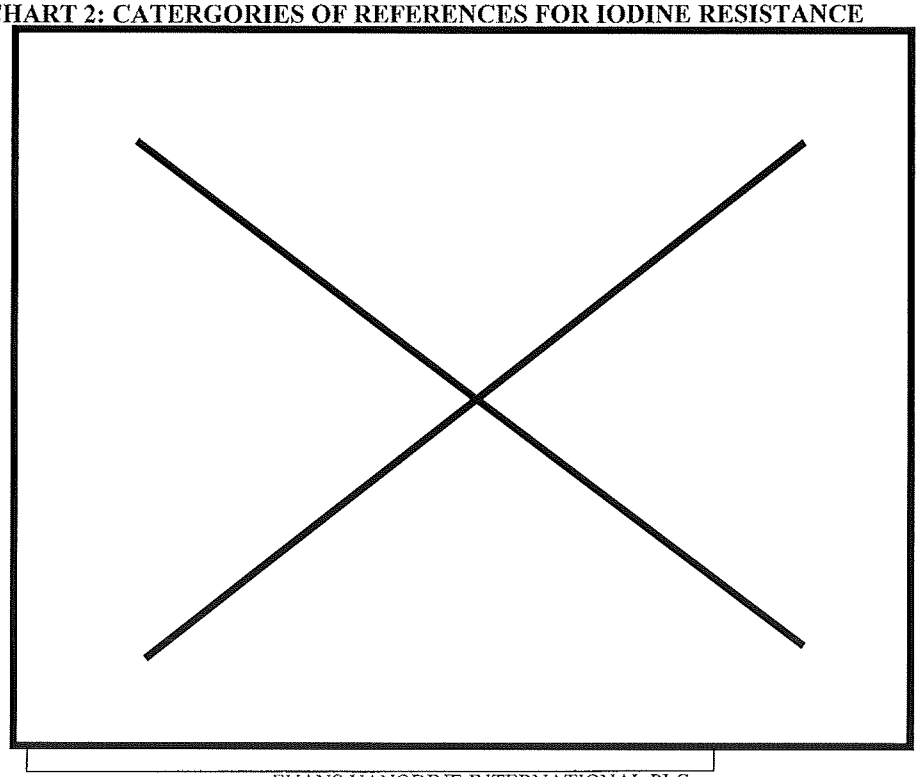
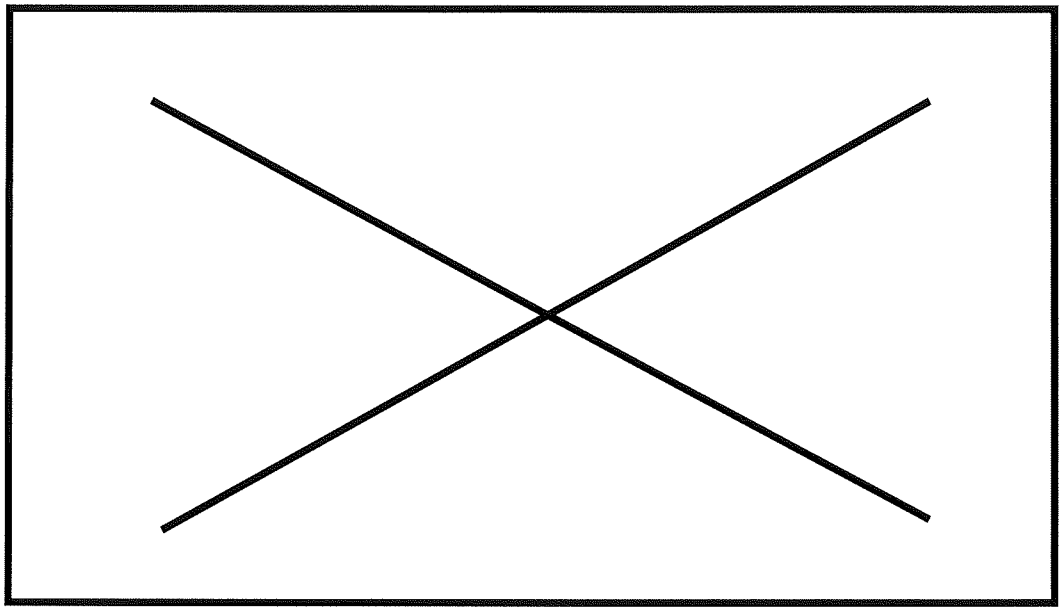


CHART 2: CATERGORIES OF REFERENCES FOR IODINE RESISTANCE



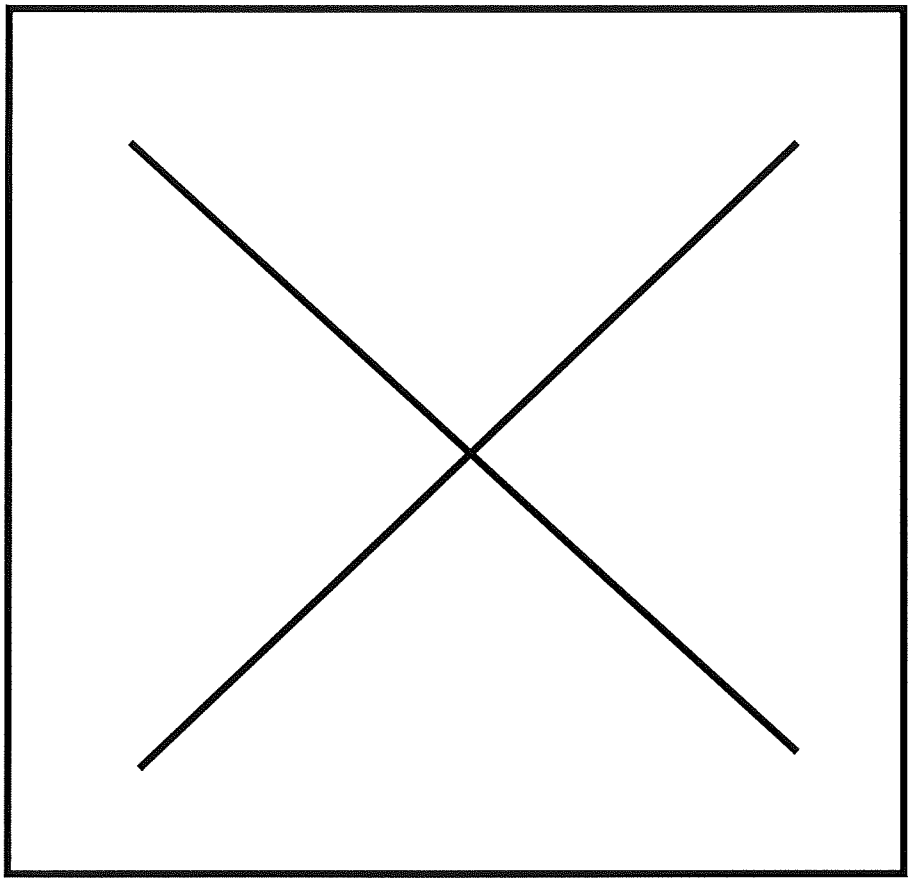
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CHART 3: Somatic cell counts in England and Wales



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CHART 4: PERCENTAGE OF TEAT DISINFECTANTS USED GLOBALLY



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BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

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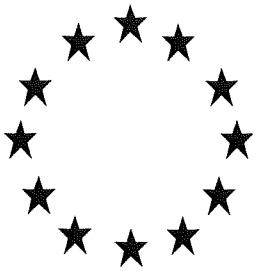
Competent Authority Report

Work Programme for Review of Active Substances in Biocidal Products
Pursuant to Council Directive 98/8/EC



IODINE (PT22)

DOCUMENT III-A5

Efficacy

Rapporteur Member State: Sweden

Draft Final May 2013

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Section A5 Effectiveness against target organisms and intended uses

Subsection Annex Point IIA V.5.1 – V.5.8			Official use only
5.1	**Function (IIA5.1)**	Bactericide, virucide and fungicide.	
5.2	**Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)**		
5.2.1	**Organism(s) to be controlled (IIA5.2)**	Iodine is used for control of various pathogenic organisms such as bacteria (including spores and mycobacteria), viruses and fungi. Examples of organisms against which Iodine was successfully tested are listed in the Tables A5.3.1-1, A5.3.1-2 and A5.3.1-3 that were already included in the dossier submitted in July 2007. Please note the available data summarised in these tables is not exhaustive due to the large number of available publications. Only the most relevant literature is described. In addition to literature data, also laboratory reports on tests performed with Iodine-based products have been included, examples of which are listed below for the relevant uses. On request of the applicant this information is provided in the Confidential part of the dossier. The above-mentioned information was submitted for PT3 but is regarded to be also relevant for the dossier for PT22. However, the cited documents are not again included in the dossier for PT22. The organisms to be controlled by embalming of cadavers are those inside or on the body at the time of death. The predominant organisms found throughout the body after death are those derived from the gut. Post mortem transgression is universal and gastrointestinal organisms can be found in the cerebral spinal fluid and elsewhere within 4-6 hours of death. With increasing hypoxia the organisms that can survive anaerobically have an advantage. Thus, the predominant organisms isolated from the various tissues are primarily coliforms such as *E.coli*, Klebsiella and anaerobes such as Clostridium. Other organisms include pseudomonas, proteus, staphylococci and various streptococci. In addition, also saprophytic fungi, moulds and yeasts and viruses (e.g. *M. tuberculosis*) may be present that are also controlled by the embalming process. The number of organisms isolated post mortem increases with time from death leading to increased decomposition of the cadaver. Since in many cases, the cause of death is not notified to the embalmer but can only be deduced from the information provided by the relatives, the prevalent micro-organisms to be controlled are largely unknown. However, cadavers with any notifiable diseases (e.g. HIV, hepatitis) would be normally bagged and sealed to reduce the risk to the public. Please refer also to Attachment 2 to this document (Attachment 2_381-019).	

Section A5 Effectiveness against target organisms and intended uses

5.2.2	**Products, organisms or objects to be protected (IIA5.2)**	Embalming is used to protect the cadaver from decaying/developing unpleasant odour until burial/cremation (preservation). In addition, embalming of cadavers is used the protect the public against pathogens (hygienisation).	
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**		
5.3.1	**Effects on target organisms (IIA5.3)**	Iodine in aqueous or alcoholic solutions or solubilised with surfactants (iodophors) is used in a variety of applications to kill harmful microorganisms and viruses. These preparations are used as skin disinfectants pre-operatively, with wound dressings, for teat dipping in dairy cows, sheep and goats and for surface disinfection in a number of industries. In addition, these preparations are used for short-term preservation of cadavers prior to burial/cremation. Iodine is suitable for all of these applications because it is a broad spectrum biocide, its efficacy has been demonstrated over 170 years of use. Iodine and iodophors are well established and accepted as having microbicidal activity. There is a huge number of papers demonstrating the microbicidal activity of iodophor products in laboratory and field tests but only a few of these are referenced here as most of them relate to specific formulations and not just to Iodine. The following information was already submitted with the dossier for PT3 in July 2007. Since the cited reports are already available to KEMI, they have not been included again in the present dossier: Table A5.3.1-1 summarises the available information in published text and reference books and in scientific reviews is summarised. Table A5.3.1-2 summarises exemplary studies from publicly available sources showing the efficacy of Iodine-based products for biocidal uses. In the present dossier an additional table is included summarising the available data on the efficacy of Iodine from PVP-Iodine based embalming product. Detailed study summaries on these studies have been included in the product dossier. Please refer to Table 5.3.1_AARDBalm arterial fluid-3 provided in the confidential part of the dossier.	X2
5.3.2	**Likely concentrations at which the A.S. will be used (IIA5.3)**		
	PT22	Arterial injection of diluted product: 0.29 - 0.39 % Iodine (w/w). Injection of undiluted product into abdominal cavity: 1.15 – 1.54 % Iodine (w/w).	
5.4	**Mode of action (including time delay) (IIA5.4)**		

Section A5 Effectiveness against target organisms and intended uses

5.4.1 Mode of action

The following mechanisms of action contribute to the high reactivity and non-selective action of Iodine against different micoorganisms:

- Iodine rapidly penetrates into micoorganisms showing a high affinity pattern of adsorption.
- Iodine combines with protein substances in the bacterial cell; these can be peptidoglycans in the cell walls or enzymes in the cytoplasm. This results in irreversible coagulation of the protein and consequent loss of function.
- Iodine is known to act on thiol groups in the cell; if a thiol enzyme is part of a metabolic chain, metabolic inhibition will result.
- Iodine reacts with key groups of proteins, in particular the free-sulfur amino acids cysteine and methionine, nucleotides and fatty acids.
- Iodine interferes at the level of the respiratory chain of the aerobic microorganisms by blocking the transport of electrons through electrophilic reactions with the enzymes of the respiratory chain.

For further details, please refer to the expert statement on resistance attached to this document (Attachment 1_381-017).

5.4.2 Time delay

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

The germicidal activity of Iodine-containing solutions is characterised by their colour. Amber solutions are active whilst pale yellow or colourless solutions are less effective and must be replaced by new solutions.

5.5 Field of use envisaged (IIA5.5)

MG01: Disinfectants, general biocidal products	PT 3: Veterinary hygiene biocidal products covered in the dossier submitted in 2007.	X1
MG04: Disinfectants, general biocidal products	PT 22: Embalming and taxidermist fluids covered in the present dossier.	

5.6 User (IIA5.6)

Industrial	No industrial use
Professional	Embalming fluid such as [redacted] will only be used by professionals. For a detailed use-description, please refer to Document IIB, Chapter 8.
General public	None

Section A5 Effectiveness against target organisms and intended uses

5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**		
5.7.1	**Development of resistance**	As described in the dossier submitted in 2007, Iodine / Iodophors have been used in teat dips since the 1960's and are still the predominant type of product used for the prevention of mastitis. No reduction in efficacy was reported to the producers indicating that no development of resistant microorganisms or viruses has occurred. An overview on the efforts made to find reports on the development of resistance to Iodine is provided in the expert statement attached to this document (Attachment 1_381-017). No resistance of target organisms to [redacted] has been reported. Development of resistance is not likely since the treated cadaver is buried/cremated after a limited period. [redacted] is not recommended for long-term preservation or repatriation cases.	X3
5.7.2	**Management strategies**	No management strategies have been developed since no occurrence of resistance has been observed. Nevertheless, it should be noted that Iodine-based products are exclusively applied by professional users, in most cases as part of professional hygiene programs, which also involve other biocidal substances of different chemical structure and different mode of action (alternating applications).	
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	Based on an estimate provided by one supplier of Iodine, the Iodine world demand in the year 2006 for the production of disinfectants was 14% of the total Iodine world demand of 25,000 – 26,000 t/year. Thus, about 3640 t Iodine/year were used for the production of disinfectants throughout the world. Doc. No. 031-013; Section A5.8/01 For information on the likely tonnage to be placed on the market per year for biocidal products per member of the Iodine Registration Group (IRG), please refer to the confidential part of the dossier.	

Section A5 Effectiveness against target organisms and intended uses

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

General

Conclusion

Reliability

Acceptability

Remarks

Section A5 Effectiveness against target organisms and intended uses

Please note, that Tables 5.3.1-1 and 5.3.1-2 were already included in the dossier for PT3 submitted in July 2007. Since the cited documents are already available to KEMI, they have not been included again in the present dossier although they are regarded relevant or supportive for PT22.

Table 5.3.1-1: Summary table of reviews available in public literature on the efficacy of Iodine

Title/Author(s)	Reference	Year	Conclusion	Section point
Review Article The Role of Iodine in Antisepsis and Wound Management: A Reappraisal G. Selvaggi, S. Monstrey, K. Van Landuyt, M. Hamdi and P. Blondeel	*Acta.chir belg*, 103 (3), 241-247	2003	[redacted]	Doc. No. 392-055, Section A5.3.1/01
Topical Antimicrobial Agents in Dermatology Candace Thornton Spann, Susan C Taylor and Jeffrey M Weinberg	*Clinics in Dermatology* 21, 70-77	2003	[redacted]	Doc. No. 392-049, Section A5.3.1/02
Review of disinfectant susceptibility of bacteria isolated in hospital to commonly used disinfectants Tadashi Shiraishi and Yoshito Nakagawa	*Postgrad Med J* 69 (Suppl.3), S70-S77	1993	[redacted]	Doc. No. 392-057, Section A5.3.1/03
Virucidal Activity of Biocides A. Activity against human viruses A.S.Sattar and S.Springthorpe	In: *Principles and Practice of Disinfection, Preservation and Sterilization* 3rd Edition p178 Edited by A.D.Russell, W.B.Hugo and G.A.J.Ayliffe Published by Blackwell Scientific Publications	1999	[redacted]	Doc. No. 392-048, Section A5.3.1/04
Virucidal Activity of Biocides A. Activity against veterinary viruses P.J.Quinn and B.K.Markey	Page 193		[redacted]	

Title/Author(s)	Reference	Year	Conclusion	Section point
Halogens - Free Iodine W.B.Hugo and A.D.Russell	Page 45-46		[redacted]	
Halogens - Iodophors W.B.Hugo and A.D.Russell	Page 45-46		[redacted]	
Iodine	In: *Martindale The Complete Drug Reference* 32nd Edition p1494	1999	[redacted]	Doc. No. 392-047, Section A53.1/05
Chemical disinfectants, antiseptics and preservatives E.M.Scott and S.P.Gorman	In: *Pharmaceutical Microbiology* 6th Edition p219	1998	[redacted]	Doc. No. 392-046, Section A5.3.1/06
Chemicals used as disinfectants: active ingredients and enhancing additives D.J. Jeffrey	*Rev.sci.tech.Off.int.Epiz.* 14 (1) 68	1995	[redacted]	Doc. No. 392-045, Section A5.3.1/07
Iodine	*The Pharmaceutical Codex* 12 Edition *Principles and Practice of Pharmaceutics* p582	1994	[redacted]	Doc. No. 392-050, Section A5.3.1/08
Iodophores		1994	[redacted]	
Bacterial Spores and Chemical Sporicidal Agents A.D.Russell	*Clinical Microbiology Reviews* Vol. 3, No. 2, p99-119	1990	[redacted]	Doc. No. 392-058, Section A5.3.1/09

Title/Author(s)	Reference	Year	Conclusion	Section point
The Bacterial Flora of 'In-Use' Teat Dips J.Bruce	In: *Disinfectants Their use and Evaluation of Effectiveness* p177-182 Edited by C.H.Collins, M.C.Allwood, Sally F. Bloomfield and A.Fox Published by Academic Press, London	1981	[redacted]	Doc. No. 392-051, Section A5.3.1/10
The inactivation of vegetative micro-organisms by chemicals in the dairying industry Christina M Cousins	In: *Inhibition and Inactivation of Vegetative Microbes* p13-30 Edited by F.A.Skinner and W.B.Hugo Published by Academic Press, London	1976	[redacted]	Doc. No. 392-052, Section A5.3.1/11
Iodophors, their physical, chemical and bactericidal properties and use in the dairy industry - A Review A Twomey	*Australian Journal of Dairy Technology*, Part II, 24, 29-32	1969	[redacted]	Doc. No. 392-053, Section A5.3.1/12
Iodine compounds	In: *A Review of Sterilization and Disinfection* p143-144 S.D. Rubbo and Joan F Gardner Published by Lloyd-Luke (Medical Books) Ltd, London	1965	[redacted]	Doc. No. 392-054, Section A5.3.1/13
Elemental Iodine as a Disinfectant for Drinking Water Shih Lu Chang and J. Carrell Morris	*Industrial and Engineering Chemistry* 45(5); 1009-1012.	1953	[redacted]	Doc. No. 392-056, Section A53.1/14

Table 5.3.1-2: Summary table of available publications describing the efficacy of Iodine and Iodine-based products to provide evidence for the intrinsic efficacy of Iodine.

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
bactericide	PT3	Iodophor teat dips	Clostridium spores Coliform counts Anaerobe spores	[redacted]	[redacted]	Iodophor premilking teat dipping followed by subsequent drying with a paper towel reduced bacterial counts in milk as well as the use of teat preparation combined with wet and dry paper towel, but it was superior in reducing new infections. By replacing the paper towel with a cotton towel, iodophor premilking teat dipping followed by drying and scrubbing of teat ends will not raise Iodine residue in milk.	Doc. No. 392-028; Section A5.3.1/15

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
bactericide	PT5	Iodine	*Escherichia coli*	[redacted]		2-5 ppm: reduction to < 5 viable colonies after treatment of 10^8 cells within 10 minutes	Doc. No. 392-056; Section A5.3.1/14
bactericide	PT5	Iodine	Water-borne pathogenic organisms such as enteric bacteria amebic cysts, cercariae, leptospira and viruses	[redacted]	[redacted]	7-8 ppm Iodine in 10 minutes at room temperature: reduction to < 5 viable colonies after treatment of 10^8 cells obtained for *E.coli, Sal. typhosa, Sh. dysenteriae*, Vibrio cholera and mixed coli aerogenes flora of sewage. Sal. Schöttmuelleri: 20 minutes treatment required	Doc. No. 392-056; Section A5.3.1/14
bactericide	PT2-4	[redacted] (1350 ppm Iodine)	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeuginosa* *Enterobacter aerogenes* *Klebsiella pneumoniae* *Streptococcus*	[redacted]	[redacted]	Percentage reduction achieved: > 99.999 for all test organisms after 30 seconds contact time. Suspensions of micro-organisms tested at concentrations of 10^7 to 10^8 in contact with disinfectant.	Doc. No 381-015; Section A5.3.1/16

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
			dysgalactiae *Streptococcus agalactiae* *Streptococcus uberus*	[redacted]			
bactericide	PT3	[redacted] (1350 ppm Iodine)	*Staphylococcus aureus* *Escherichia coli*	[redacted]	[redacted]	5.62 and 5.49 log reduction for S. aureus and E. coli, respectively. Pass level for this kind of test is a 3 log reduction in the initial populations. Conclusion: [redacted] shows a significant and effective disinfecting action.	
Bactericide /fungicide	PT3	[redacted] (1350 ppm Iodine)	*P. aeruginosa* CIP 82.118 *S. aureus* CIP 4.83 *C. albicans* IP 48.72 *A. niger* IP 1431.83	[redacted]	[redacted]	The number of colonies per mL of product tested following contact with the product was analysed after 24 hours, 7, 14, 21 and 28 days. Less than 10 colonies per mL were counted indicating that the preserving action of [redacted] is guaranteed. Pass level: at least 4 log reduction after 24 hours.	
virucide	PT2	[redacted] and	Enterovirus	[redacted]	[redacted]	% disinfectant to achieve	Doc. No. 392-019; Section

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
		[redacted] (28,000 ppm Iodine) 7 other disinfectants (not containing Iodine)	(Talfan) Reovirus Type 1 WBR 26 Coronavirus: Transmissible gastroenteritis (TGE) Togavirus: Bovine virus diarrhoea (BVD) NADL Myxovirus: Parainfluenza Type 3 T1 Adenovirus type 3 WBR1 Herpesvirus: Infectious bovine rhinotracheitis (IBR) Oxford Poxvirus: Contagious pustular dermatitis (CPD) WVRS	[redacted]	[redacted]	4 log reduction in titer Talfan: 4% [redacted] Reovirus-1: Partial reduction only TGE: 4% [redacted], 3% [redacted] BVD: Partial reduction only Parainfluenza Type 3T1: 2% [redacted] or [redacted] Adenovirus type 3: 3% [redacted] or [redacted] IBR: 1% [redacted], 0.5% [redacted] CPD: 3% [redacted], 2% [redacted]	A5.3.1/17
virucide	PT2 and PT5	Iodine	Poliomyelitis virus, strain Lansing (mouse adapted)	[redacted]	[redacted]	Results were variable but at the concentrations needed for killing amebic cysts, it is also effective against Poliomyelitis virus.	Doc. No. 392-056; Section A5..3.1/14

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
				[redacted]			
Bactericide /fungicide/ virucide	PT3	[redacted] (28,000 ppm Iodine)	Lots of organisms/Pig stables	[redacted]	[redacted]	Bacteria: effective dilutions range from 1:30 for Mycobacterium spp. up to 1:150 for *Bordetella bronchiseptica.* Fungi: effective dilutions are 1:100 for all four relevant fungi. Viruses: effective dilutions range from 1:40 for the virus causing Transmissible Gastroenteritis to 1:600 for the virus causing Swine Vesicular Disease. [redacted] is not effective against Procine parvovirus.	Doc. No. 392-005; Section A5.3.1/18
bactericide	PT3	Iodine	*Staphylococcus aureus* *Staphylococcus agalactiae* *Corynebacterium bovis* Or grouped as Staphylococci and Streptococci	[redacted]	[redacted]	Concentrations of Iodine in products showing significant efficacy for postmilking treatment against: *S. aureus*: 0.05% to 1% Iodine *S. agalactiae*: 0.1% to 1% Iodine *C. bovis*: 0.25% to 1%	Doc. No. 392-030, Section A5..3.1/19

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
						Iodine Staph. species. 0.25% to 1% Iodine Streptococci: 1% Iodine	
bactericide	PT3	[redacted] (Iodophor: 0.1% Iodine) [redacted] (Iodophor: 0.25%) [redacted] (Iodine: 0.25%) [redacted] (Iodophor: 0.55% Iodine plus linear dodecyl benzene sulfonic acid at 1.9%)	No details provided. Test organisms are grouped as "Environmental pathogens", "major pathogens" and "Gram-negative bacteria".	[redacted]	[redacted]	Significant efficacy of product for premilking treatment against: [redacted] environmental pathogens (P>.10) and major pathogens (P<.05) [redacted], environmental pathogens (P>.05) and major pathogens (P<.025) [redacted] Gram-negative bacteria (P<.025) and major pathogens (P<.001) [redacted] environmental pathogens (P>.10) and major pathogens (P<.10)	
amoebicide	PT5	Iodine	Entamoeba histolytica cysts	[redacted]	[redacted]	A suitable dose for emergency disinfection was calculated to be about 8 ppm for a 10 minute treatment at 23 °C. In water with high organic color or Iodine demand > 3 ppm, an increase in dosage was needed. 16	Doc. No. 392-056; Section A5..3.1/14

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
				[redacted]		ppm was effective for all waters tested. At low temperatures (0-5 °C) the required contact time was 20 minutes.	

*) References:

Section A5.3.1/15: Rasmussen, M.D. et al. (1991): Effects of premilking teat preparation on spores of anaerobes, bacteria and Iodine residues in milk; J. Dairy Sci., Vol. 74, pp. 2472-2478; Doc. No. 392-028. (published)

Section A5..3.1/16: Anonymous (n.i.): Technical file-[redacted]; Doc. No. 381-015 (published).

Section A5..3.1/17: Evans, D.H. (19779: Disinfection of animal viruses; Fr. Vet. J., pages 133 and 356; Doc. No. 392-019 (published).

Section A5.3.1/18: Anonymous (n.i.): Pig disinfection programme; Evans brochure; Doc. No. 392-005 (published).

Section A5..3.1/19: Anonymous (1996): 35th annual meeting-national mastitis council, Inc.: Summary of peer-reviewed publications on efficacy of premilking and postmilking teat disinfectants published since 1980; National Mastitis Council Annual Meeting Proceedings, pages 245-256; Doc. No. 392-030 (published).

Please refer also to Table 5.3.1_I-3 and Table 5.3.1_PVP-I-3 in the corresponding confidential parts of the dossier submitted in July 2007 (not included again in the present dossier) for a summary of available data provided by the applicant which is considered confidential.

In addition to the information submitted in 2007 in the dossier for PT3, please refer to Table 5.3.1-4 in the confidential part of the present dossier for a summary of available data provided by the applicant which is considered confidential.

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

Official use only

1 REFERENCE

1.1	**Reference**	Chang, S.L.and Morris, J.C.(1953): ELEMENTAL IODINE AS A DISINFECTANT FOR DRINKING WATER; Industrial and Engineering Chemistry, 45, 5, May 1953, 1009-1012; Doc. No.: 392-056 (published). This document was first cited under section point A5.3.1/14.
1.2	**Data protection**	[redacted]
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
1.3	**Guideline study**	No but the studies described in the publication were conducted as suspension tests resembling the EN1040 method.
1.4	**Deviations**	Not applicable

2 METHOD

2.1	**Test Substance (Biocidal Product)**	Elemental iodine
2.1.1	Trade name/ proposed trade name	[redacted]
2.1.2	Composition of Product tested	[redacted]
2.1.3	Physical state and nature	[redacted]
2.1.4	Monitoring of active substance concentration	[redacted]
2.1.5	Method of analysis	[redacted]
2.2	**Reference substance**	[redacted]
2.2.1	Method of analysis for reference substance	[redacted]
2.3	**Testing procedure**	[redacted]
2.3.1	Test population / inoculum / test organism	[redacted]
2.3.2	Test system	[redacted]
2.3.3	Application of TS	[redacted]

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

2.3.4 Test conditions

2.3.5 Duration of the test / Exposure time

2.3.6 Number of replicates performed

2.3.7 Controls

2.4 Examination

2.4.1 Effect investigated

2.4.2 Method for recording / scoring of the effect

2.4.3 Intervals of examination

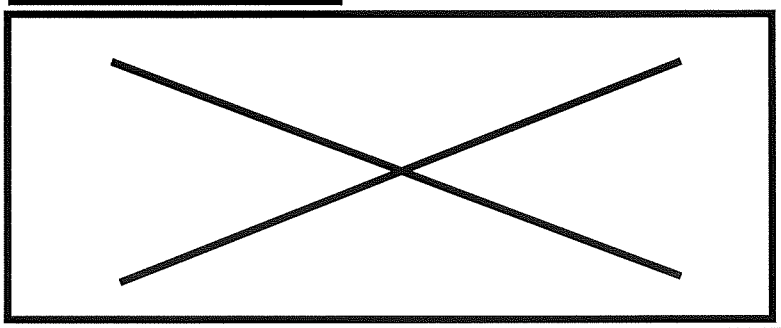
2.4.4 Statistics

2.4.5 Post monitoring of the test organism

3

3.1 Efficacy

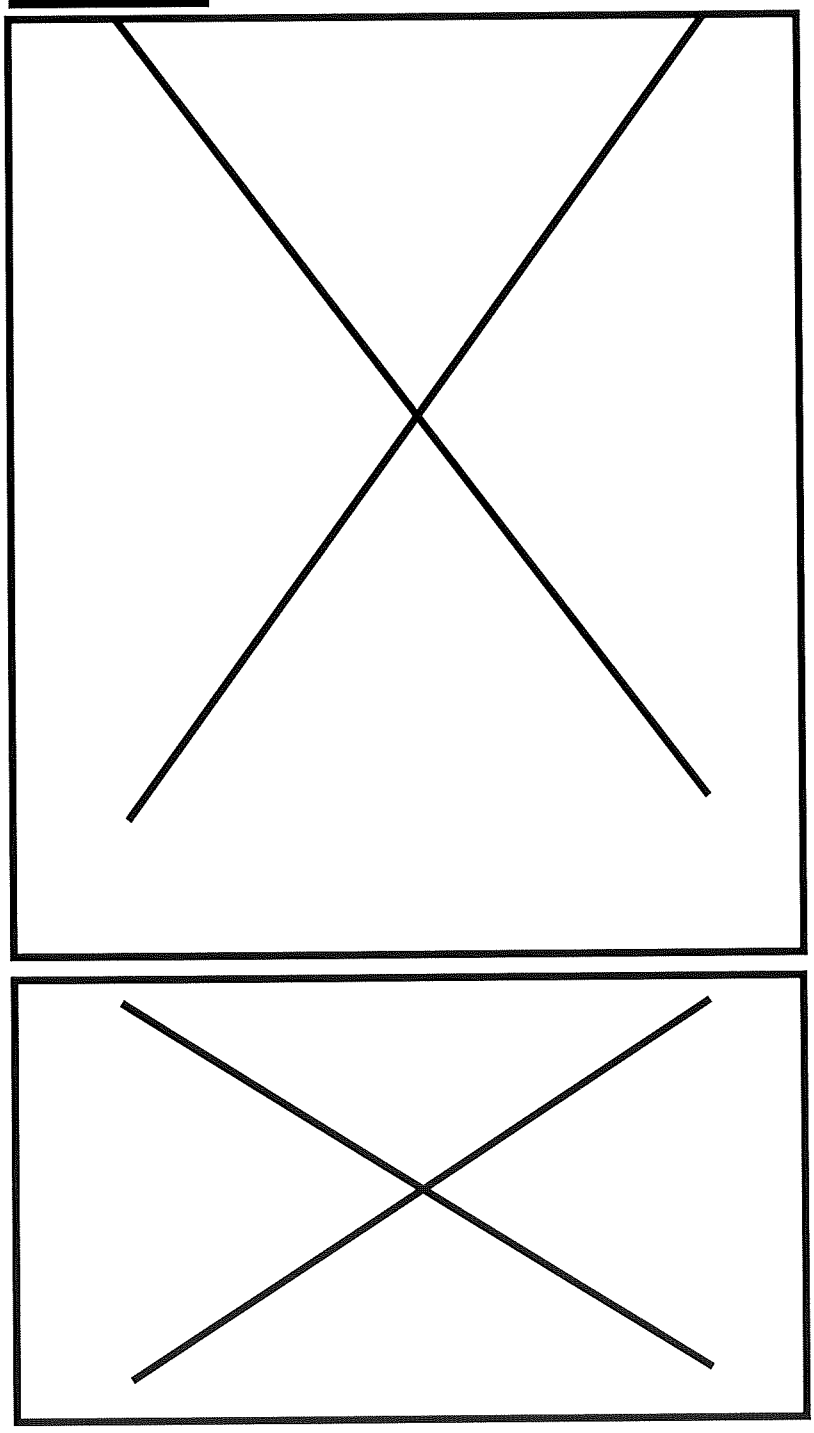
3.1.1 Dose/Efficacy curve



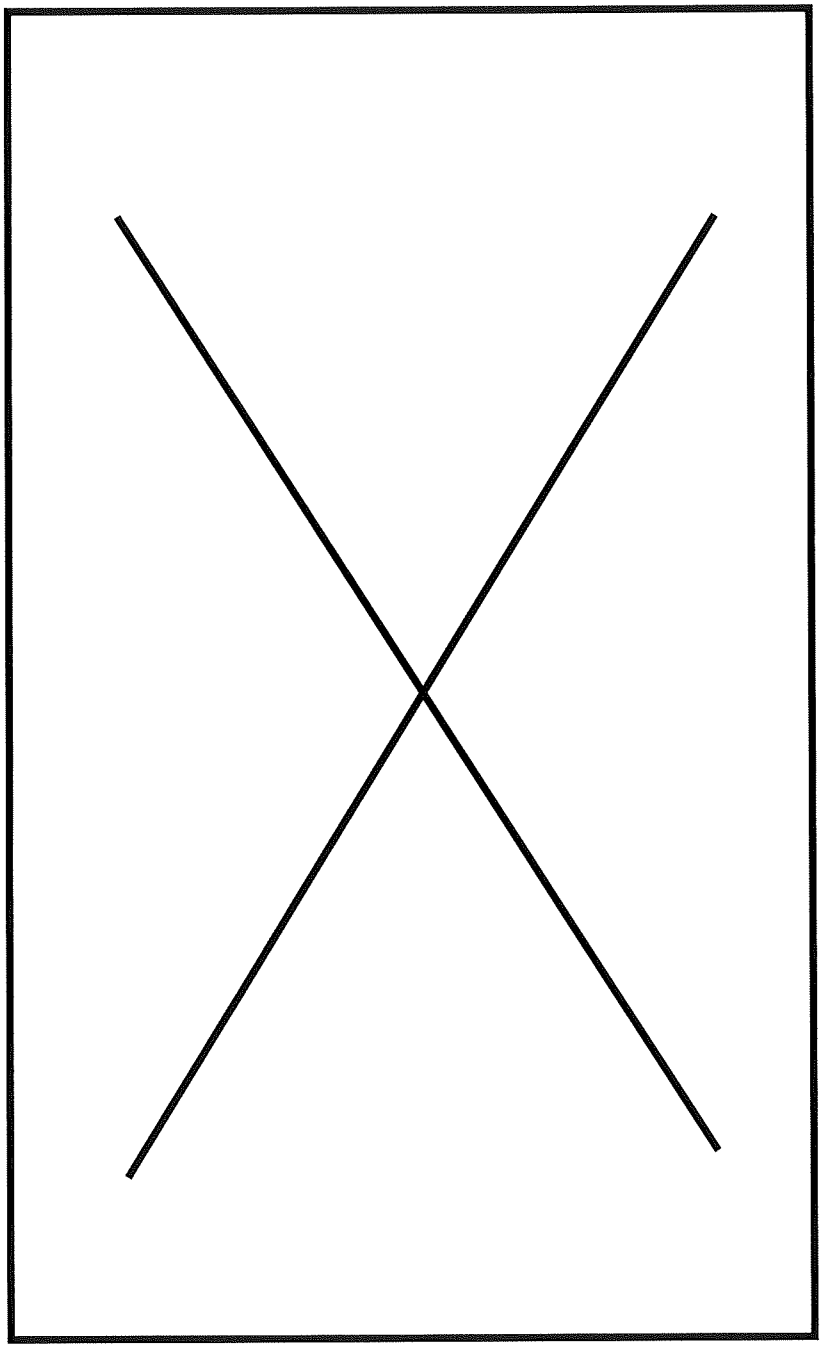
3.1.2 Begin and duration of effects

3.1.3 Observed effects in the post monitoring phase

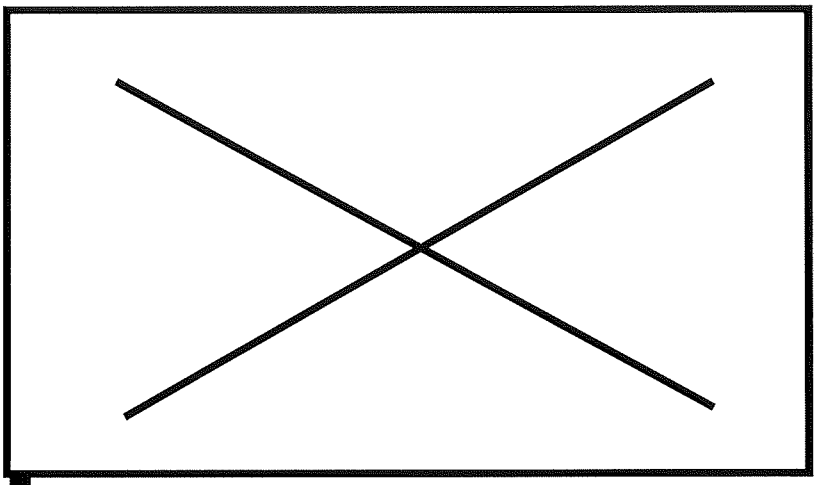
3.2 Effects against

	organisms or objects to be protected	
3.3	**Other effects**	[redacted]
3.4	**Efficacy of the reference substance**	[redacted]
3.5	**Tabular and/or graphical presentation of the summarised results**	

Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*



Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*



3.6 Efficacy limiting factors

3.6.1 Occurrences of resistances

3.6.2 Other limiting factors

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing

4.2 Intended actual scale of biocide application

4.3 Relevance compared to field conditions

4.3.1 Application method

4.3.2 Test organism

4.3.3 Observed effect

4.4 Relevance for read-across

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and

Section A5/01
Annex Point IIB V.5.10

Efficacy Data
Suspension tests with bacteria and viruses

methods

[redacted]

5.2 Reliability

[redacted]

5.3 Assessment of efficacy, data analysis and interpretation

[redacted]

5.4 Conclusion

Iodine has innate efficacy against bacteria, amoebae and viruses in water.

5.5 Proposed efficacy specification

[redacted]

Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Comments	[redacted]
Summary and conclusion	[redacted]

COVER PAGE

Doc. No.: 381-017

Title:	BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD
Author(s):	Fotheringham, V.J.C.
Report date:	Apr/2007

SCC Project No.:	854-005
Name of database:	Iodine

EVANS VANODINE
INTERNATIONAL PLC
Global Hygiene Solutions

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW

Prepared by Valerie J C Fotheringham
Chief Microbiologist, Evans Vanodine International plc

FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD

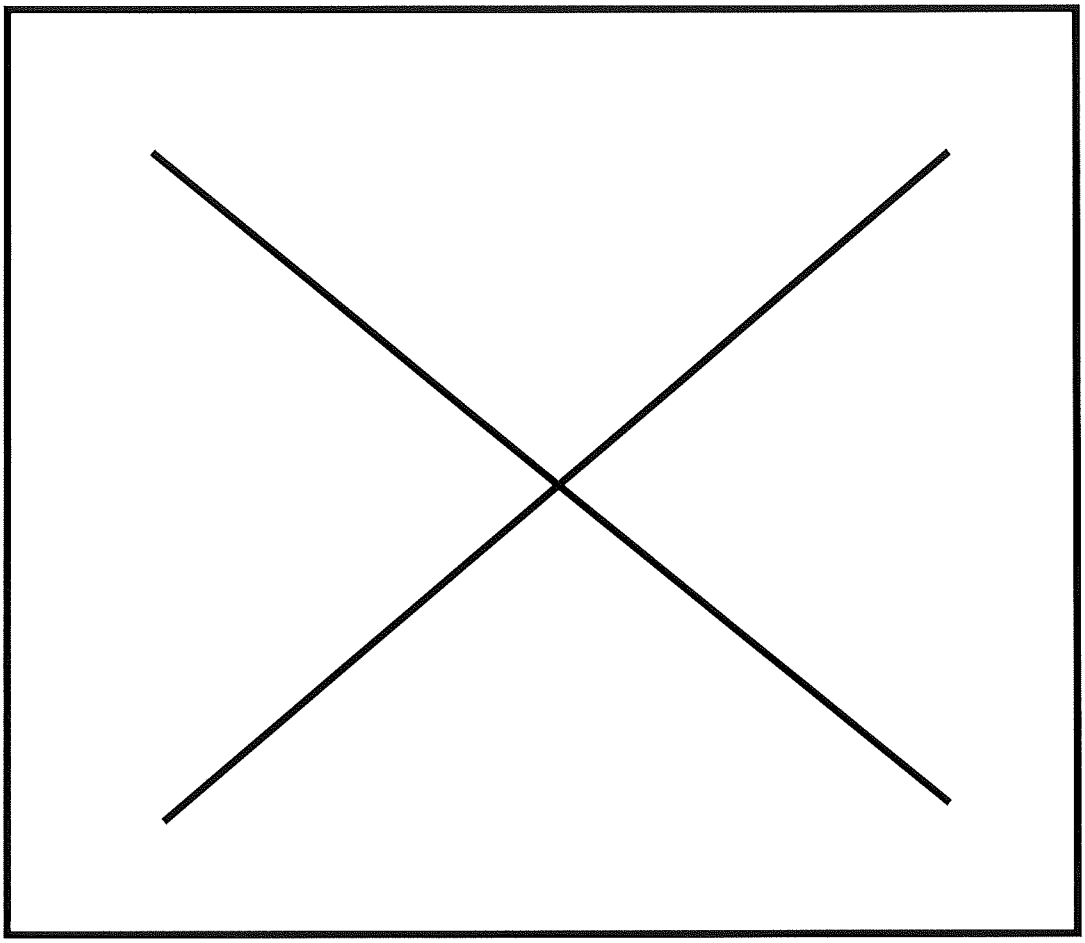
APRIL 2007

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CONTENTS

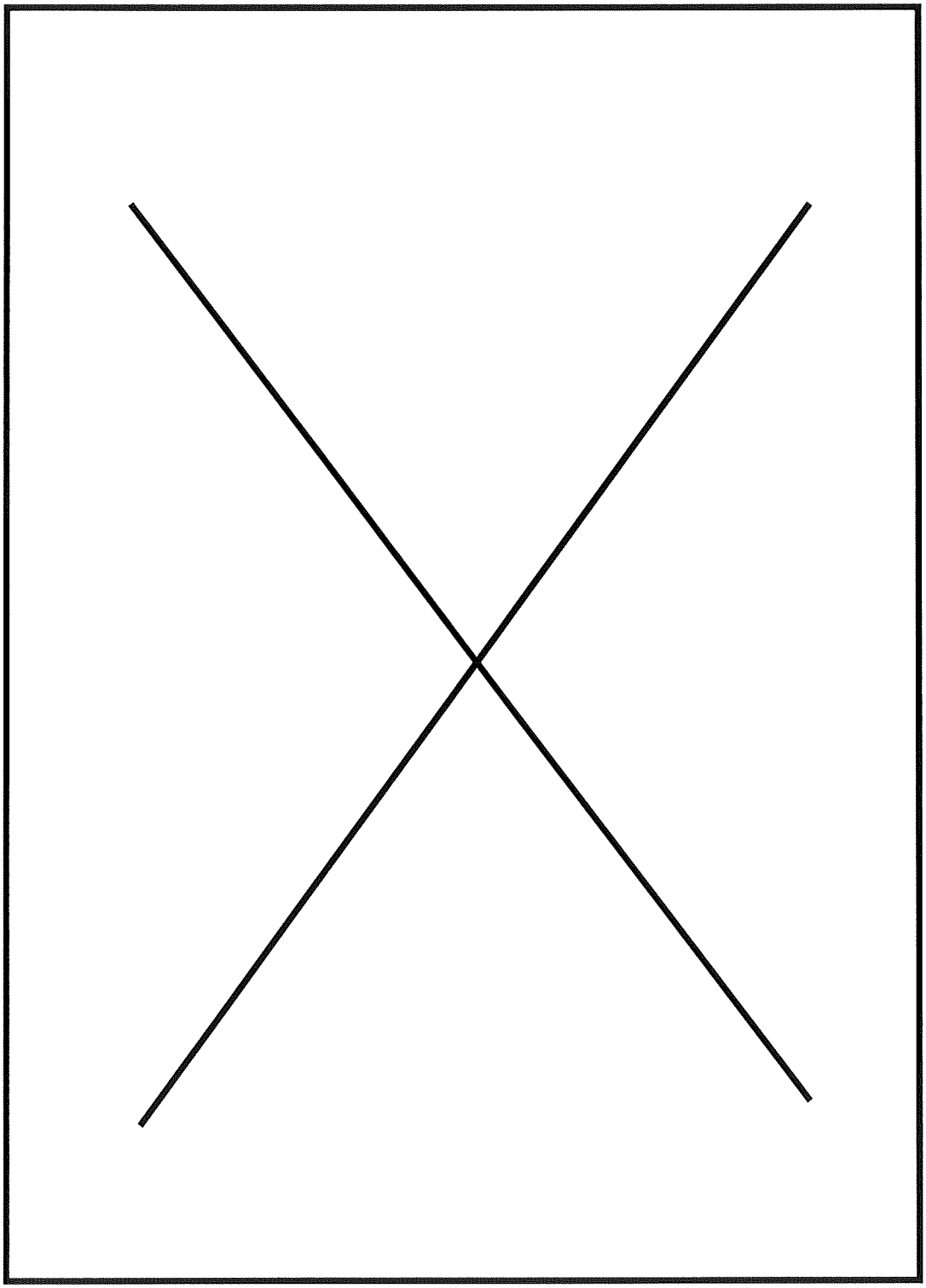
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

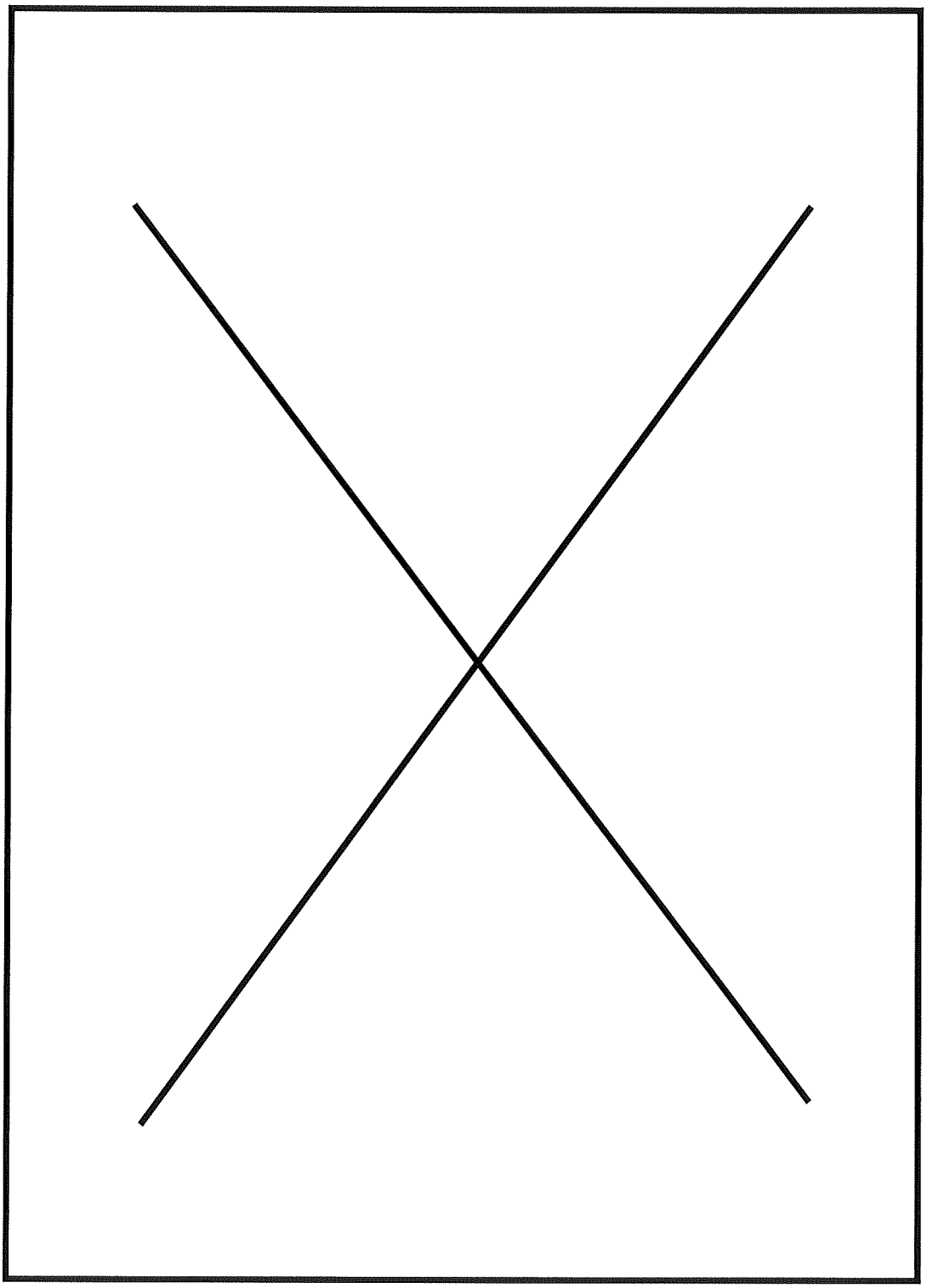


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

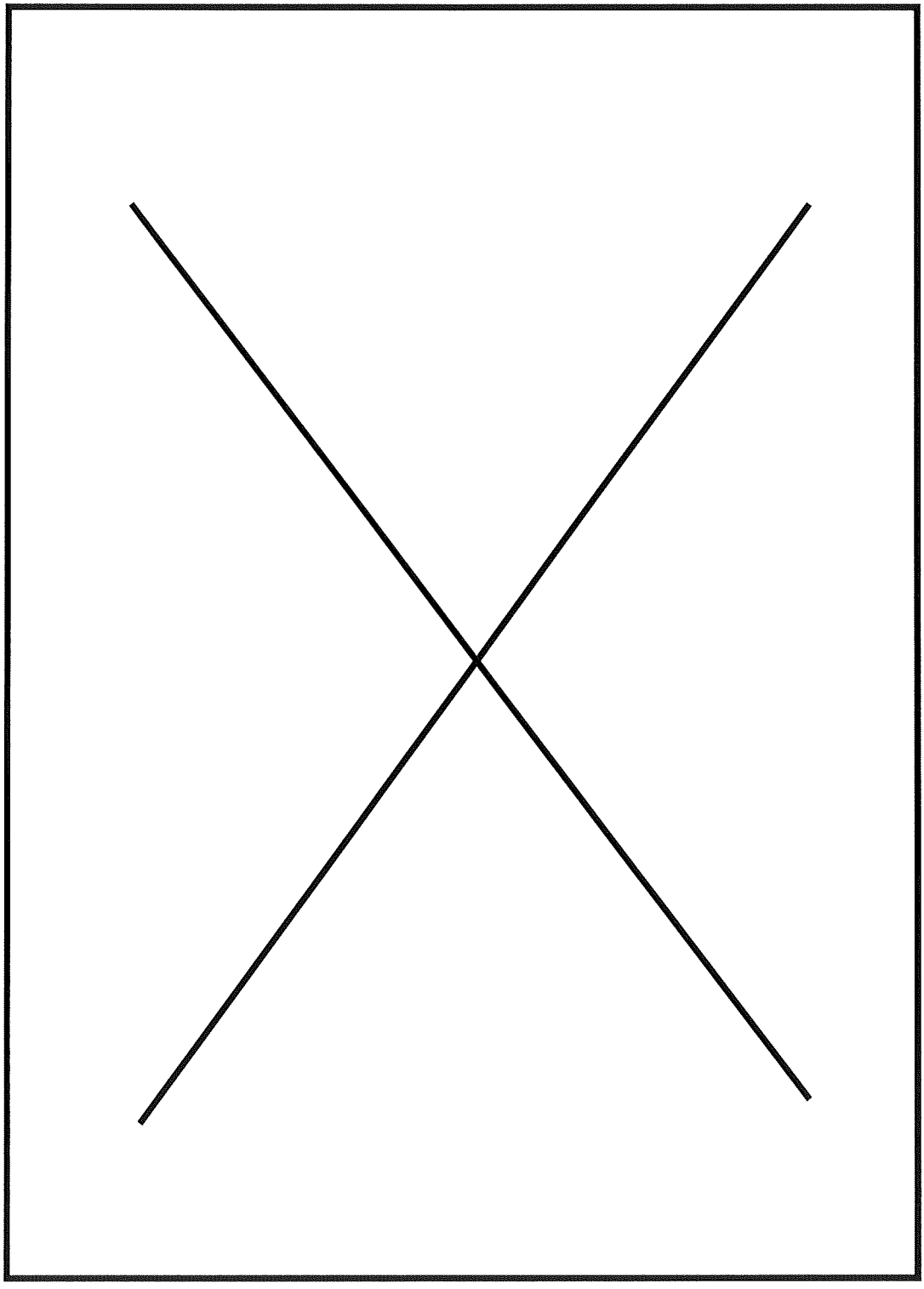


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

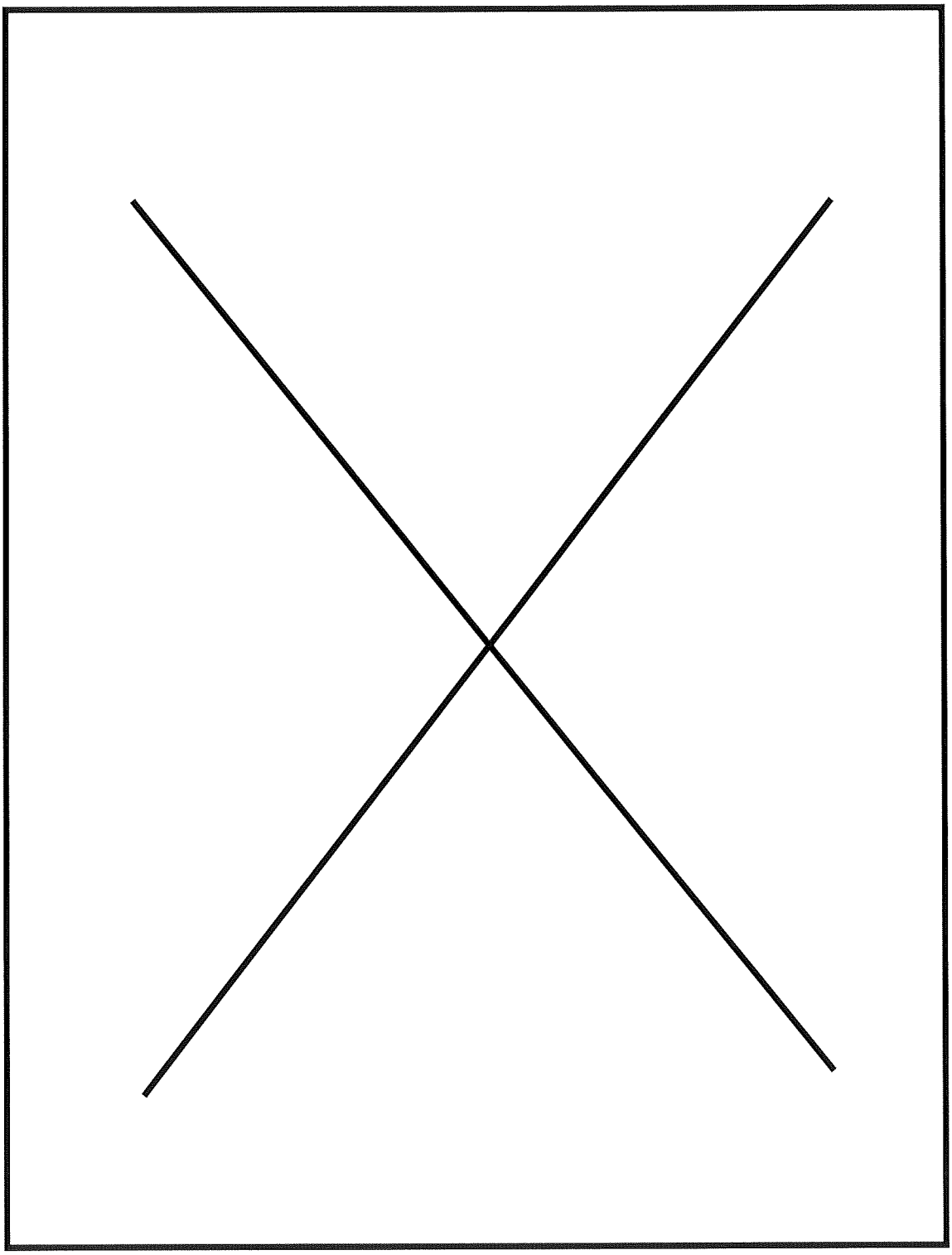


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

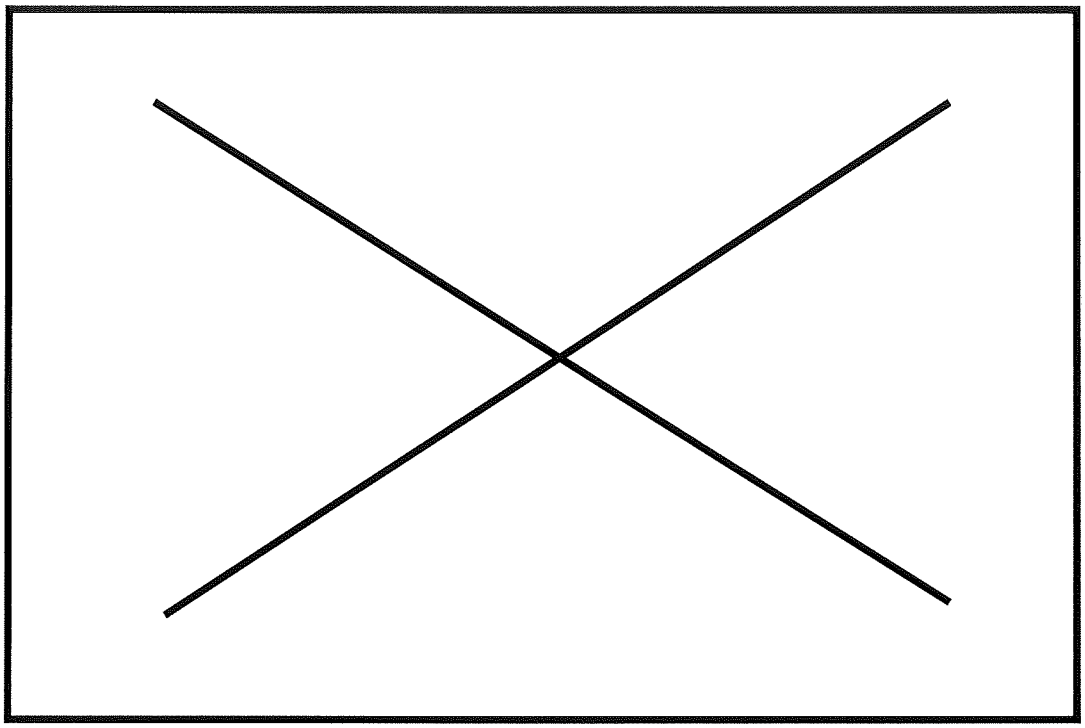


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

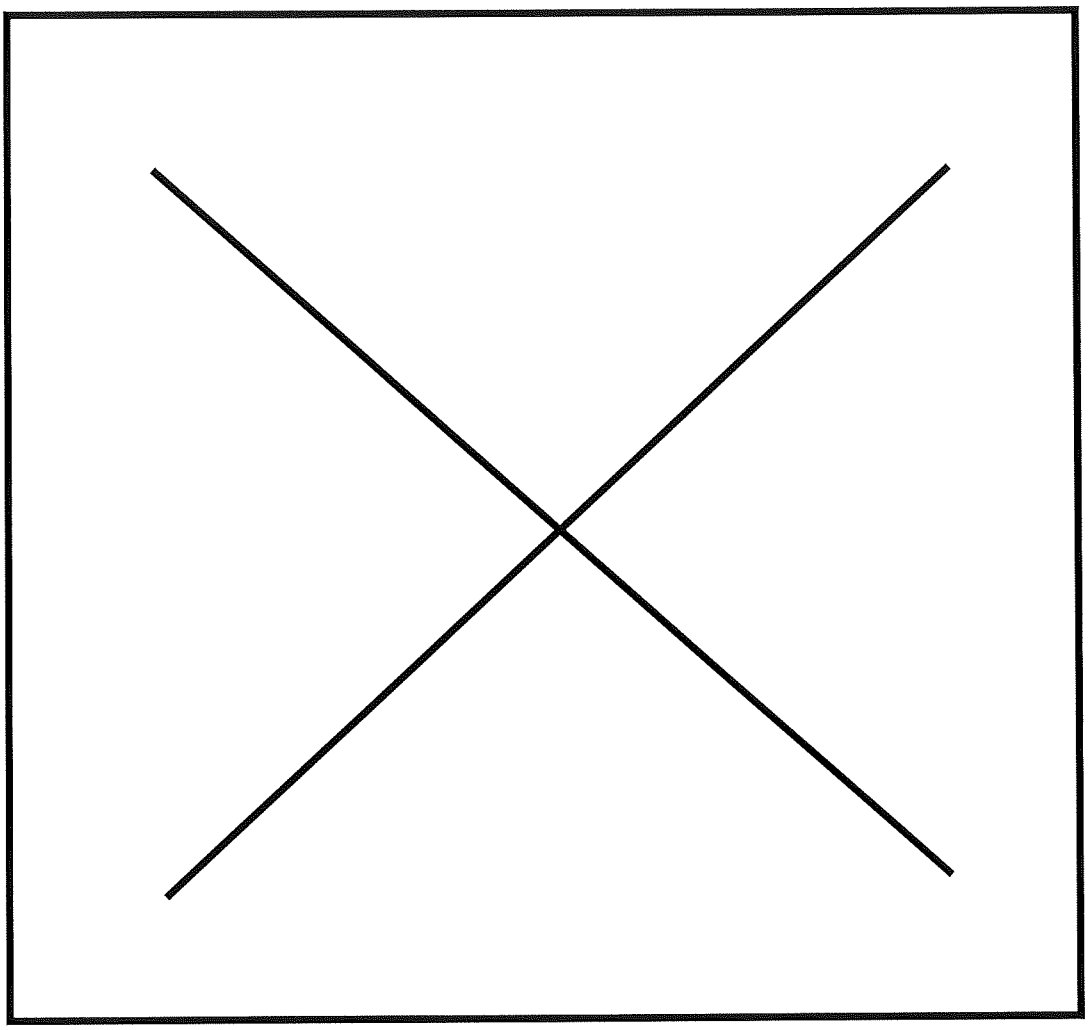


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW



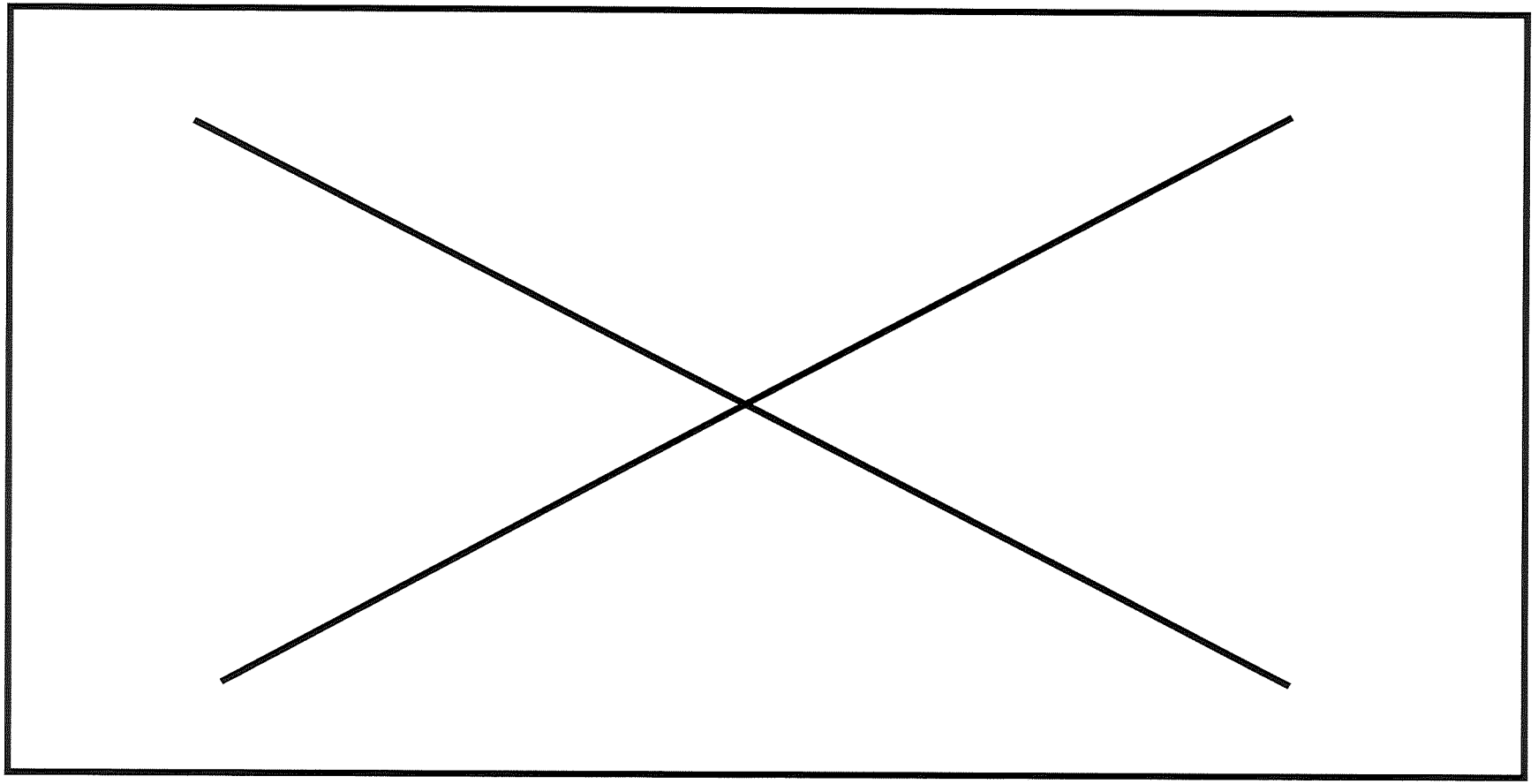
Valerie J C Fotheringham B.Sc., C.Biol, M.I.Biol.
Chief Microbiologist

DATE: 30 April 2007.

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 1: PASS DILUTIONS FOR IODOPHOR SURFACE DISINFECTANT* AGAINST A RANGE OF MICRO-ORGANISMS



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 2: PASS DILUTIONS FOR IODOPHOR TEAT DISINFECTANT*** AGAINST A RANGE OF BACTERIA

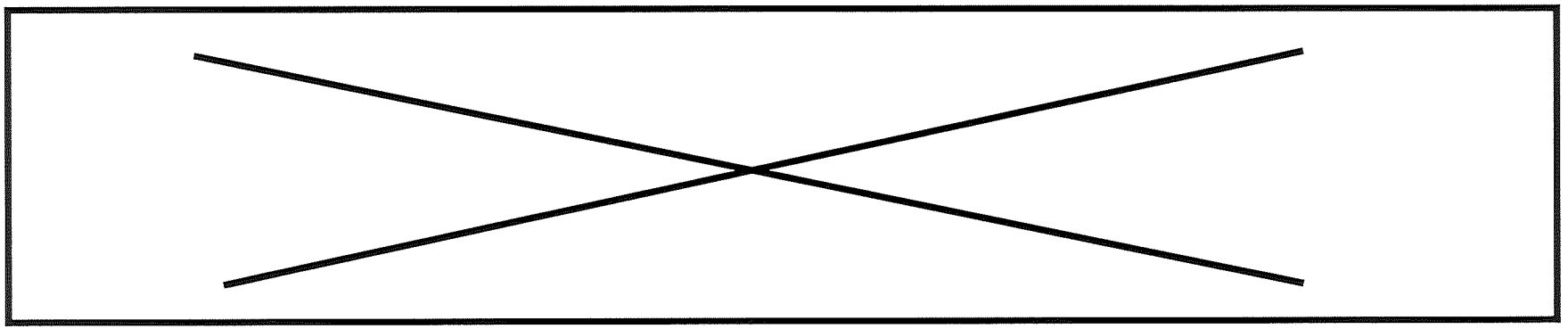
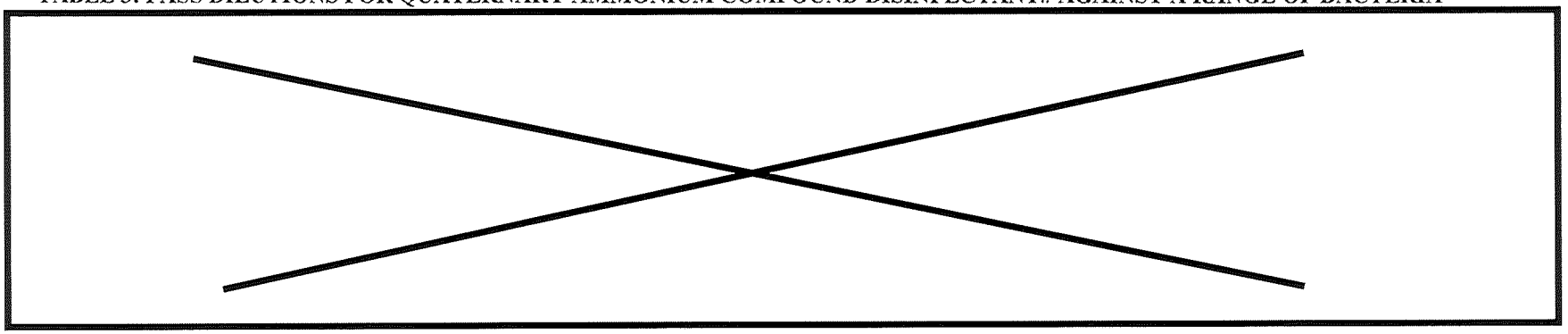


TABLE 3: PASS DILUTIONS FOR QUATERNARY AMMONIUM COMPOUND DISINFECTANT# AGAINST A RANGE OF BACTERIA



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

CHART 1: RELEVANCE OF REFERENCES SITED FOR IODINE RESISTANCE

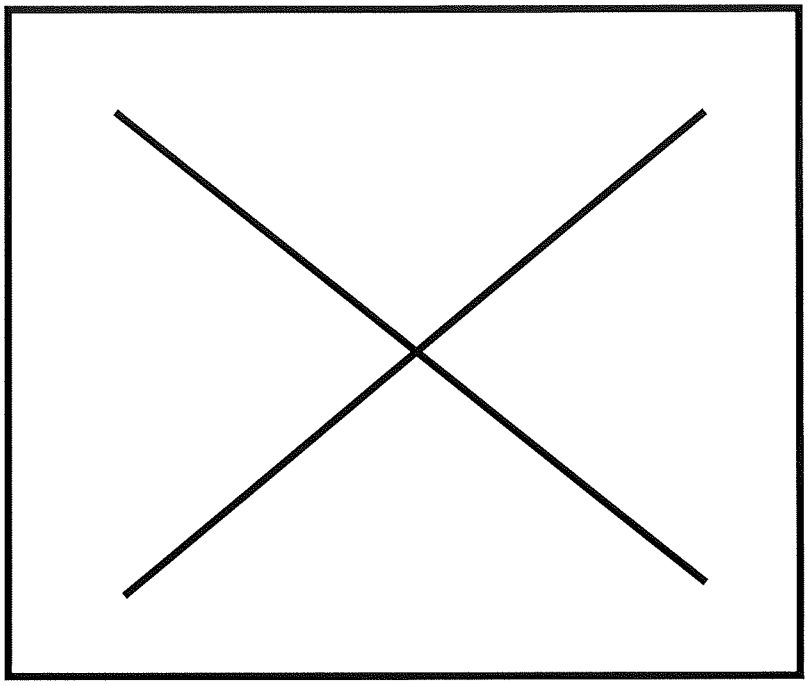
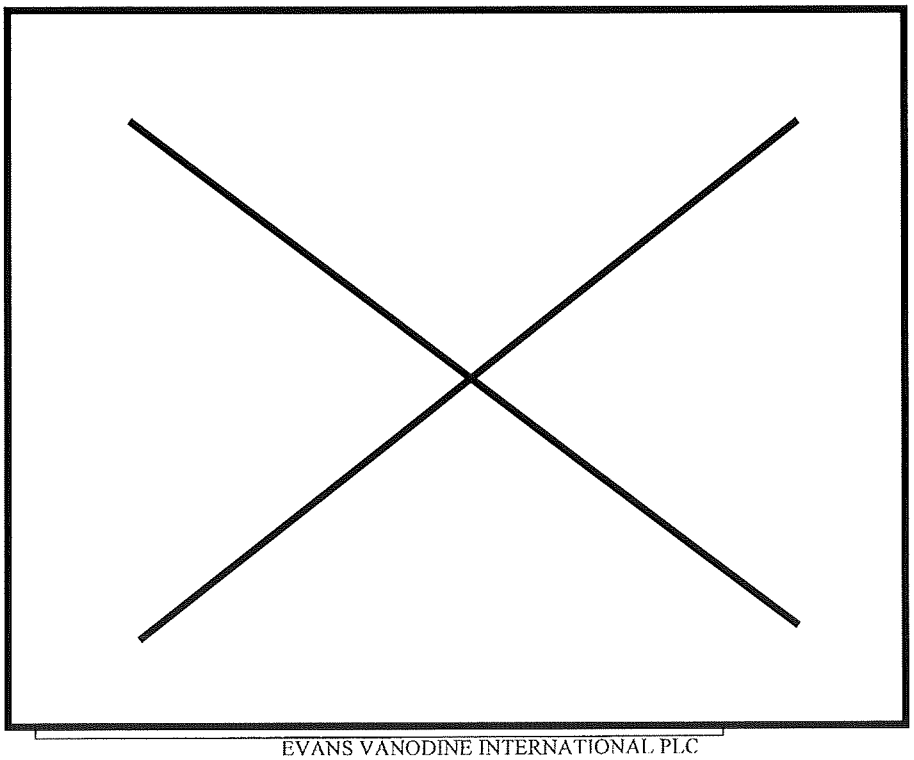
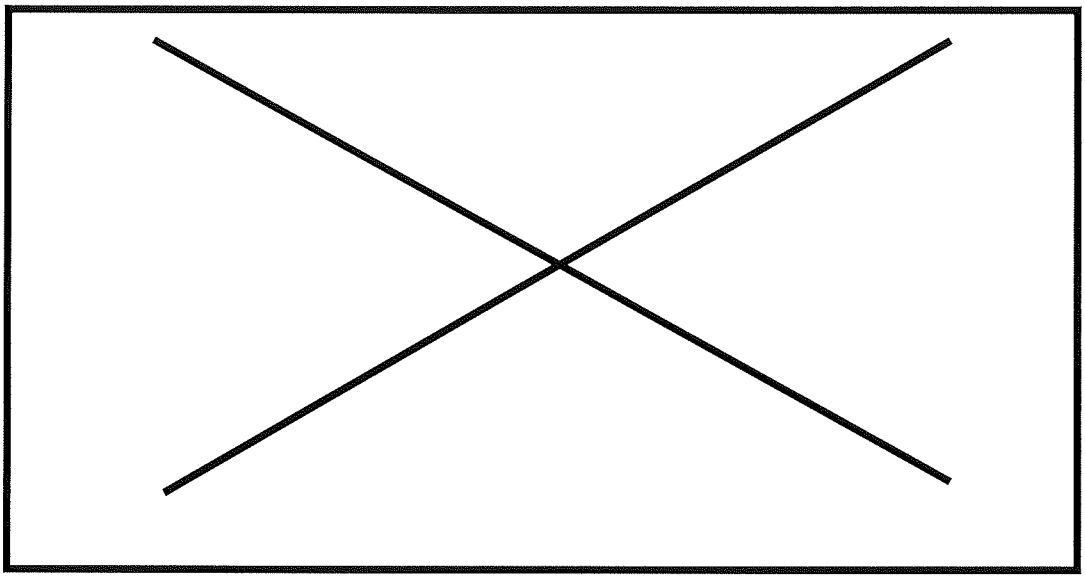


CHART 2: CATERGORIES OF REFERENCES FOR IODINE RESISTANCE



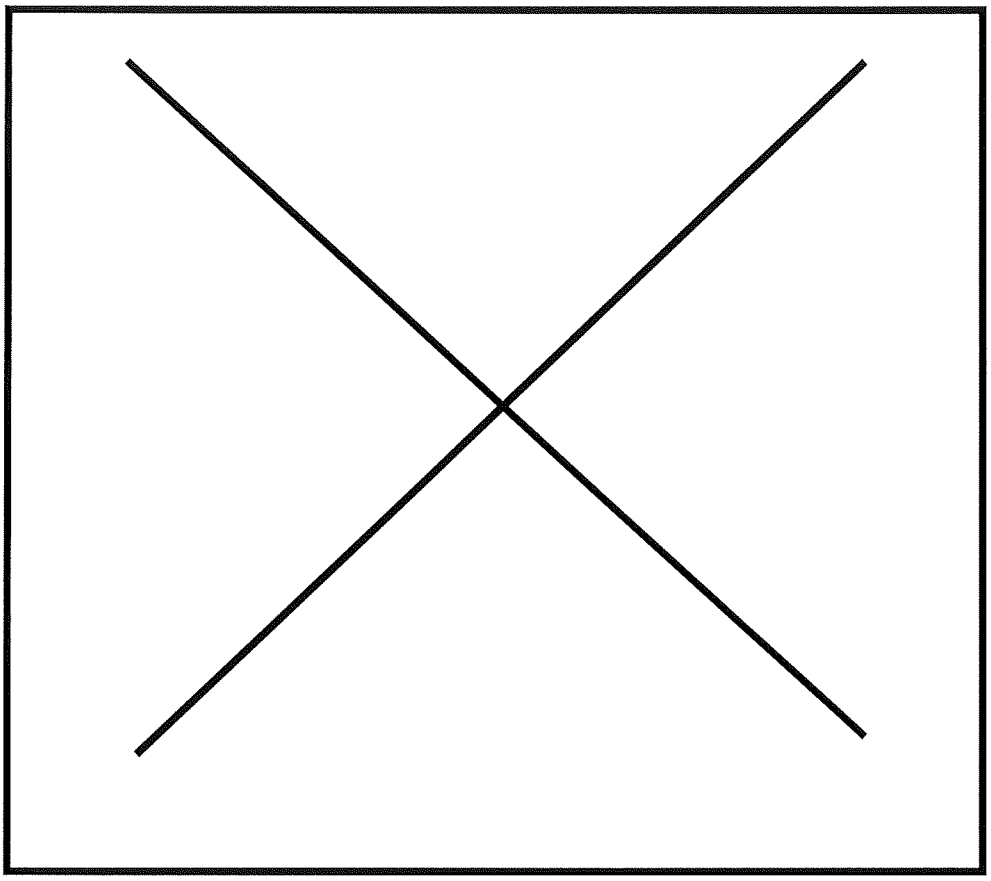
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CHART 3: Somatic cell counts in England and Wales



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CHART 4: PERCENTAGE OF TEAT DISINFECTANTS USED GLOBALLY



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

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BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

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Statement on the organisms to be controlled:

COVER PAGE

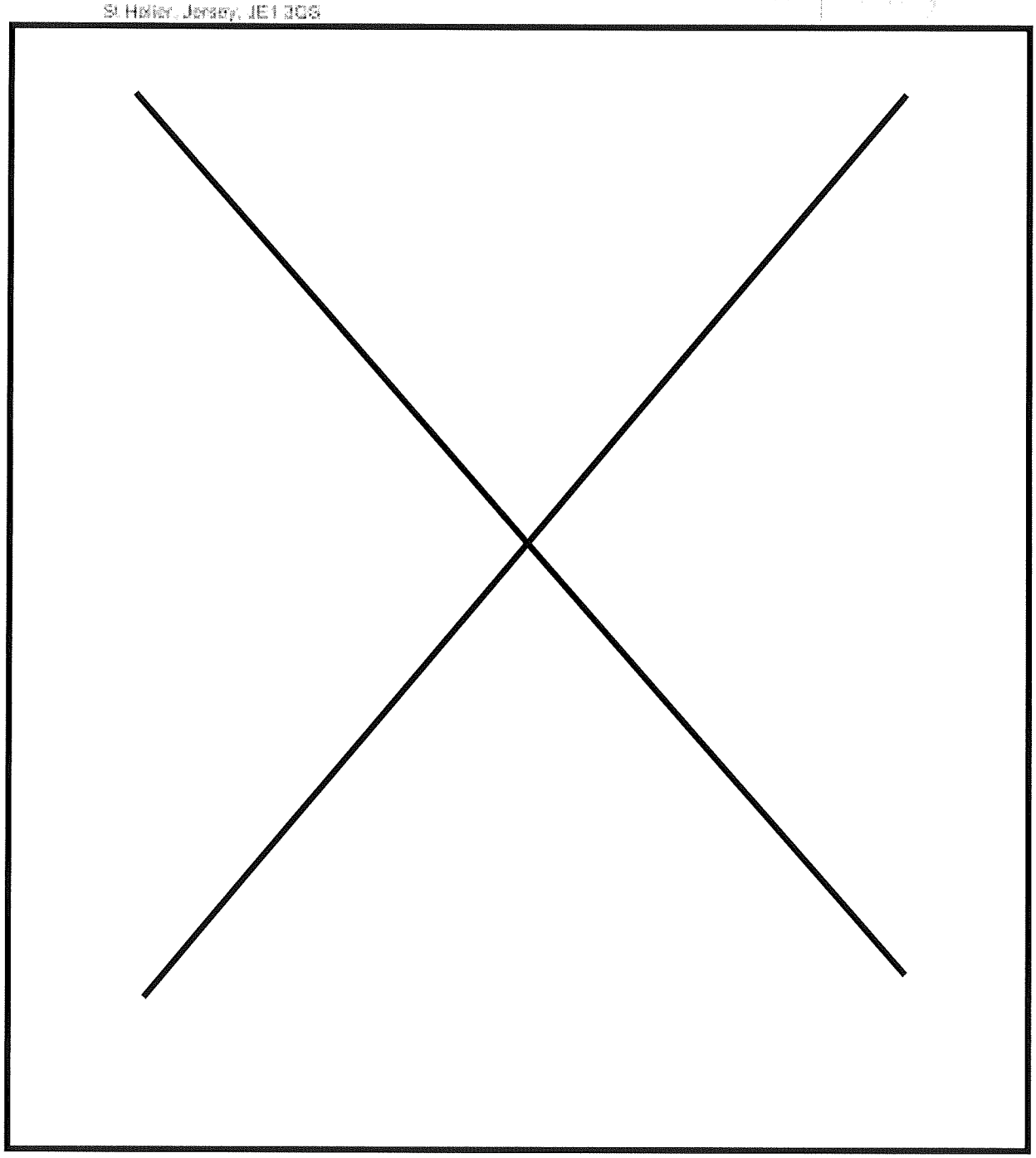
Doc. No.: 381-019

Title:	LETTER HEALTH AND SOCIAL SERVICES DEPARTMENT TO DR. HIGGINS - PREDOMINANT ORGANISMS IN A CADAVER
Author(s):	Anonymous
Report date:	09/04/2006

SCC Project No.:	954-005
Name of database:	Iodine

faxed 9th Sept
Hard copy in post

Health and Social Services Department
Microbiology and Genito Urinary Medicine Department
General Hospital, Gloucester Street
St Helier, Jersey, JE1 3QS

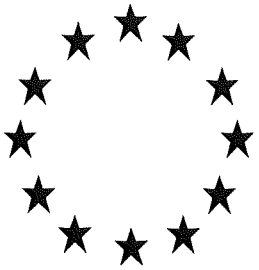


Yours sincerely,

Dr I Muscat FRC Path., Dip.Clin.Micro., Dip GUM.
Consultant Microbiologist

Competent Authority Report

Work Programme for Review of Active Substances in Biocidal Products
Pursuant to Council Directive 98/8/EC



IODINE (PT3)

DOCUMENT III-A5

Efficacy

Rapporteur Member State: Sweden

Draft Final May 2013

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Section A5 Effectiveness against target organisms and intended uses

Subsection Annex Point IIA V.5.1 – V.5.8			Official use only
5.1	**Function (IIA5.1)**	Bactericide, virucide and fungicide.	
5.2	**Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)**		
5.2.1	**Organism(s) to be controlled (IIA5.2)**	Iodine is used for control of various pathogenic organisms such as bacteria (including spores and mycobacteria), viruses and fungi. Examples of organisms against which Iodine was successfully tested are listed in Tables A5.3.1-1, A5.3.1-2 and A5.3.1-3. Please note the available data summarised in these tables is not exhaustive due to the large number of available publications. Only the most relevant literature is described. In addition to literature data, also laboratory reports on tests performed with Iodine-based products have been included, examples of which are listed below for the relevant uses. On request of the applicant this information is provided in the Confidential part of the dossier	
5.2.2	**Products, organisms or objects to be protected (IIA5.2)**	**Manual non-medical teat disinfection and udder washes** Dairy cows, sheep and goats are protected from pathogens causing inflammation of the mammary gland. Man is protected as consumer of milk. **Surface disinfection in animal houses (including milking equipment and milk tanks)** Cows, pigs, poultry and other livestock kept in animal houses are protected from contagious diseases. Man is indirectly protected as consumer of animal products (e.g. milk and meat).	X5
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**		

Section A5 Effectiveness against target organisms and intended uses

5.3.1 Effects on target organisms (IIA5.3)

Iodine in aqueous or alcoholic solutions or solubilised with surfactants (iodophors) is used in a variety of applications to kill harmful microorganisms and viruses. These preparataions are used as skin disinfectants pre-operatively, with wound dressings, for teat dipping in dairy cows, sheep and goats and for surface disinfection in a number of industries. X6 X1

Iodine is suitable for all of these applications because it is a broad spectrum biocide, its efficacy has been demonstrated over 170 years of use. Iodine and iodophors are well established and accepted as having microbicidal activity.

There is a huge number of papers demonstrating the microbicidal activity of iodophor products in laboratory and field tests but only a few of these are referenced here as most of them relate to specific formulations and not just to Iodine.

In Table A5.3.1-1, the available information in published text and reference books and in scientific reviews is summarised.

In Table A5.3.1-2, exemplary studies from publicly available sources are included showing the efficacy of Iodine-based products for biocidal uses.

In Tables A5.3.1_I-3 and A5.3.1_PVP-I-3, provided in the corresponding confidential parts of the dossier, exemplary studies provided by the applicant are included showing the efficacy of Iodine-based products.

5.3.2 Likely concentrations at which the A.S. will be used (IIA5.3)

PT3

Manual non-medical teat disinfection and udder washes: X2 X3 X4
0.0025 – 1.0 % Iodine corresponding to 25 – 10,000 ppm Iodine

Surface disinfection in animal houses (including equipment and milk tanks): X5
0.0025 – 0.020 % Iodine corresponding to 25 – 200 ppm Iodine

5.4 Mode of action (including time delay) (IIA5.4)

5.4.1 Mode of action

The following mechanisms of action contribute to the high reactivity and non-selective action of Iodine against different micoorganisms:

- Iodine rapidly penetrates into micoorganisms showing a high affinity pattern of adsorption.
- Iodine combines with protein substances in the bacterial cell; these can be peptidoglycans in the cell walls or enzymes in the cytoplasm. This results in irreversible coagulation of the protein and consequent loss of function.
- Iodine is known to act on thiol groups in the cell; if a thiol enzyme is part of a metabolic chain, metabolic inhibition will result.
- Iodine reacts with key groups of proteins, in particular the free-sulfur amino acids cysteine and methionine, nucleotides

		and fatty acids. • Iodine interferes at the level of the respiratory chain of the aerobic microorganisms by blocking the transport of electrons through electrophilic reactions with the enzymes of the respiratory chain. For further details, please refer to the expert statement on resistance attached to this document (Attachment 1_381-017.pdf).	
5.4.2	**Time delay**	The rapid penetration of Iodine into microorganisms and its mode of action indicate that the time-delay i.e. contact time required for sufficient efficacy depends on the tolerance of the organism to Iodine and the concentration of Iodine used for treatment. Iodine is more effective at higher temperatures. The germicidal activity of Iodine-containing solutions is characterised by their colour. Amber solutions are active whilst pale yellow or colourless solutions are less effective and must be replaced by new solutions.	
5.5	**Field of use envisaged (IIA5.5)**		
	MG01: Disinfectants, general biocidal products	PT 3: Veterinary hygiene biocidal products.	
5.6	**User (IIA5.6)**		
	Industrial	No industrial use	
	Professional	**Manual non-medical teat disinfection and udder washes:** Depending on the product, the biocidal product is diluted or used as ready-to-use product. Teats of cows, sheep or goats are treated with the use solution by spraying, or by dipping of the teats into the solution. Alternatively, milking machines with integrated automated dipping in a closed system are being used.	
		Surface disinfection in animal houses (including equipment and milk tanks): Biocidal product is diluted and surfaces are sprayed with the use solution. Equipment is either sprayed with use solution or immersed into use solution. Milking equipment and holding tanks can also be disinfected by CIP procedures. For detailed use-descriptions, please refer to Document IIB, Chapter 8. For further illustration of the procedures, please refer to the video (Doc. No. 998-005; Section A5.6/01).	X5
	General public	None	

Section A5 Effectiveness against target organisms and intended uses

5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**		
5.7.1	**Development of resistance**	Iodine / Iodophors have been used in teat dips since the 1960's and are still the predominant type of product used for the prevention of mastitis. No reduction in efficacy was reported to the producers indicating that no development of resistant microorganisms or viruses has occurred. An overview on the efforts made to find reports on the development of resistance to Iodine is provided in the expert statement attached to this document (Attachment 1_381-017.pdf).	X7
5.7.2	**Management strategies**	No management strategies have been developed since no occurrence of resistance has been observed. Nevertheless, it should be noted that Iodine-based products are exclusively applied by professional users, in most cases as part of professional hygiene programs, which also involve other biocidal substances of different chemical structure and different mode of action (alternating applications).	
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	Based on an estimate provided by one supplier of Iodine, the Iodine world demand in the year 2006 for the production of disinfectants was 14% of the total Iodine world demand of 25,000 – 26,000 t/year. Thus, about 3640 t Iodine/year were used for the production of disinfectants throughout the world. Doc. No. 031-013; Section A5.8/01 For information on the likely tonnage to be placed on the market per year for biocidal products per member of the Iodine Registration Group (IRG), please refer to the confidential part of the dossier.	

Section A5 Effectiveness against target organisms and intended uses

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

General

Conclusion

Reliability

Acceptability

Remarks

Section A5 Effectiveness against target organisms and intended uses

Table 5.3.1-1: Summary table of reviews available in public literature on the efficacy of Iodine

Title/Author(s)	Reference	Year	Conclusion	Section point
Review Article The Role of Iodine in Antisepsis and Wound Management: A Reappraisal G. Selvaggi, S. Monstrey, K. Van Landuyt, M. Hamdi and P. Blondeel	*Acta.chir belg*, 103 (3), 241-247	2003	[redacted]	Doc. No. 392-055, Section A5.3.1/01
Topical Antimicrobial Agents in Dermatology Candace Thornton Spann, Susan C Taylor and Jeffrey M Weinberg	*Clinics in Dermatology* 21, 70-77	2003	[redacted]	Doc. No. 392-049, Section A5.3.1/02
Review of disinfectant susceptibility of bacteria isolated in hospital to commonly used disinfectants Tadashi Shiraishi and Yoshito Nakagawa	*Postgrad Med J* 69 (Suppl.3), S70-S77	1993		Doc. No. 392-057, Section A5.3.1/03
Virucidal Activity of Biocides A. Activity against human viruses A.S.Sattar and S.Springthorpe	In: *Principles and Practice of Disinfection, Preservation and Sterilization* 3rd Edition p178 Edited by A.D.Russell, W.B.Hugo and G.A.J.Ayliffe Published by Blackwell Scientific Publications	1999	[redacted]	Doc. No. 392-048, Section A5.3.1/04
Virucidal Activity of Biocides A. Activity against veterinary viruses P.J.Quinn and B.K.Markey	Page 193		[redacted]	

Title/Author(s)	Reference	Year	Conclusion	Section point
Halogens - Free Iodine W.B.Hugo and A.D.Russell	Page 45-46		[redacted]	
Halogens - Iodophors W.B.Hugo and A.D.Russell	Page 45-46		[redacted]	
Iodine	In: *Martindale The Complete Drug Reference* 32nd Edition p1494	1999	[redacted]	Doc. No. 392-047, Section A53.1/05
Chemical disinfectants, antiseptics and preservatives E.M.Scott and S.P.Gorman	In: *Pharmaceutical Microbiology* 6th Edition p219	1998	[redacted]	Doc. No. 392-046, Section A5.3.1/06
Chemicals used as disinfectants: active ingredients and enhancing additives D.J. Jeffrey	*Rev.sci.tech.Off.int.Epiz.* 14 (1) 68	1995	[redacted]	Doc. No. 392-045, Section A5.3.1/07
Iodine	*The Pharmaceutical Codex* 12 Edition *Principles and Practice of Pharmaceutics* p582	1994	[redacted]	Doc. No. 392-050, Section A5.3.1/08
Iodophores		1994	[redacted]	
Bacterial Spores and Chemical Sporicidal Agents A.D.Russell	*Clinical Microbiology Reviews* Vol. 3, No. 2, p99-119	1990	[redacted]	Doc. No. 392-058, Section A5.3.1/09

Title/Author(s)	Reference	Year	Conclusion	Section point
The Bacterial Flora of 'In-Use' Teat Dips J.Bruce	In: *Disinfectants Their use and Evaluation of Effectiveness* p177-182 Edited by C.H.Collins, M.C.Allwood, Sally F. Bloomfield and A.Fox Published by Academic Press, London	1981	[redacted]	Doc. No. 392-051, Section A5.3.1/10
The inactivation of vegetative micro-organisms by chemicals in the dairying industry Christina M Cousins	In: *Inhibition and Inactivation of Vegetative Microbes* p13-30 Edited by F.A.Skinner and W.B.Hugo Published by Academic Press, London	1976	[redacted]	Doc. No. 392-052, Section A5.3.1/11
Iodophors, their physical, chemical and bactericidal properties and use in the dairy industry - A Review A Twomey	*Australian Journal of Dairy Technology*, Part II, 24, 29-32	1969	[redacted]	Doc. No. 392-053, Section A5.3.1/12
Iodine compounds	In: *A Review of Sterilization and Disinfection* p143-144 S.D. Rubbo and Joan F Gardner Published by Lloyd-Luke (Medical Books) Ltd, London	1965	[redacted]	Doc. No. 392-054, Section A5.3.1/13
Elemental Iodine as a Disinfectant for Drinking Water Shih Lu Chang and J. Carrell Morris	*Industrial and Engineering Chemistry* 45(5); 1009-1012.	1953	[redacted]	Doc. No. 392-056, Section A5**Fehler! Textmarke nicht definiert.**.3.1/14

Table 5.3.1-2: Summary table of available publications describing the efficacy of Iodine and Iodine-based products to provide evidence for the intrinsic efficacy of Iodine.

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
bactericide	PT3	Iodophor teat dips	Clostridium spores Coliform counts Anaerobe spores	[redacted]	[redacted]	Iodophor premilking teat dipping followed by subsequent drying with a paper towel reduced bacterial counts in milk as well as the use of teat preparation combined with wet and dry paper towel, but it was superior in reducing new infections. By replacing the paper towel with a cotton towel, iodophor premilking teat dipping followed by drying and scrubbing of teat ends will not raise Iodine residue in milk.	Doc. No. 392-028; Section A5.3.1/15

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
bactericide	PT5	Iodine	*Escherichia coli*	[redacted]		2-5 ppm: reduction to < 5 viable colonies after treatment of 10^8 cells within 10 minutes	Doc. No. 392-056; Section A5.3.1/14
bactericide	PT5	Iodine	Water-borne pathogenic organisms such as enteric bacteria amebic cysts, cercariae, leptospira and viruses	[redacted]	[redacted]	7-8 ppm Iodine in 10 minutes at room temperature: reduction to < 5 viable colonies after treatment of 10^8 cells obtained for *E.coli, Sal. typhosa, Sh. dysenteriae*, Vibrio cholera and mixed coli aerogenes flora of sewage. Sal. Schöttmuelleri: 20 minutes treatment required	Doc. No. 392-056; Section A5.3.1/14
bactericide	PT2-4	[redacted] (1350 ppm Iodine)	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeuginosa* *Enterobacter aerogenes* *Klebsiella pneumoniae* *Streptococcus dysgalactiae* *Streptococcus*	[redacted]	[redacted]	Percentage reduction achieved: > 99.999 for all test organisms after 30 seconds contact time. Suspensions of micro-organisms tested at concentrations of 10^7 to 10^8 in contact with disinfectant.	Doc. No 381-015; Section A5.3.1/16

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
			agalactiae *Streptococcus uberus*	[redacted]			
bactericide	PT3	[redacted] (1350 ppm Iodine)	*Staphylococcus aureus* *Escherichia coli*	[redacted]	[redacted]	5.62 and 5.49 log reduction for S. aureus and E. coli, respectively. Pass level for this kind of test is a 3 log reduction in the initial populations. Conclusion: [redacted] shows a significant and effective disinfecting action.	
Bactericide /fungicide	PT3	[redacted] (1350 ppm Iodine)	*P. aeruginosa* CIP 82.118 *S. aureus* CIP 4.83 *C. albicans* IP 48.72 *A. niger* IP 1431.83	[redacted]	[redacted]	The number of colonies per mL of product tested following contact with the product was analysed after 24 hours, 7, 14, 21 and 28 days. Less than 10 colonies per mL were counted indicating that the preserving action of [redacted] is guaranteed. Pass level: at least 4 log reduction after 24 hours.	
virucide	PT2	[redacted] (28,000 ppm Iodine) 7 other	Enterovirus (Talfan) Reovirus Type 1 WBR 26 Coronavirus:	[redacted]	[redacted]	% disinfectant to achieve 4 log reduction in titer Talfan: 4% [redacted] Reovirus-1:	Doc. No. 392-019; Section A5.3.1/17

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
		disinfectants (not containing Iodine)	Transmissible gastroenteritis (TGE) Togavirus: Bovine virus diarrhoea (BVD) NADL Myxovirus: Parainfluenza Type 3 T1 Adenovirus type 3 WBR1 Herpesvirus: Infectious bovine rhinotracheitis (IBR) Oxford Poxvirus: Contagious pustular dermatitis (CPD) WVRS	[redacted]	[redacted]	Partial reduction only TGE: 4% [redacted] 3% [redacted] BVD: Partial reduction only Parainfluenza Type 3T1: 2% [redacted] Adenovirus type 3: 3% [redacted] IBR: 1% [redacted] 0.5% [redacted] CPD: 3% [redacted] 2% [redacted]	
virucide	PT2 and PT5	Iodine	Poliomyelitis virus, strain Lansing (mouse adapted)	[redacted]	[redacted]	Results were variable but at the concentrations needed for killing amebic cysts, it is also effective against Poliomyelitis virus.	Doc. No. 392-056; Section A5..3.1/14
Bactericide /fungicide/ virucide	PT3	[redacted] (28,000 ppm Iodine)	Lots of organisms/Pig stables	[redacted]	[redacted]	Bacteria: effective dilutions range from 1:30 for Mycobacterium spp.	Doc. No. 392-005; Section A5.3.1/18

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
						up to 1:150 for *Bordetella bronchiseptica.* Fungi: effective dilutions are 1:100 for all four relevant fungi. Viruses: effective dilutions range from 1:40 for the virus causing Transmissible Gastroenteritis to 1:600 for the virus causing Swine Vesicular Disease. [redacted] is not effective against Procine parvovirus.	
bactericide	PT3	Iodine	*Staphylococcus aureus* *Staphylococcus agalactiae* *Corynebacterium bovis* Or grouped as Staphylococci and Streptococci	[redacted]	[redacted]	Concentrations of Iodine in products showing significant efficacy for postmilking treatment against: *S. aureus*: 0.05% to 1% Iodine *S. agalactiae*: 0.1% to 1% Iodine *C. bovis*: 0.25% to 1% Iodine Staph. species. 0.25% to 1% Iodine Streptococci: 1% Iodine	Doc. No. 392-030, Section A5..3.1/19
bactericide	PT3	[redacted]	No details	[redacted]	[redacted]	Significant efficacy of	

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
		(Iodophor: 0.1% Iodine) [redacted] (Iodophor: 0.25%) [redacted] (Iodine: 0.25%) [redacted] (Iodophor: 0.55% Iodine [redacted]	provided. Test organisms are grouped as "Environmental pathogens", "major pathogens" and "Gram-negative bacteria".	[redacted]	[redacted]	product for premilking treatment against: [redacted] environmental pathogens (P>.10) and major pathogens (P<.05) [redacted] environmental pathogens (P>.05) and major pathogens (P<.025) [redacted] Gram-negative bacteria (P<.025) and major pathogens (P<.001) [redacted] environmental pathogens (P>.10) and major pathogens (P<.10)	
amoebicide	PT5	Iodine	Entamoeba histolytica cysts	[redacted]	[redacted]	A suitable dose for emergency disinfection was calculated to be about 8 ppm for a 10 minute treatment at 23 °C. In water with high organic color or Iodine demand > 3 ppm, an increase in dosage was needed. 16 ppm was effective for all waters tested. At low temperatures (0-5 °C) the required contact time was 20 minutes.	Doc. No. 392-056; Section A5..3.1/14

*) References:

Section A5.3.1/15: Rasmussen, M.D. et al. (1991): Effects of premilking teat preparation on spores of anaerobes, bacteria and Iodine residues in milk; J. Dairy Sci., Vol. 74, pp. 2472-2478; Doc. No. 392-028. (published)

Section A5..3.1/16: Anonymous (n.i.): Technical file- [redacted] Doc. No. 381-015 (published).

Section A5..3.1/17: Evans, D.H. (19779: Disinfection of animal viruses; Fr. Vet. J., pages 133 and 356; Doc. No. 392-019 (published).

Section A5.3.1/18: Anonymous (n.i.): Pig disinfection programme; Evans brochure; Doc. No. 392-005 (published).

Section A5..3.1/19: Anonymous (1996): 35th annual meeting-national mastitis council, Inc.: Summary of peer-reviewed publications on efficacy of premilking and postmilking teat disinfectants published since 1980; National Mastitis Council Annual Meeting Proceedings, pages 245-256; Doc. No. 392-030 (published).

Please refer also to Table 5.3.1_I-3 and Table 5.3.1_PVP-I-3 in the corresponding confidential parts of the dossier for a summary of available data provided by the applicant which is considered confidential.

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

Official use only

1 REFERENCE

1.1	**Reference**	Chang, S.L.and Morris, J.C.(1953): ELEMENTAL IODINE AS A DISINFECTANT FOR DRINKING WATER; Industrial and Engineering Chemistry, 45, 5, May 1953, 1009-1012; Doc. No.: 392-056 (published). This document was first cited under section point A5.3.1/14.
1.2	**Data protection**	[redacted]
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
1.3	**Guideline study**	No but the studies described in the publication were conducted as suspension tests resembling the EN1040 method.
1.4	**Deviations**	Not applicable

2 METHOD

2.1	**Test Substance (Biocidal Product)**	Elemental iodine
2.1.1	Trade name/ proposed trade name	[redacted]
2.1.2	Composition of Product tested	[redacted]
2.1.3	Physical state and nature	[redacted]
2.1.4	Monitoring of active substance concentration	[redacted]
2.1.5	Method of analysis	[redacted]
2.2	**Reference substance**	[redacted]
2.2.1	Method of analysis for reference substance	[redacted]
2.3	**Testing procedure**	[redacted]
2.3.1	Test population / inoculum / test organism	[redacted]
2.3.2	Test system	[redacted]
2.3.3	Application of TS	[redacted]

Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*

2.3.4 Test conditions

2.3.5 Duration of the test / Exposure time

2.3.6 Number of replicates performed

2.3.7 Controls

2.4 Examination

2.4.1 Effect investigated

2.4.2 Method for recording / scoring of the effect

2.4.3 Intervals of examination

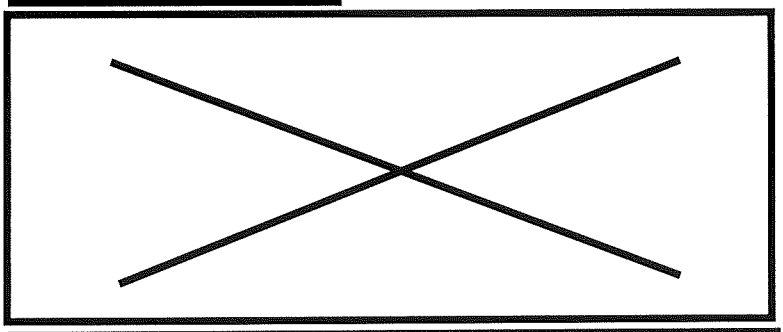
2.4.4 Statistics

2.4.5 Post monitoring of the test organism

3 RESULTS

3.1 Efficacy --

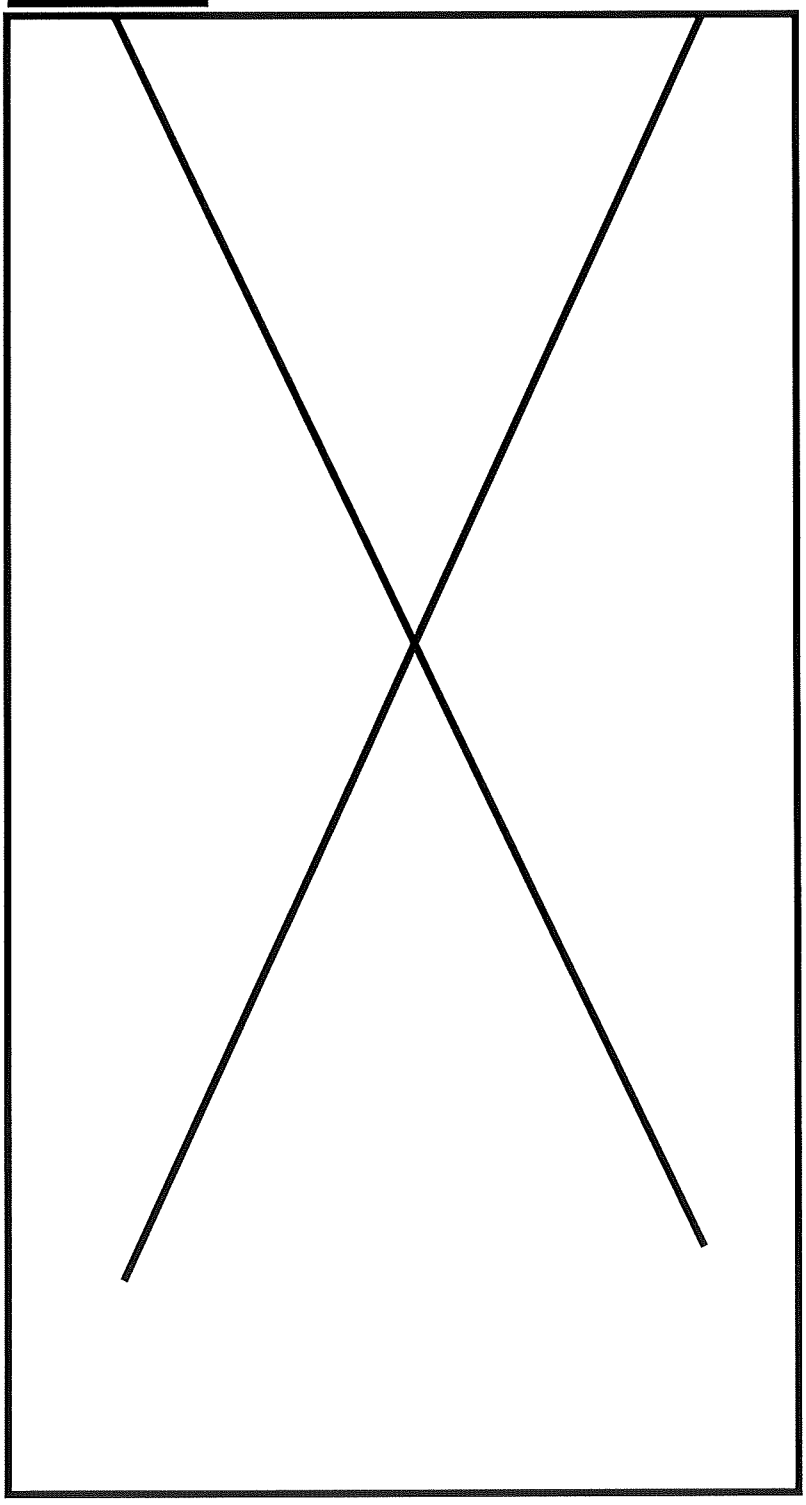
3.1.1 Dose/Efficacy curve



3.1.2 Begin and duration of effects

3.1.3 Observed effects in the post monitoring phase

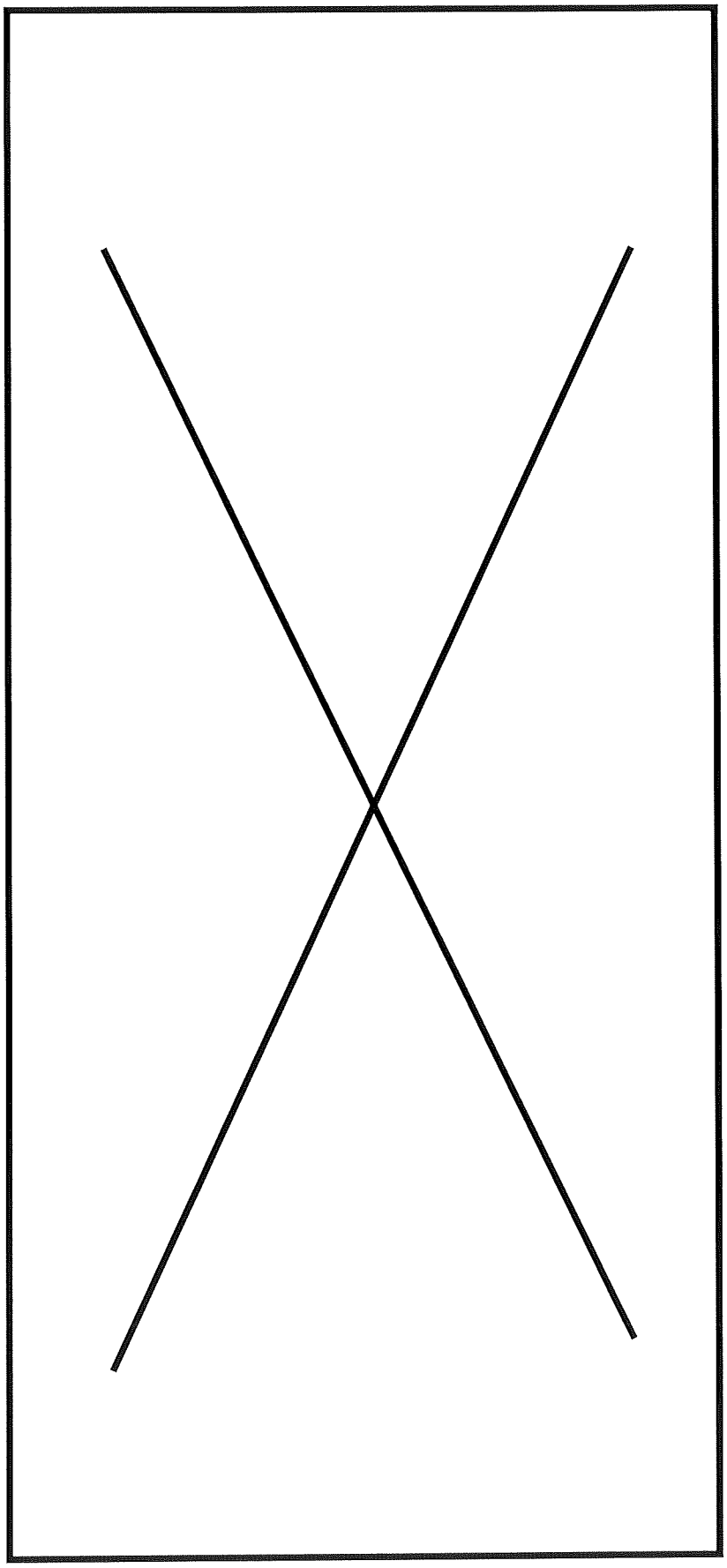
3.2 Effects against organisms or

	objects to be protected	
3.3	**Other effects**	[redacted]
3.4	**Efficacy of the reference substance**	[redacted]
3.5	**Tabular and/or graphical presentation of the summarised results**	

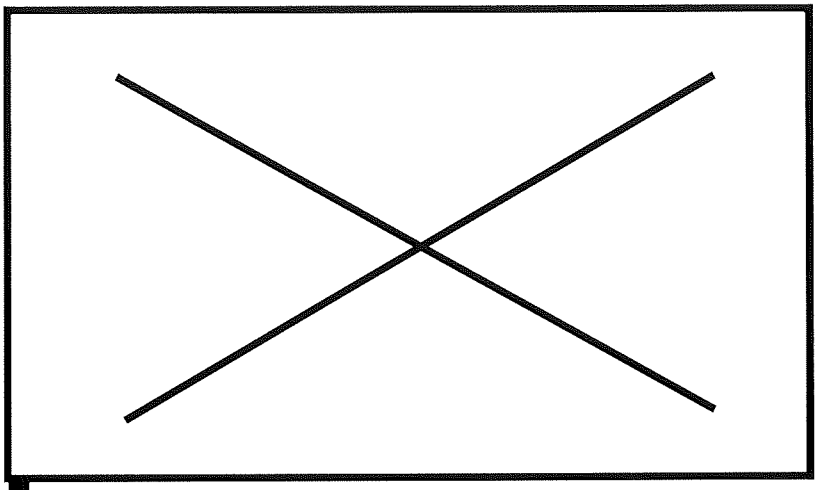
Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses



Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*



3.6 Efficacy limiting factors

3.6.1 Occurrences of resistances

3.6.2 Other limiting factors

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing

4.2 Intended actual scale of biocide application

4.3 Relevance compared to field conditions

4.3.1 Application method

4.3.2 Test organism

4.3.3 Observed effect

4.4 Relevance for read-across

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*

[redacted]

5.2 Reliability

[redacted]

5.3 Assessment of efficacy, data analysis and interpretation

[redacted]

5.4 Conclusion

Iodine has innate efficacy against bacteria, amoebae and viruses in water.

5.5 Proposed efficacy specification

[redacted]

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

Comments	[redacted]
Summary and conclusion	[redacted]

COVER PAGE

Doc. No.: 381-017

Title:	BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD
Author(s):	Fotheringham, V.J.C.
Report date:	Apr/2007

SCC Project No.:	854-005
Name of database:	Iodine

EVANS VANODINE

INTERNATIONAL PLC

Global Hygiene Solutions

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW

Prepared by Valerie J C Fotheringham
Chief Microbiologist, Evans Vanodine International plc

FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD

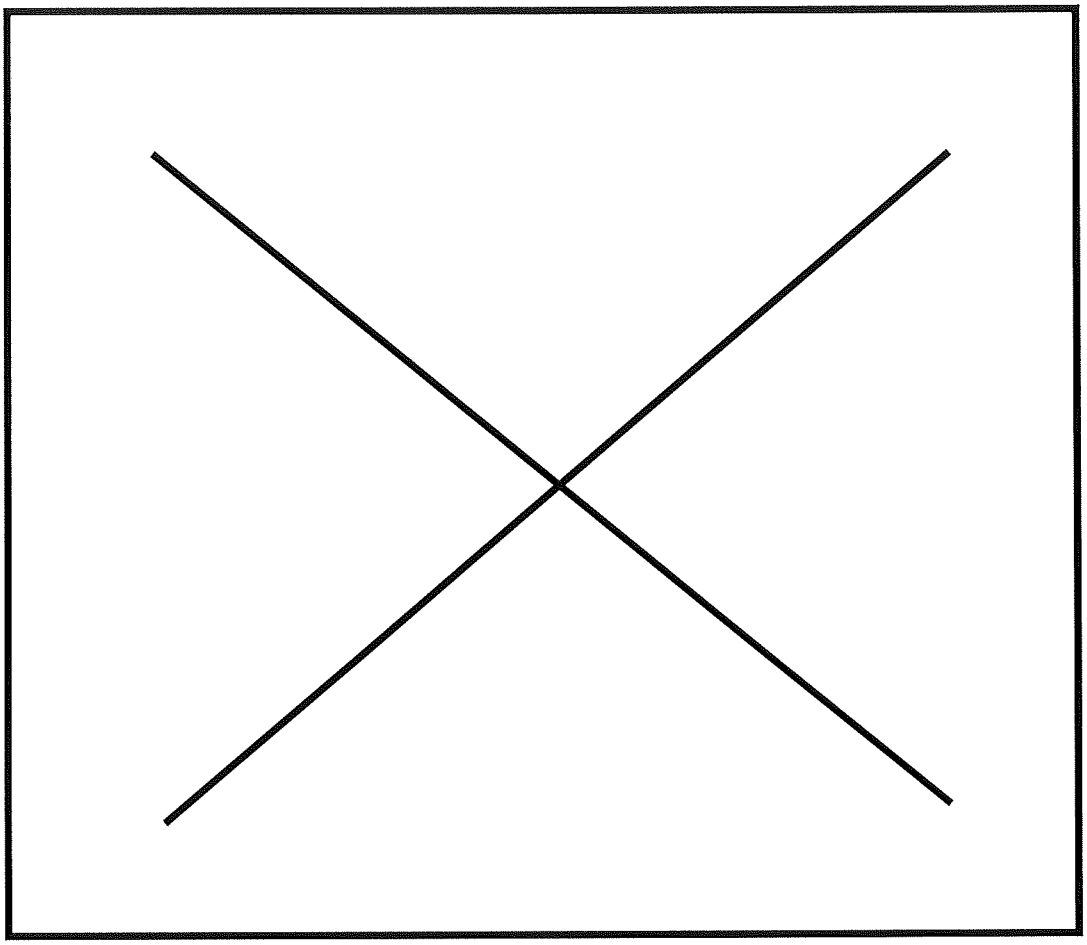
APRIL 2007

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CONTENTS

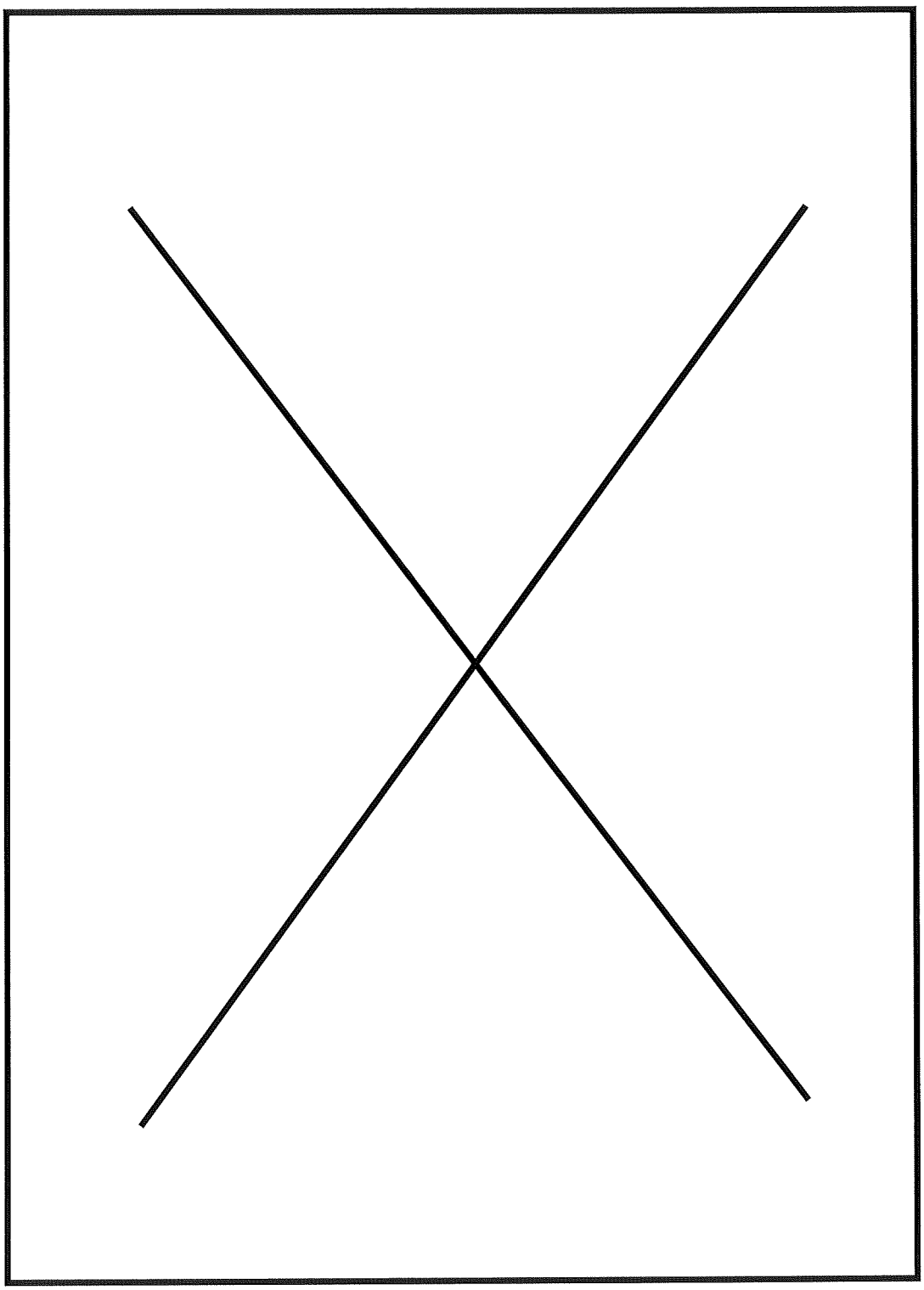
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



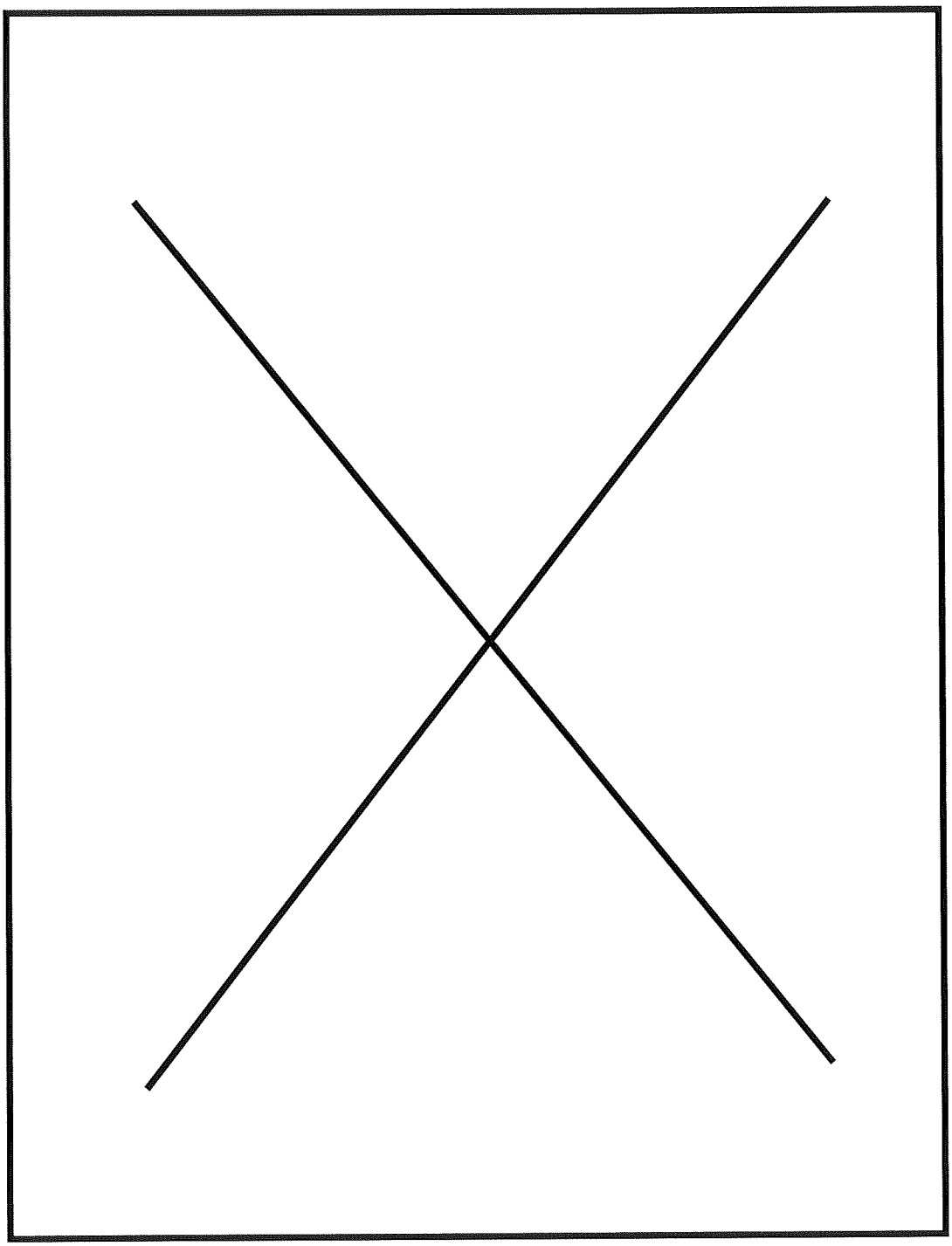
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



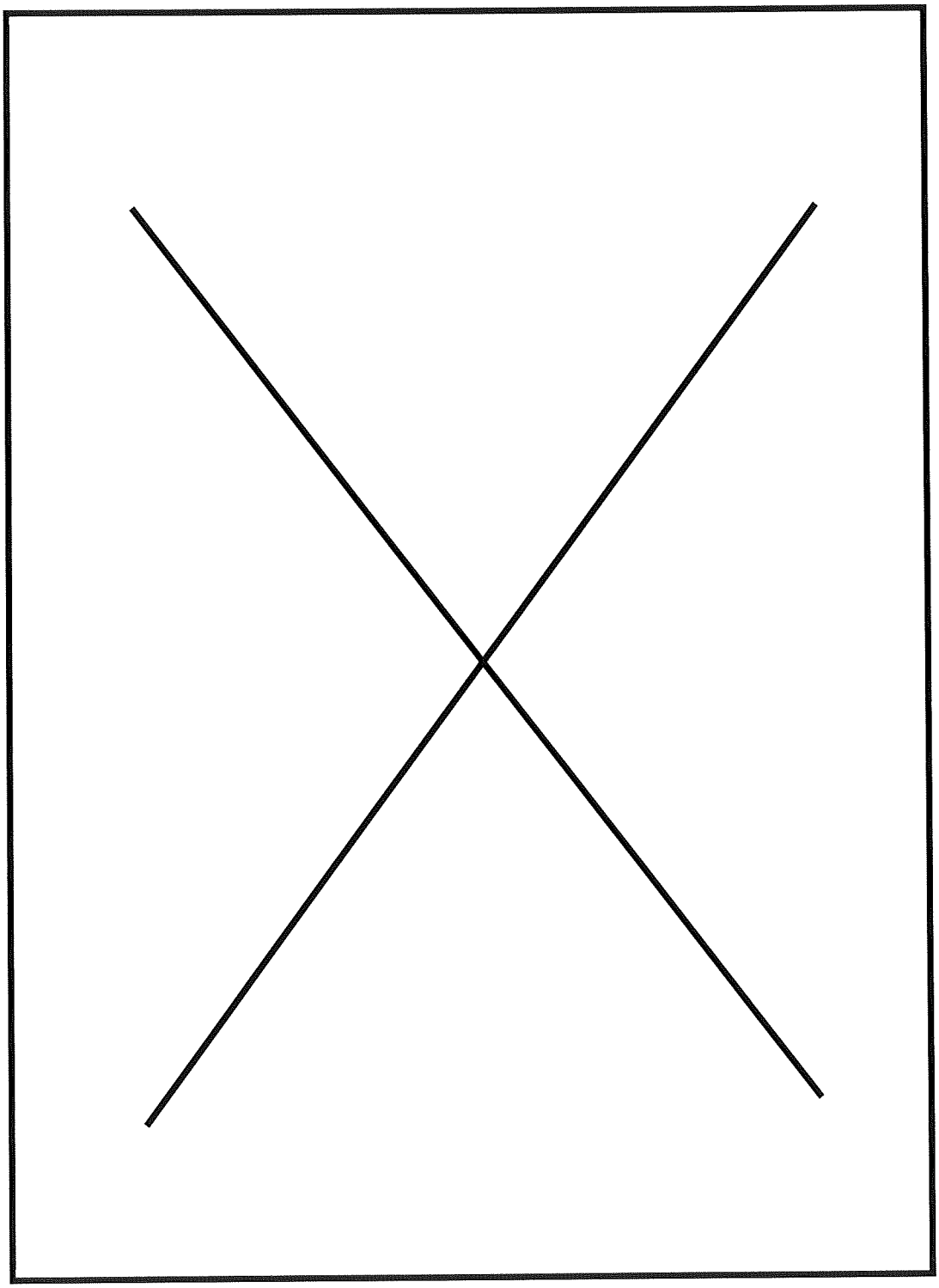
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



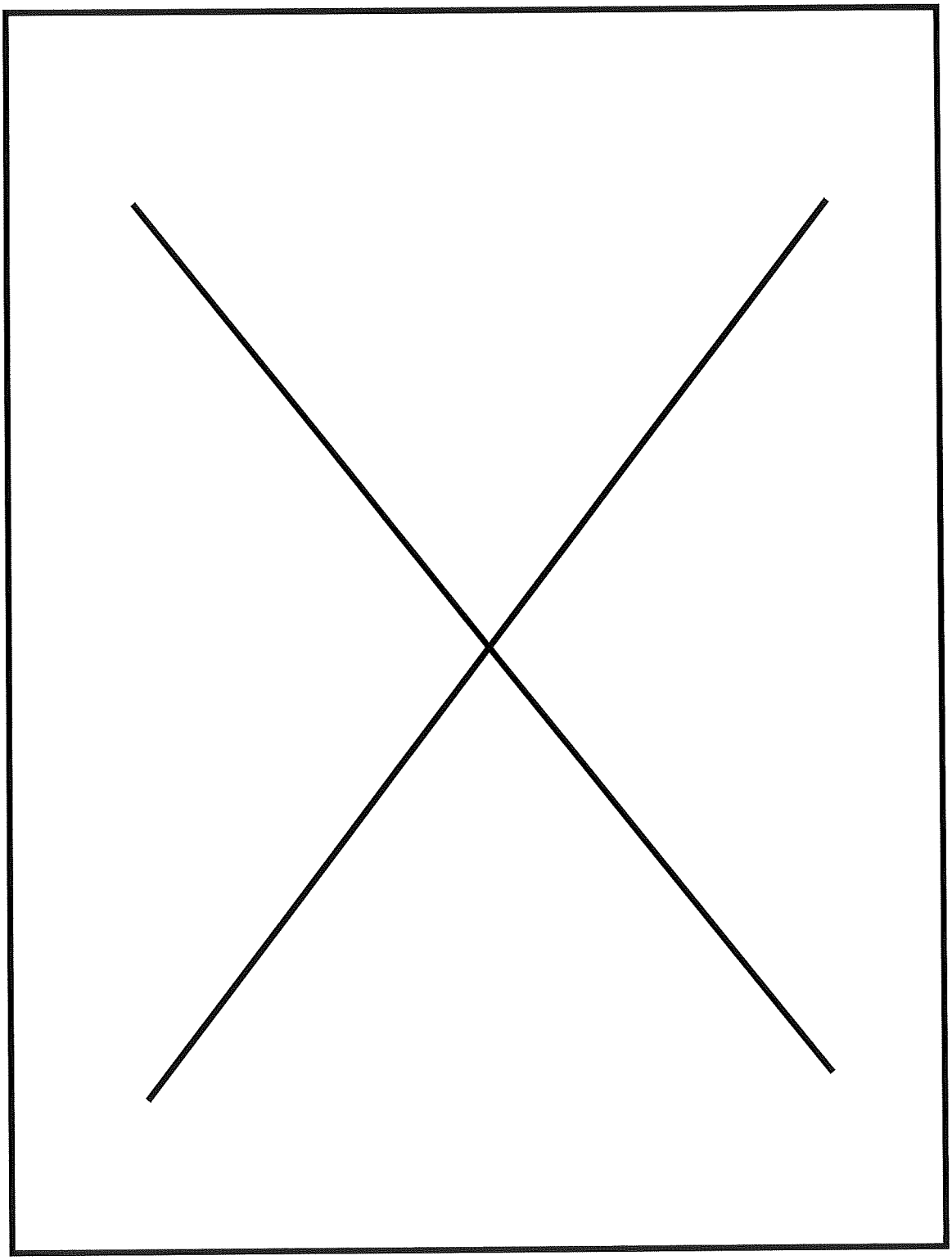
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



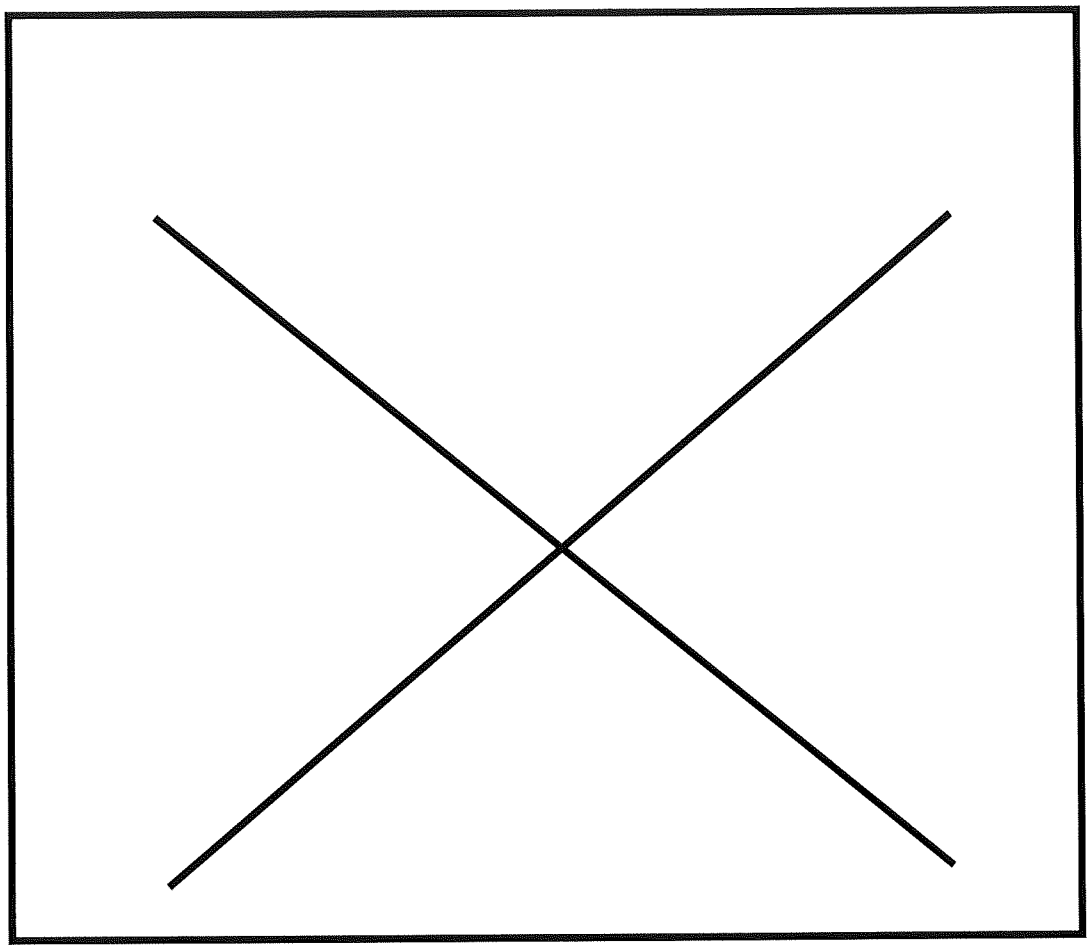
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



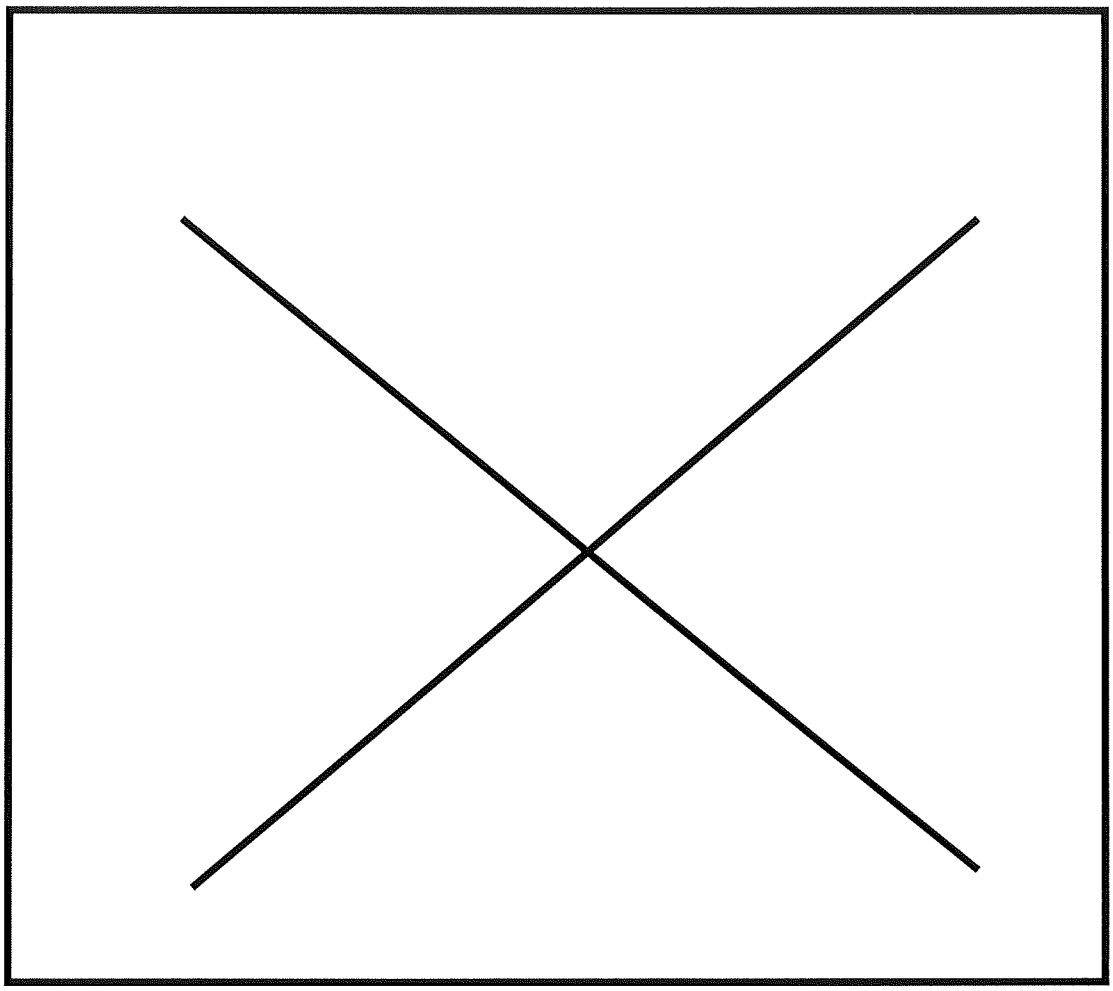
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



Valerie J C Fotheringham

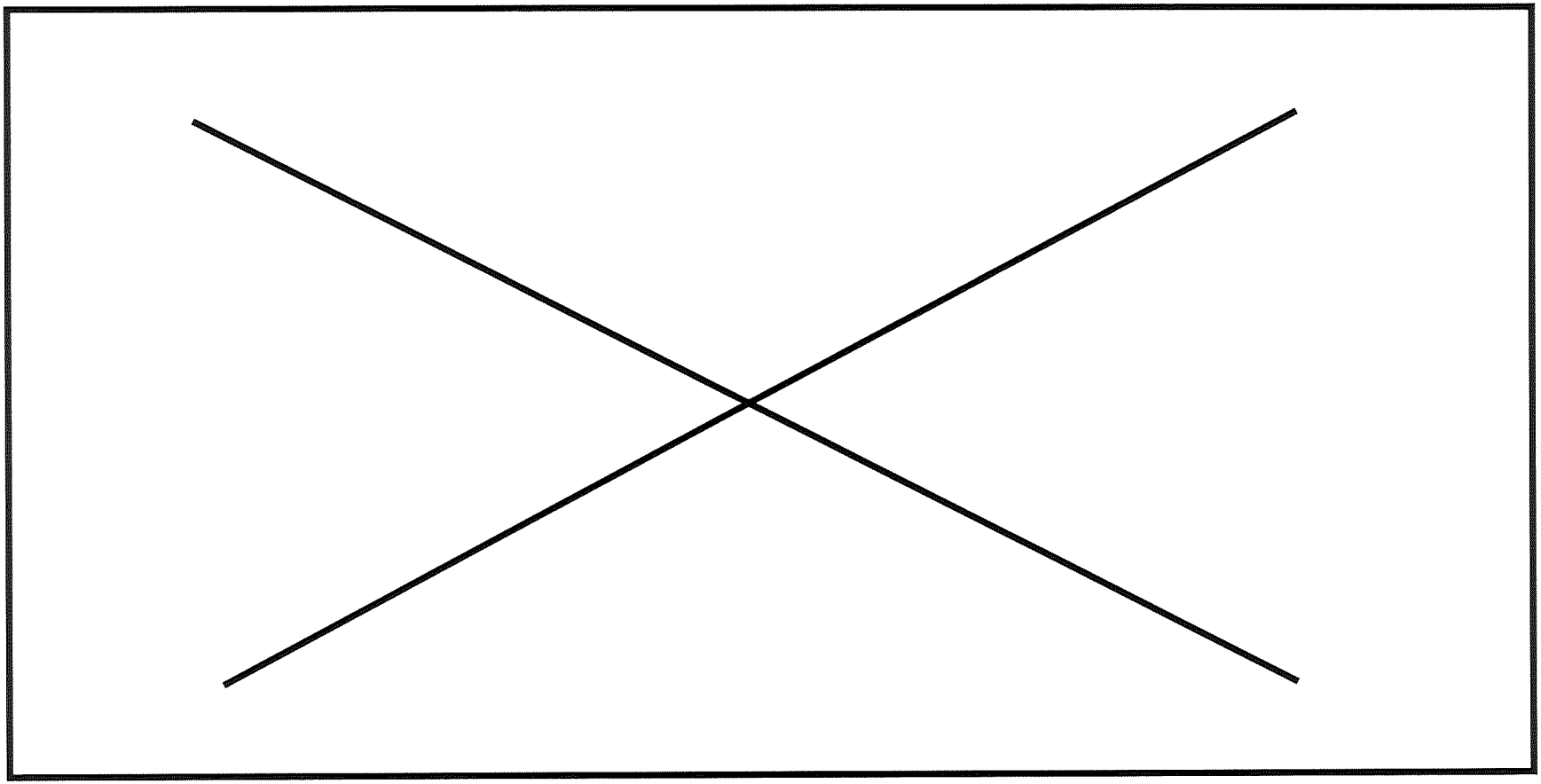
Valerie J C Fotheringham B.Sc., C.Biol, M.I.Biol.
Chief Microbiologist

DATE: 30 April 2007.

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 1: PASS DILUTIONS FOR IODOPHOR SURFACE DISINFECTANT* AGAINST A RANGE OF MICRO-ORGANISMS



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 2: PASS DILUTIONS FOR IODOPHOR TEAT DISINFECTANT*** AGAINST A RANGE OF BACTERIA

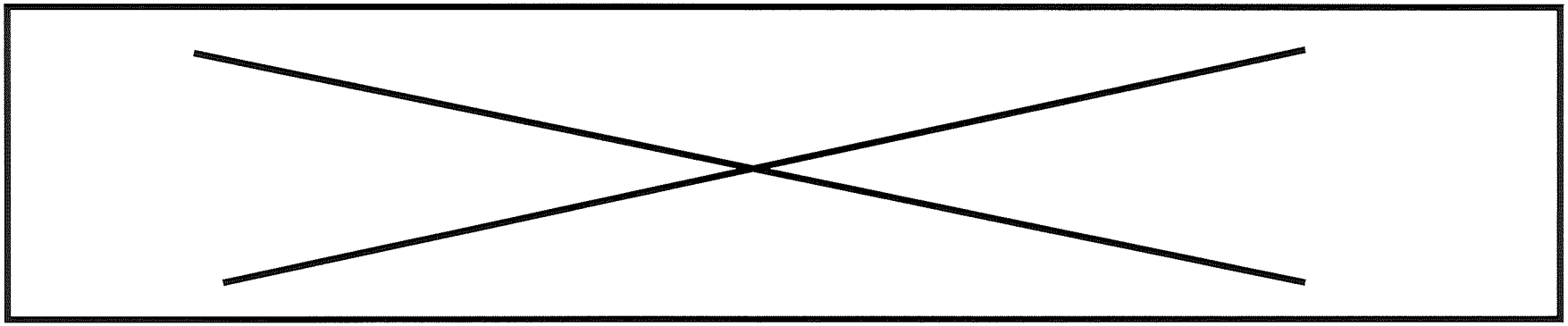
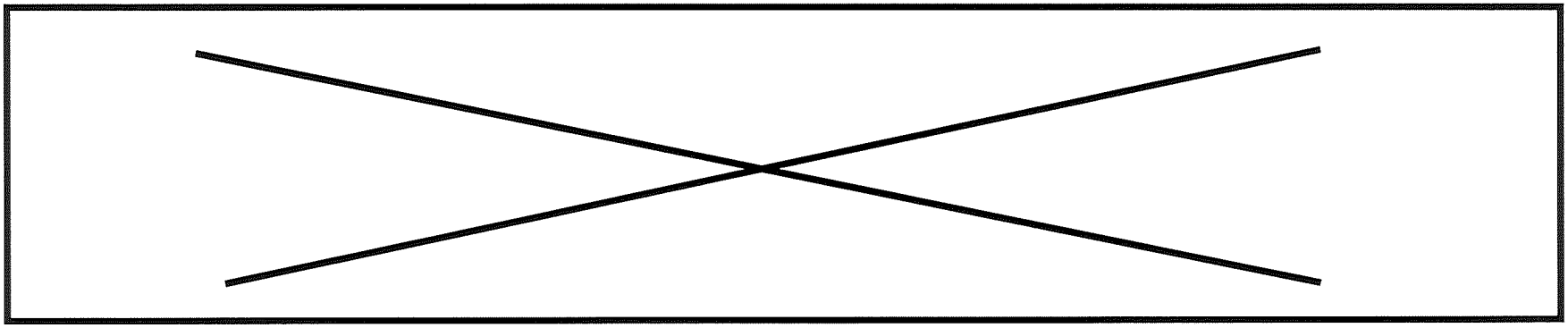


TABLE 3: PASS DILUTIONS FOR QUATERNARY AMMONIUM COMPOUND DISINFECTANT# AGAINST A RANGE OF BACTERIA



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

CHART 1: RELEVANCE OF REFERENCES SITED FOR IODINE RESISTANCE

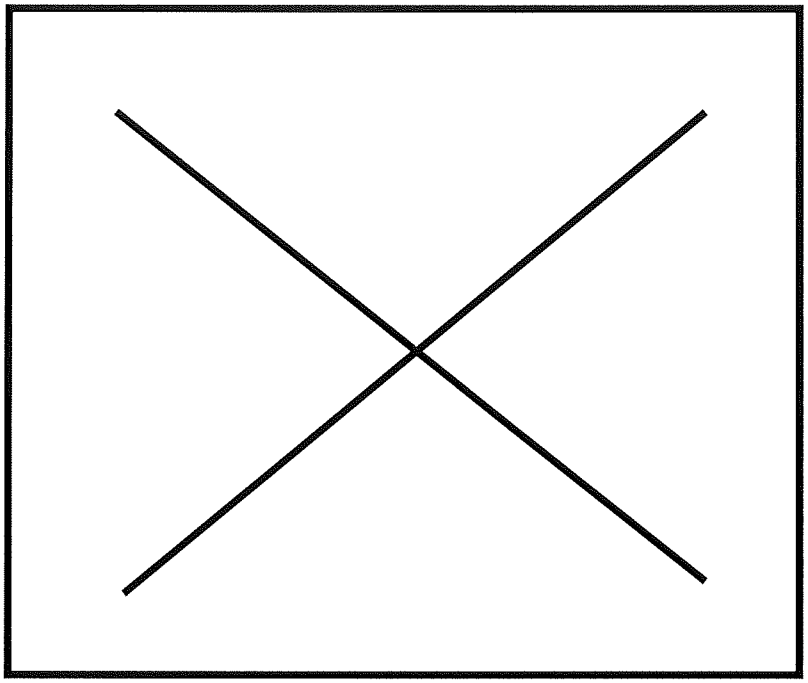
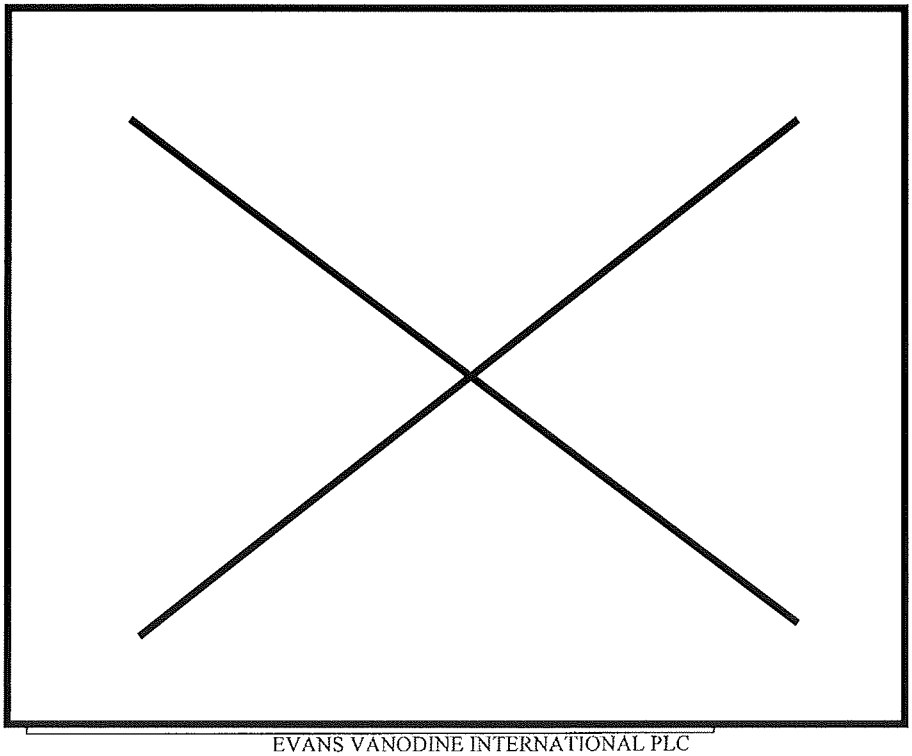


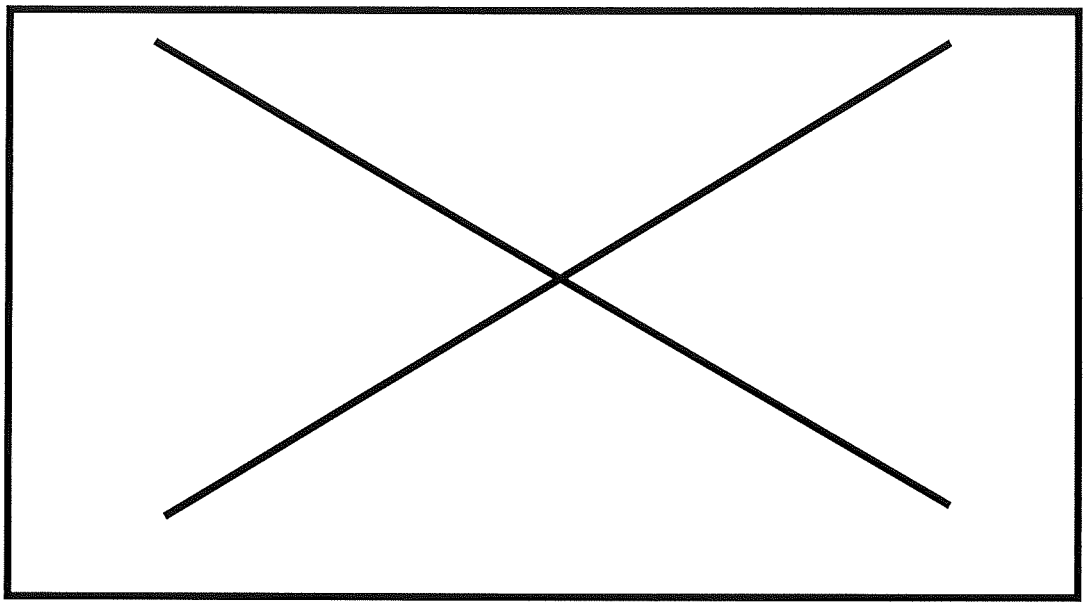
CHART 2: CATERGORIES OF REFERENCES FOR IODINE RESISTANCE



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

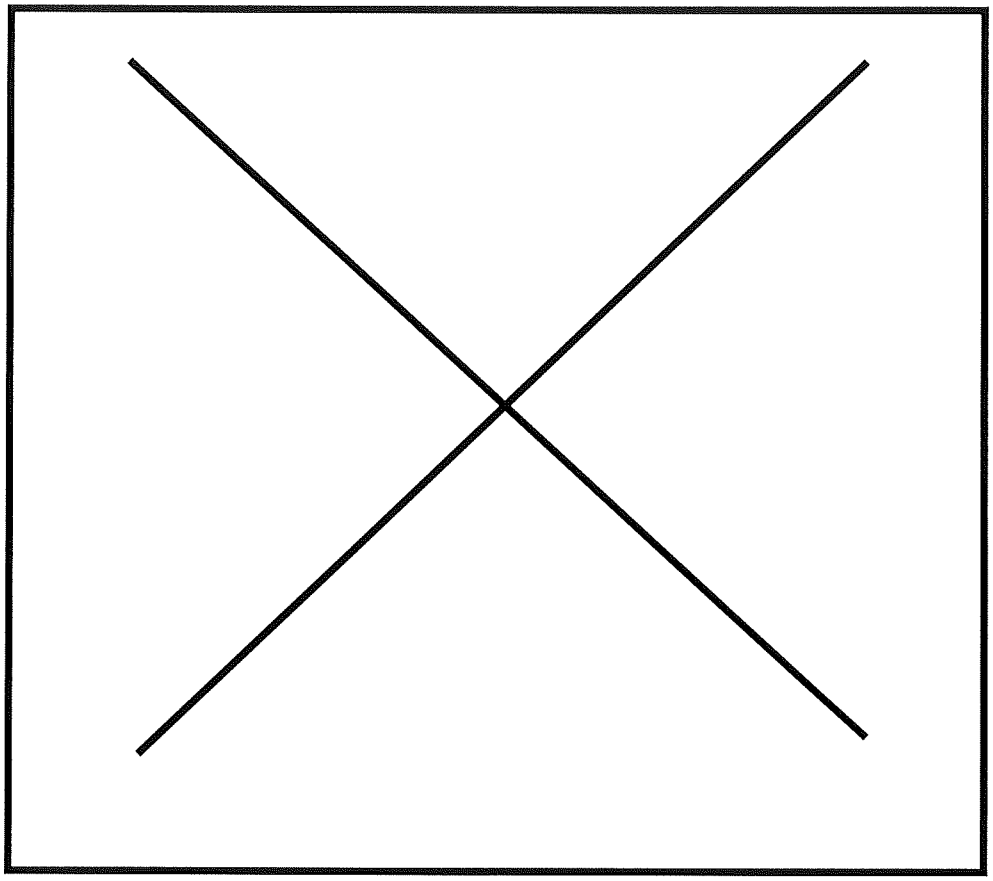
CHART 3: Somatic cell counts in England and Wales



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

CHART 4: PERCENTAGE OF TEAT DISINFECTANTS USED GLOBALLY



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

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BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

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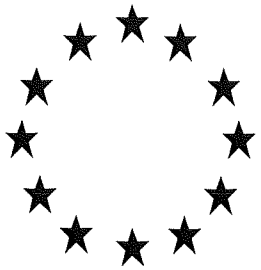
Competent Authority Report

Work Programme for Review of Active Substances in Biocidal Products
Pursuant to Council Directive 98/8/EC



IODINE (PT4)

DOCUMENT III-A5

Efficacy

Rapporteur Member State: Sweden

Draft Final May 2013

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Section A5 Effectiveness against target organisms and intended uses

Subsection Annex Point IIA V.5.1 – V.5.8			Official use only
5.1	**Function (IIA5.1)**	Bactericide, virucide and fungicide.	
5.2	**Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)**		
5.2.1	**Organism(s) to be controlled (IIA5.2)**	Iodine is used for control of various pathogenic organisms such as bacteria (including spores and mycobacteria), viruses and fungi. Examples of organisms against which Iodine was successfully tested are listed in Tables A5.3.1-1, A5.3.1-2 and A5.3.1-3. Please note the available data summarised in these tables is not exhaustive due to the large number of available publications. Only the most relevant literature is described. In addition to literature data, also laboratory reports on tests performed with Iodine-based products have been included, examples of which are listed below for the relevant uses. On request of the applicant this information is provided in the Confidential part of the dossier	
5.2.2	**Products, organisms or objects to be protected (IIA5.2)**	**Disinfection of milking equipment and milk tanks** Man is indirectly protected as consumer of milk. Disinfection of equipment directly in contact with the cows' teats also prevents the spread of contagious diseases.	
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**		

Section A5 Effectiveness against target organisms and intended uses

5.3.1 Effects on target organisms (IIA5.3)

Iodine in aqueous or alcoholic solutions or solubilised with surfactants (iodophors) is used in a variety of applications to kill harmful microorganisms and viruses. These preparations are used as skin disinfectants pre-operatively, with wound dressings, for teat dipping in dairy cows, sheep and goats and for surface disinfection in a number of industries.

Iodine is suitable for all of these applications because it is a broad spectrum biocide, its efficacy has been demonstrated over 170 years of use. Iodine and iodophors are well established and accepted as having microbicidal activity.

There is a huge number of papers demonstrating the microbicidal activity of iodophor products in laboratory and field tests but only a few of these are referenced here as most of them relate to specific formulations and not just to Iodine.

In Table A5.3.1-1, the available information in published text and reference books and in scientific reviews is summarised.

In Table A5.3.1-2, exemplary studies from publicly available sources are included showing the efficacy of Iodine-based products for biocidal uses.

In Table A5.3.1_I-3, provided in the corresponding confidential parts of the dossier, exemplary studies provided by the applicant are included showing the efficacy of Iodine-based products.

The innate efficacy of iodine in water (suspension tests) is described in Document IIIA5/01.

5.3.2 Likely concentrations at which the A.S. will be used (IIA5.3)

PT4

Dsinfection of milking equipment and milk tanks:
0.0025 – 0.020 % Iodine corresponding to 25 – 200 ppm Iodine

X1

5.4 Mode of action (including time delay) (IIA5.4)

5.4.1 Mode of action

The following mechanisms of action contribute to the high reactivity and non-selective action of Iodine against different micoorganisms:

- Iodine rapidly penetrates into micoorganisms showing a high affinity pattern of adsorption.
- Iodine combines with protein substances in the bacterial cell; these can be peptidoglycans in the cell walls or enzymes in the cytoplasm. This results in irreversible coagulation of the protein and consequent loss of function.
- Iodine is known to act on thiol groups in the cell; if a thiol enzyme is part of a metabolic chain, metabolic inhibition will result.
- Iodine reacts with key groups of proteins, in particular the free-sulfur amino acids cysteine and methionine, nucleotides

Section A5 Effectiveness against target organisms and intended uses

		and fatty acids. • Iodine interferes at the level of the respiratory chain of the aerobic microorganisms by blocking the transport of electrons through electrophilic reactions with the enzymes of the respiratory chain. For further details, please refer to the expert statement on resistance attached to this document (Attachment 1_381-017.pdf).
5.4.2	**Time delay**	The rapid penetration of Iodine into microorganisms and its mode of action indicate that the time-delay i.e. contact time required for sufficient efficacy depends on the tolerance of the organism to Iodine and the concentration of Iodine used for treatment. Iodine is more effective at higher temperatures. The germicidal activity of Iodine-containing solutions is characterised by their colour. Amber solutions are active whilst pale yellow or colourless solutions are less effective and must be replaced by new solutions.
5.5	**Field of use envisaged (IIA5.5)**	
	MG01: Disinfectants, general biocidal products	PT 4: Food and feed area disinfectants
5.6	**User (IIA5.6)**	
	Industrial	No industrial use
	Professional	**Disinfection of milking equipment and milk tanks**: Biocidal product is diluted and surfaces are sprayed with the use solution. Equipment is either sprayed with use solution or immersed into use solution. Milking equipment and holding tanks can also be disinfected by CIP procedures. For detailed use-descriptions, please refer to Document IIB, Chapter 8.
	General public	None

Section A5 Effectiveness against target organisms and intended uses

5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**	
5.7.1	**Development of resistance**	Taking into account the mode of action of iodine which is non-selective, development of resistance against iodine is unlikely. Iodine / Iodophors have been used for over 170 years as disinfectants for a variety of applications. Such applications include disinfection of skin in the human hygiene and medical area but also skin of animals using teat dips as well as surfaces such as milk tanks. No reduction in efficacy was reported to the producers of iodine/iodophor-based products for such applications indicating that no development of resistant microorganisms or viruses has occurred. An overview on the efforts made to find reports on the development of resistance to Iodine is provided in the expert statement attached to this document (Attachment 1_381-017.pdf). This literature search covers all uses of iodine for disinfection and of the first 94 hits, 91 were from a medical source and 3 related to the veterinary field. 14 papers were related to resistance or absence of resistance as detailed in the expert statement. It was concluded that no information was found in the public domain which gives rise to concern of development of resistance to iodine.
5.7.2	**Management strategies**	No management strategies have been developed since no occurrence of resistance has been observed. Nevertheless, it should be noted that Iodine-based products are exclusively applied by professional users, in most cases as part of professional hygiene programs, which also involve other biocidal substances of different chemical structure and different mode of action (alternating applications).
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	Based on an estimate provided by one supplier of Iodine, the Iodine world demand in the year 2006 for the production of disinfectants was 14% of the total Iodine world demand of 25,000 – 26,000 t/year. Thus, about 3640 t Iodine/year were used for the production of disinfectants throughout the world. Doc. No. 031-013; Section A5.8/01 For information on the likely tonnage to be placed on the market per year for biocidal products per member of the Iodine Registration Group (IRG), please refer to the confidential part of the dossier.

Section A5 Effectiveness against target organisms and intended uses

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
General	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

Section A5 Effectiveness against target organisms and intended uses

Table 5.3.1-1: Summary table of reviews available in public literature on the efficacy of Iodine

Title/Author(s)	Reference	Year	Conclusion	Section point
Review Article The Role of Iodine in Antisepsis and Wound Management: A Reappraisal G. Selvaggi, S. Monstrey, K. Van Landuyt, M. Hamdi and P. Blondeel	*Acta.chir belg*, 103 (3), 241-247	2003	[redacted]	Doc. No. 392-055, Section A5.3.1/01
Topical Antimicrobial Agents in Dermatology Candace Thornton Spann, Susan C Taylor and Jeffrey M Weinberg	*Clinics in Dermatology* 21, 70-77	2003	[redacted]	Doc. No. 392-049, Section A5.3.1/02
Review of disinfectant susceptibility of bacteria isolated in hospital to commonly used disinfectants Tadashi Shiraishi and Yoshito Nakagawa	*Postgrad Med J* 69 (Suppl.3), S70-S77	1993	[redacted]	Doc. No. 392-057, Section A5.3.1/03
Virucidal Activity of Biocides A. Activity against human viruses A.S.Sattar and S.Springthorpe	In: *Principles and Practice of Disinfection, Preservation and Sterilization* 3rd Edition p178 Edited by A.D.Russell, W.B.Hugo and G.A.J.Ayliffe Published by Blackwell Scientific Publications	1999	[redacted]	Doc. No. 392-048, Section A5.3.1/04
Virucidal Activity of Biocides A. Activity against veterinary viruses P.J.Quinn and B.K.Markey	Page 193		[redacted]	

Title/Author(s)	Reference	Year	Conclusion	Section point
Halogens - Free Iodine W.B.Hugo and A.D.Russell	Page 45-46		[redacted]	
Halogens - Iodophors W.B.Hugo and A.D.Russell	Page 45-46		[redacted]	
Iodine	In: *Martindale The Complete Drug Reference* 32nd Edition p1494	1999	[redacted]	Doc. No. 392-047, Section A53.1/05
Chemical disinfectants, antiseptics and preservatives E.M.Scott and S.P.Gorman	In: *Pharmaceutical Microbiology* 6th Edition p219	1998	[redacted]	Doc. No. 392-046, Section A5.3.1/06
Chemicals used as disinfectants: active ingredients and enhancing additives D.J. Jeffrey	*Rev.sci.tech.Off.int.Epiz.* 14 (1) 68	1995	[redacted]	Doc. No. 392-045, Section A5.3.1/07
Iodine	*The Pharmaceutical Codex* 12 Edition *Principles and Practice of Pharmaceutics* p582	1994	[redacted]	Doc. No. 392-050, Section A5.3.1/08
Iodophores		1994	[redacted]	
Bacterial Spores and Chemical Sporicidal Agents A.D.Russell	*Clinical Microbiology Reviews* Vol. 3, No. 2, p99-119	1990	[redacted]	Doc. No. 392-058, Section A5.3.1/09

Title/Author(s)	Reference	Year	Conclusion	Section point
The Bacterial Flora of 'In-Use' Teat Dips J.Bruce	In: *Disinfectants Their use and Evaluation of Effectiveness* p177-182 Edited by C.H.Collins, M.C.Allwood, Sally F. Bloomfield and A.Fox Published by Academic Press, London	1981	[redacted]	Doc. No. 392-051, Section A5.3.1/10
The inactivation of vegetative micro-organisms by chemicals in the dairying industry Christina M Cousins	In: *Inhibition and Inactivation of Vegetative Microbes* p13-30 Edited by F.A.Skinner and W.B.Hugo Published by Academic Press, London	1976	[redacted]	Doc. No. 392-052, Section A5.3.1/11
Iodophors, their physical, chemical and bactericidal properties and use in the dairy industry - A Review A Twomey	*Australian Journal of Dairy Technology*, Part II, 24, 29-32	1969	[redacted]	Doc. No. 392-053, Section A5.3.1/12
Iodine compounds	In: *A Review of Sterilization and Disinfection* p143-144 S.D. Rubbo and Joan F Gardner Published by Lloyd-Luke (Medical Books) Ltd, London	1965	[redacted]	Doc. No. 392-054, Section A5.3.1/13
Elemental Iodine as a Disinfectant for Drinking Water Shih Lu Chang and J. Carrell Morris	*Industrial and Engineering Chemistry* 45(5); 1009-1012.	1953	[redacted]	Doc. No. 392-056, Section A5**Fehler! Textmarke nicht definiert.**.3.1/14

Table 5.3.1-2: Summary table of available publications describing the efficacy of Iodine and Iodine-based products to provide evidence for the intrinsic efficacy of Iodine.

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
bactericide	PT3	Iodophor teat dips	Clostridium spores Coliform counts Anaerobe spores	[redacted]	[redacted]	Iodophor premilking teat dipping followed by subsequent drying with a paper towel reduced bacterial counts in milk as well as the use of teat preparation combined with wet and dry paper towel, but it was superior in reducing new infections. By replacing the paper towel with a cotton towel, iodophor premilking teat dipping followed by drying and scrubbing of teat ends will not raise Iodine residue in milk.	Doc. No. 392-028; Section A5.3.1/15

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
bactericide	PT5	Iodine	*Escherichia coli*	[redacted]		2-5 ppm: reduction to < 5 viable colonies after treatment of 10^8 cells within 10 minutes	Doc. No. 392-056; Section A5.3.1/14
bactericide	PT5	Iodine	Water-borne pathogenic organisms such as enteric bacteria amebic cysts, cercariae, leptospira and viruses	[redacted]	[redacted]	7-8 ppm Iodine in 10 minutes at room temperature: reduction to < 5 viable colonies after treatment of 10^8 cells obtained for *E.coli, Sal. typhosa, Sh. dysenteriae*, Vibrio cholera and mixed coli aerogenes flora of sewage. Sal. Schöttmuelleri: 20 minutes treatment required	Doc. No. 392-056; Section A5.3.1/14
bactericide	PT2-4	[redacted] (1350 ppm Iodine)	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeuginosa* *Enterobacter aerogenes* *Klebsiella pneumoniae* *Streptococcus dysgalactiae*	[redacted]	[redacted]	Percentage reduction achieved: > 99.999 for all test organisms after 30 seconds contact time. Suspensions of micro-organisms tested at concentrations of 10^7 to 10^8 in contact with disinfectant.	Doc. No 381-015; Section A5.3.1/16

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
			Streptococcus agalactiae *Streptococcus uberus*	[redacted]			
bactericide	PT3	[redacted] (1350 ppm Iodine)	*Staphylococcus aureus* *Escherichia coli*	[redacted]	[redacted]	5.62 and 5.49 log reduction for S. aureus and E. coli, respectively. Pass level for this kind of test is a 3 log reduction in the initial populations. Conclusion: [redacted] shows a significant and effective disinfecting action.	
Bactericide /fungicide	PT3	[redacted] (1350 ppm Iodine)	*P. aeruginosa* CIP 82.118 *S. aureus* CIP 4.83 *C. albicans* IP 48.72 *A. niger* IP 1431.83	[redacted]	[redacted]	The number of colonies per mL of product tested following contact with the product was analysed after 24 hours, 7, 14, 21 and 28 days. Less than 10 colonies per mL were counted indicating that the preserving action of [redacted] is guaranteed. Pass level: at least 4 log reduction after 24 hours.	
virucide	PT2	[redacted] and (28,000 ppm	Enterovirus (Talfan) Reovirus Type 1	[redacted]	[redacted]	% disinfectant to achieve 4 log reduction in titer Talfan:	Doc. No. 392-019; Section A5.3.1/17

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
		Iodine) 7 other disinfectants (not containing Iodine)	WBR 26 Coronavirus: Transmissible gastroenteritis (TGE) Togavirus: Bovine virus diarrhoea (BVD) NADL Myxovirus: Parainfluenza Type 3 T1 Adenovirus type 3 WBR1 Herpesvirus: Infectious bovine rhinotracheitis (IBR) Oxford Poxvirus: Contagious pustular dermatitis (CPD) WVRS	[redacted]	[redacted]	4% [redacted] Reovirus-1: Partial reduction only TGE: 4% [redacted] 3% [redacted] BVD: Partial reduction only Parainfluenza Type 3T1: 2% [redacted] or [redacted] Adenovirus type 3: 3% [redacted] or [redacted] IBR: 1% [redacted] 0.5% [redacted] CPD: 3% [redacted] 2% [redacted]	
virucide	PT2 and PT5	Iodine	Poliomyelitis virus, strain Lansing (mouse adapted)	[redacted]	[redacted]	Results were variable but at the concentrations needed for killing amebic cysts, it is also effective against Poliomyelitis virus.	Doc. No. 392-056; Section A5..3.1/14

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
Bactericide /fungicide/ virucide	PT3	[redacted] (28,000 ppm Iodine)	Lots of organisms/Pig stables	[redacted]	[redacted]	[redacted]	Doc. No. 392-005; Section A5.3.1/18
bactericide	PT3	Iodine	*Staphylococcus aureus* *Staphylococcus agalactiae* *Corynebacterium bovis* Or grouped as Staphylococci and Streptococci	[redacted]	[redacted]	Concentrations of Iodine in products showing significant efficacy for postmilking treatment against: *S. aureus*: 0.05% to 1% Iodine *S. agalactiae*: 0.1% to 1% Iodine *C. bovis*: 0.25% to 1% Iodine Staph. species. 0.25% to	Doc. No. 392-030, Section A5..3.1/19

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
						1% Iodine Streptococci: 1% Iodine	
bactericide	PT3	[redacted] (Iodophor: 0.1% Iodine) [redacted] (Iodophor: 0.25%) [redacted] (Iodine: 0.25%) [redacted] (Iodophor: 0.55% Iodine plus linear dodecyl benzene sulfonic acid at 1.9%)	No details provided. Test organisms are grouped as "Environmental pathogens", "major pathogens" and "Gram-negative bacteria".	[redacted]	[redacted]	Significant efficacy of product for premilking treatment against: [redacted] environmental pathogens (P>.10) and major pathogens (P<.05) [redacted] environmental pathogens (P>.05) and major pathogens (P<.025) [redacted] Gram-negative bacteria (P<.025) and major pathogens (P<.001) [redacted] environmental pathogens (P>.10) and major pathogens (P<.10)	
amoebicide	PT5	Iodine	Entamoeba histolytica cysts	[redacted]	[redacted]	A suitable dose for emergency disinfection was calculated to be about 8 ppm for a 10 minute treatment at 23 °C. In water with high organic color or Iodine demand > 3 ppm, an increase in dosage was needed. 16 ppm was effective for all waters tested. At low temperatures (0-5 °C) the	Doc. No. 392-056; Section A5..3.1/14

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
						required contact time was 20 minutes.	

*) References:

Section A5.3.1/15: Rasmussen, M.D. et al. (1991): Effects of premilking teat preparation on spores of anaerobes, bacteria and Iodine residues in milk; J. Dairy Sci., Vol. 74, pp. 2472-2478; Doc. No. 392-028. (published)

Section A5..3.1/16: Anonymous (n.i.): Technical file-[redacted] Doc. No. 381-015 (published).

Section A5..3.1/17: Evans, D.H. (19779: Disinfection of animal viruses; Fr. Vet. J., pages 133 and 356; Doc. No. 392-019 (published).

Section A5.3.1/18: Anonymous (n.i.): Pig disinfection programme; Evans brochure; Doc. No. 392-005 (published).

Section A5..3.1/19: Anonymous (1996): 35th annual meeting-national mastitis council, Inc.: Summary of peer-reviewed publications on efficacy of premilking and postmilking teat disinfectants published since 1980; National Mastitis Council Annual Meeting Proceedings, pages 245-256; Doc. No. 392-030 (published).

Please refer also to Table 5.3.1_I-3 and Table 5.3.1_PVP-I-3 in the corresponding confidential parts of the dossier for a summary of available data provided by the applicant which is considered confidential.

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

Official use only

1 REFERENCE

1.1	**Reference**	Chang, S.L.and Morris, J.C.(1953): ELEMENTAL IODINE AS A DISINFECTANT FOR DRINKING WATER; Industrial and Engineering Chemistry, 45, 5, May 1953, 1009-1012; Doc. No.: 392-056 (published). This document was first cited under section point A5.3.1/14.
1.2	**Data protection**	[redacted]
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
1.3	**Guideline study**	No but the studies described in the publication were conducted as suspension tests resembling the EN1040 method.
1.4	**Deviations**	Not applicable

2 METHOD

2.1	**Test Substance (Biocidal Product)**	Elemental iodine
2.1.1	Trade name/ proposed trade name	[redacted]
2.1.2	Composition of Product tested	[redacted]
2.1.3	Physical state and nature	[redacted]
2.1.4	Monitoring of active substance concentration	[redacted]
2.1.5	Method of analysis	[redacted]
2.2	**Reference substance**	[redacted]
2.2.1	Method of analysis for reference substance	[redacted]
2.3	**Testing procedure**	[redacted]
2.3.1	Test population / inoculum / test organism	[redacted]
2.3.2	Test system	[redacted]
2.3.3	Application of TS	[redacted]

Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*

2.3.4 Test conditions

2.3.5 Duration of the test / Exposure time

2.3.6 Number of replicates performed

2.3.7 Controls

2.4 Examination

2.4.1 Effect investigated

2.4.2 Method for recording / scoring of the effect

2.4.3 Intervals of examination

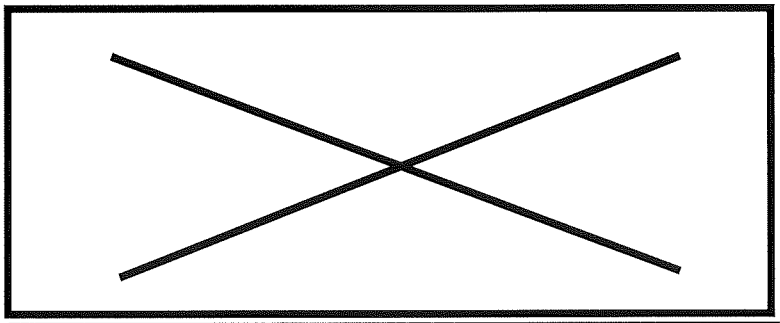
2.4.4 Statistics

2.4.5 Post monitoring of the test organism

3 RESULTS

3.1 Efficacy

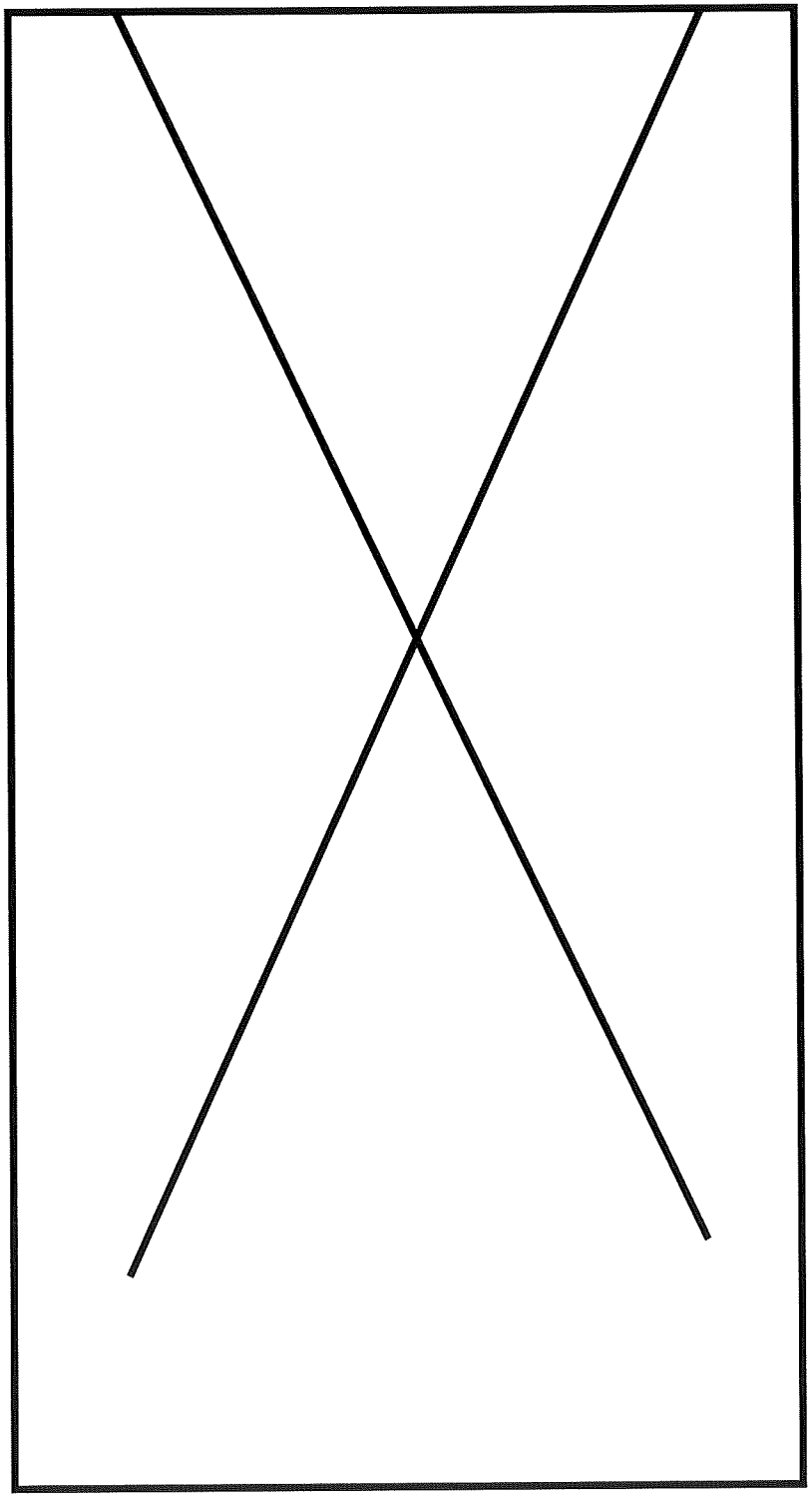
3.1.1 Dose/Efficacy curve



3.1.2 Begin and duration of effects

3.1.3 Observed effects in the post monitoring phase

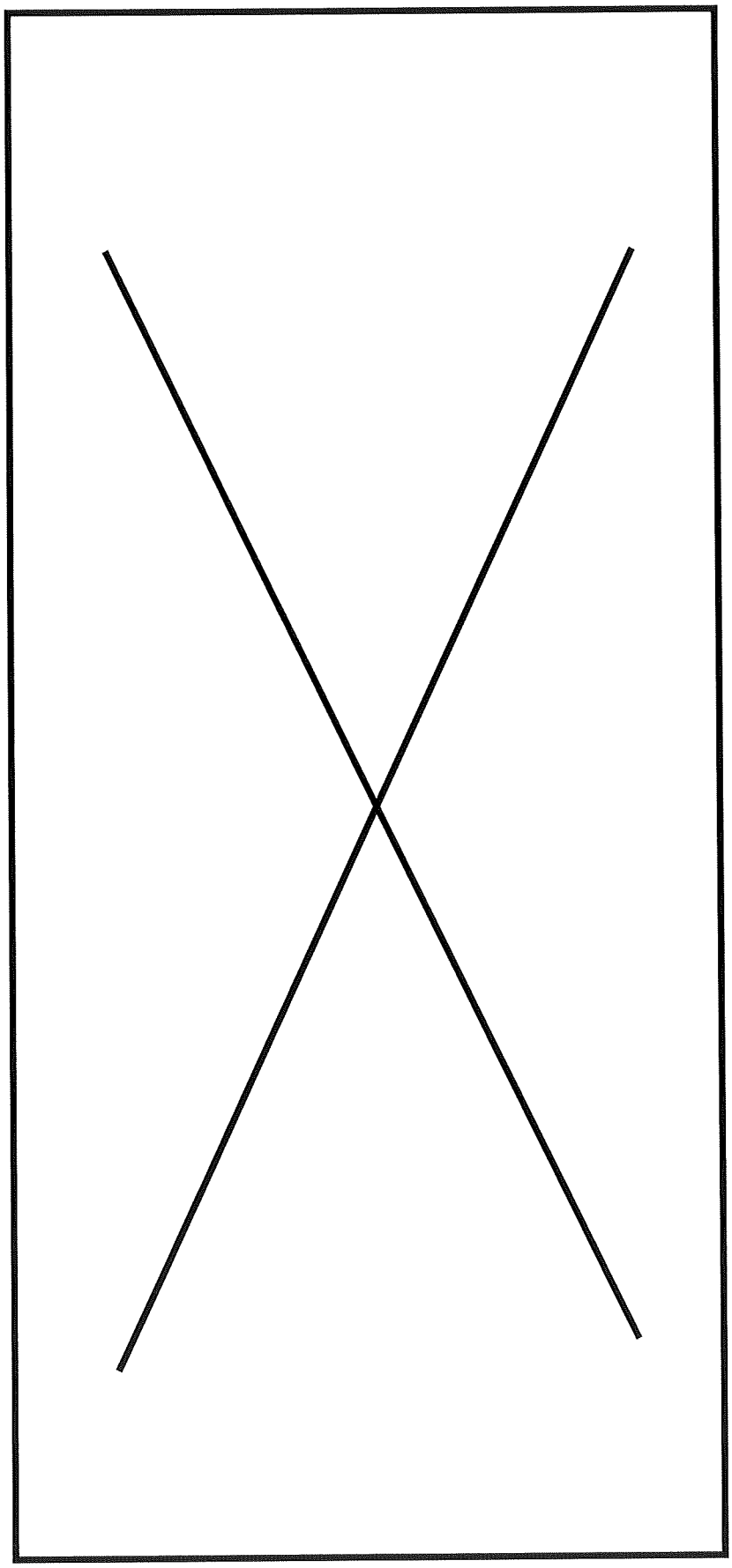
3.2 Effects against organisms or

	objects to be protected	
3.3	**Other effects**	[redacted]
3.4	**Efficacy of the reference substance**	[redacted]
3.5	**Tabular and/or graphical presentation of the summarised results**	

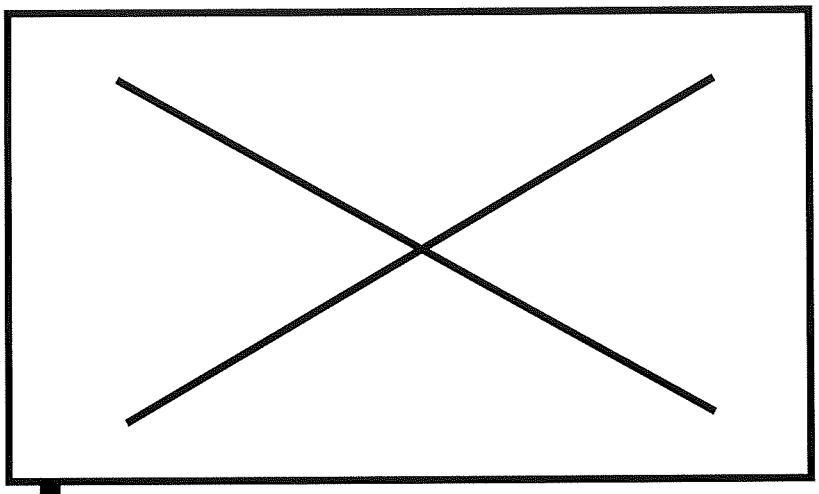
Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses



Section A5/01 **Efficacy Data**
Annex Point IIB V.5.10 *Suspension tests with bacteria and viruses*



3.6 Efficacy limiting factors

3.6.1 Occurrences of resistances

3.6.2 Other limiting factors

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing

4.2 Intended actual scale of biocide application

4.3 Relevance compared to field conditions

4.3.1 Application method

4.3.2 Test organism

4.3.3 Observed effect

4.4 Relevance for read-across

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

[redacted]

5.2 Reliability

[redacted]

5.3 Assessment of efficacy, data analysis and interpretation

[redacted]

5.4 Conclusion

Iodine has innate efficacy against bacteria, amoebae and viruses in water.

5.5 Proposed efficacy specification

[redacted]

Section A5/01
Annex Point IIB V.5.10

Efficacy Data

Suspension tests with bacteria and viruses

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Comments	[redacted]
Summary and conclusion	[redacted]

COVER PAGE

Doc. No.: 381-017

Title:	BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD
Author(s):	Fotheringham, V.J.C.
Report date:	Apr/2007

SCC Project No.:	854-005
Name of database:	Iodine

EVANS VANODINE
INTERNATIONAL PLC
Global Hygiene Solutions

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS A REVIEW

Prepared by Valerie J C Fotheringham
Chief Microbiologist, Evans Vanodine International plc

FOR INCLUSION IN THE DOSSIER FOR THE EVALUATION OF IODINE FOR INCLUSION IN ANNEX I TO THE BPD

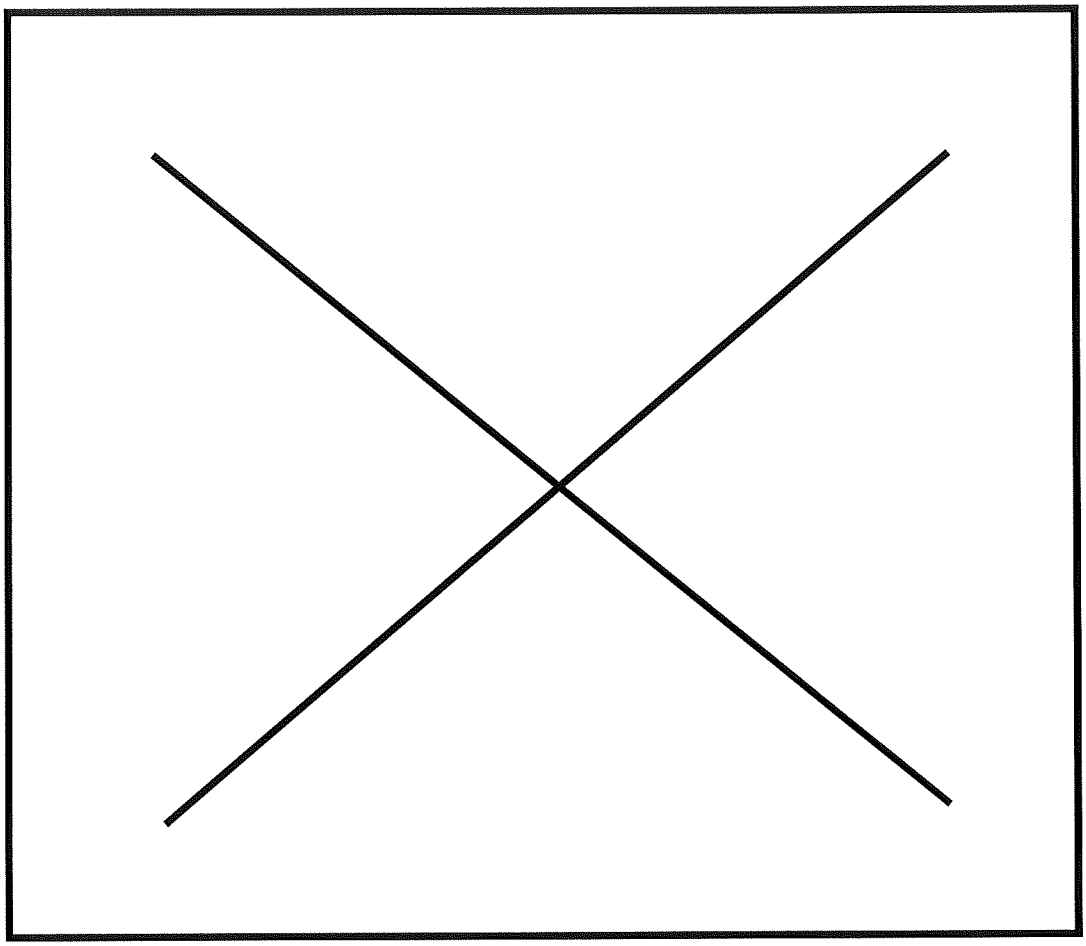
APRIL 2007

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW

CONTENTS

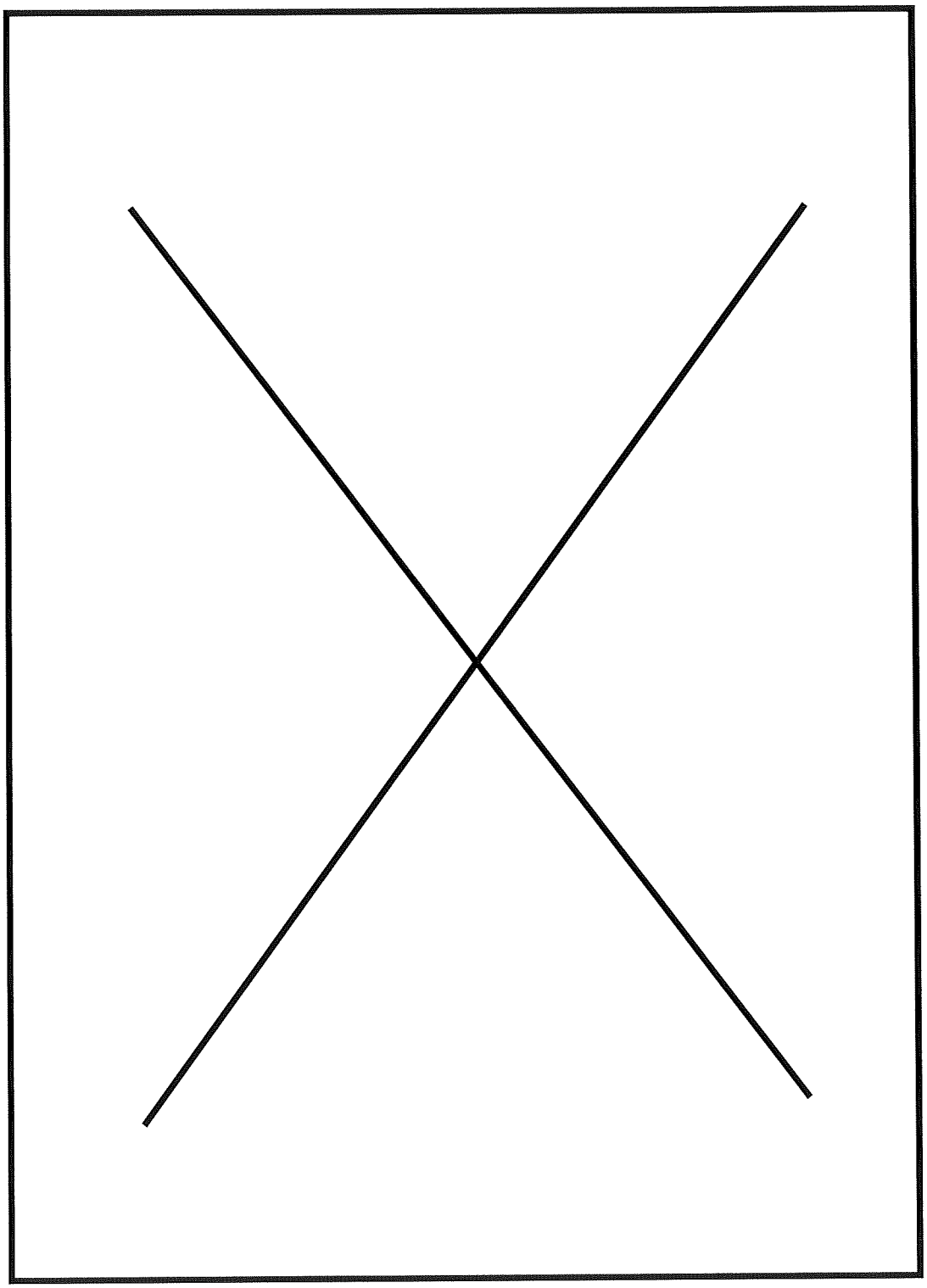
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

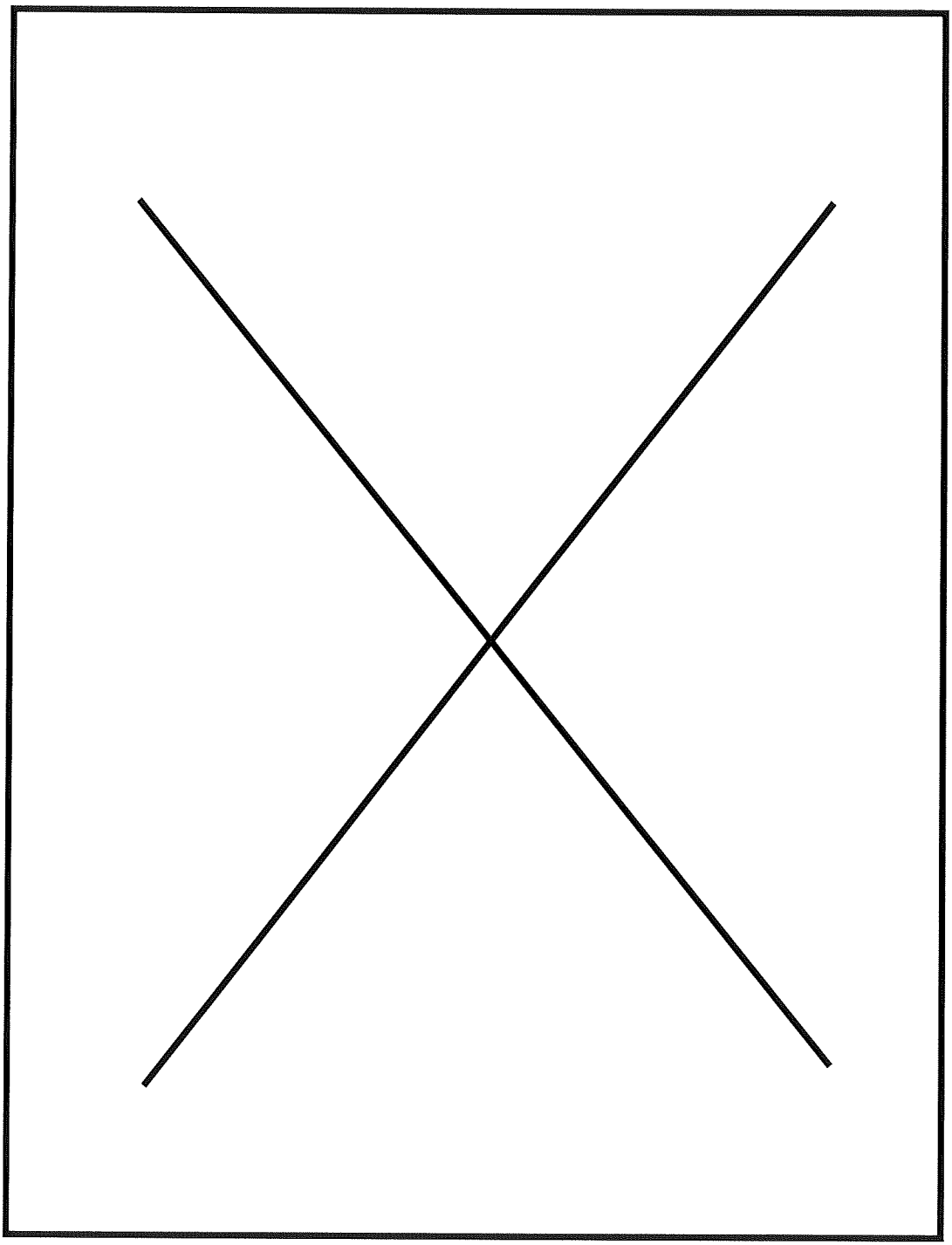


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

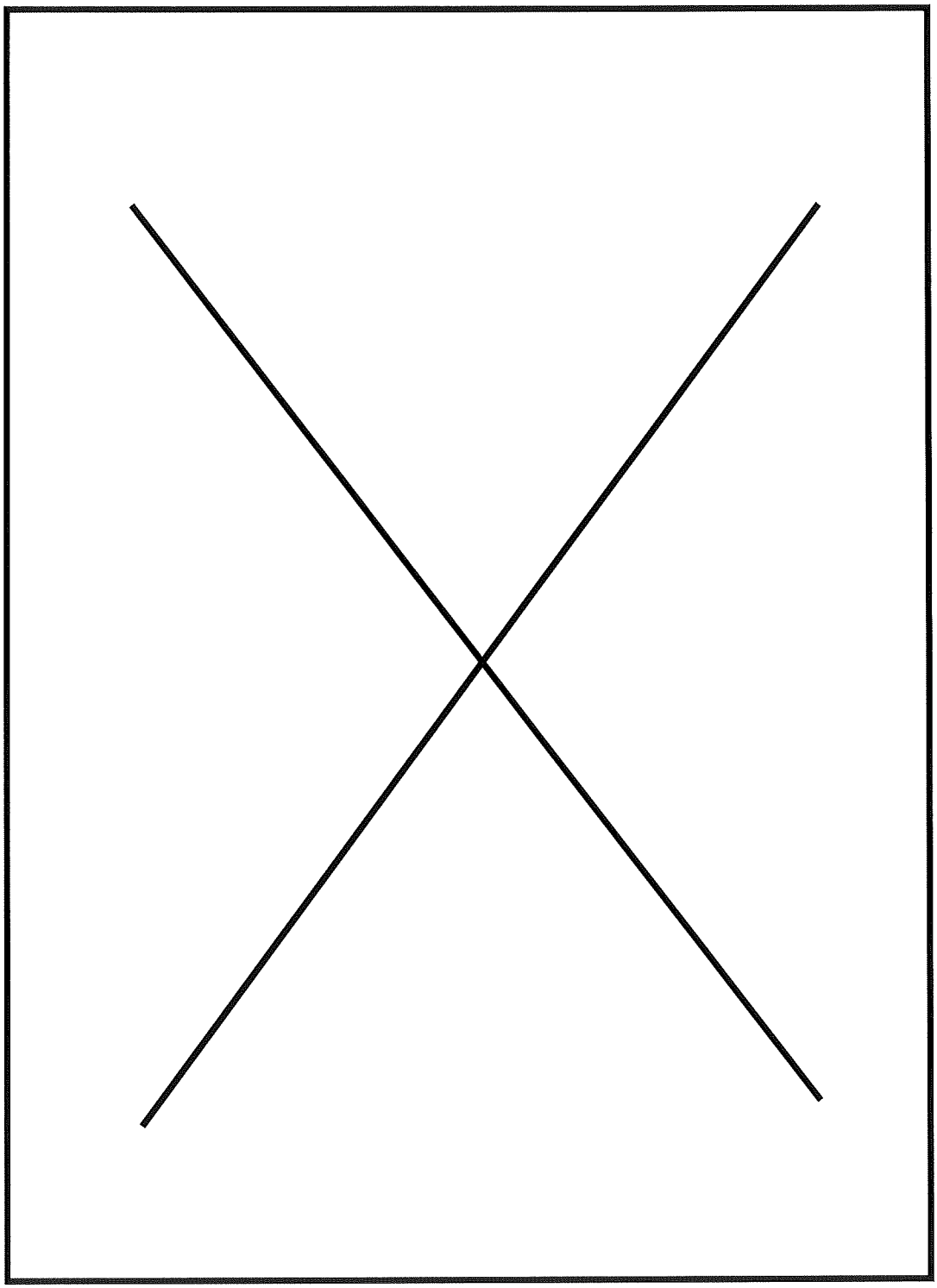


BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS
A REVIEW



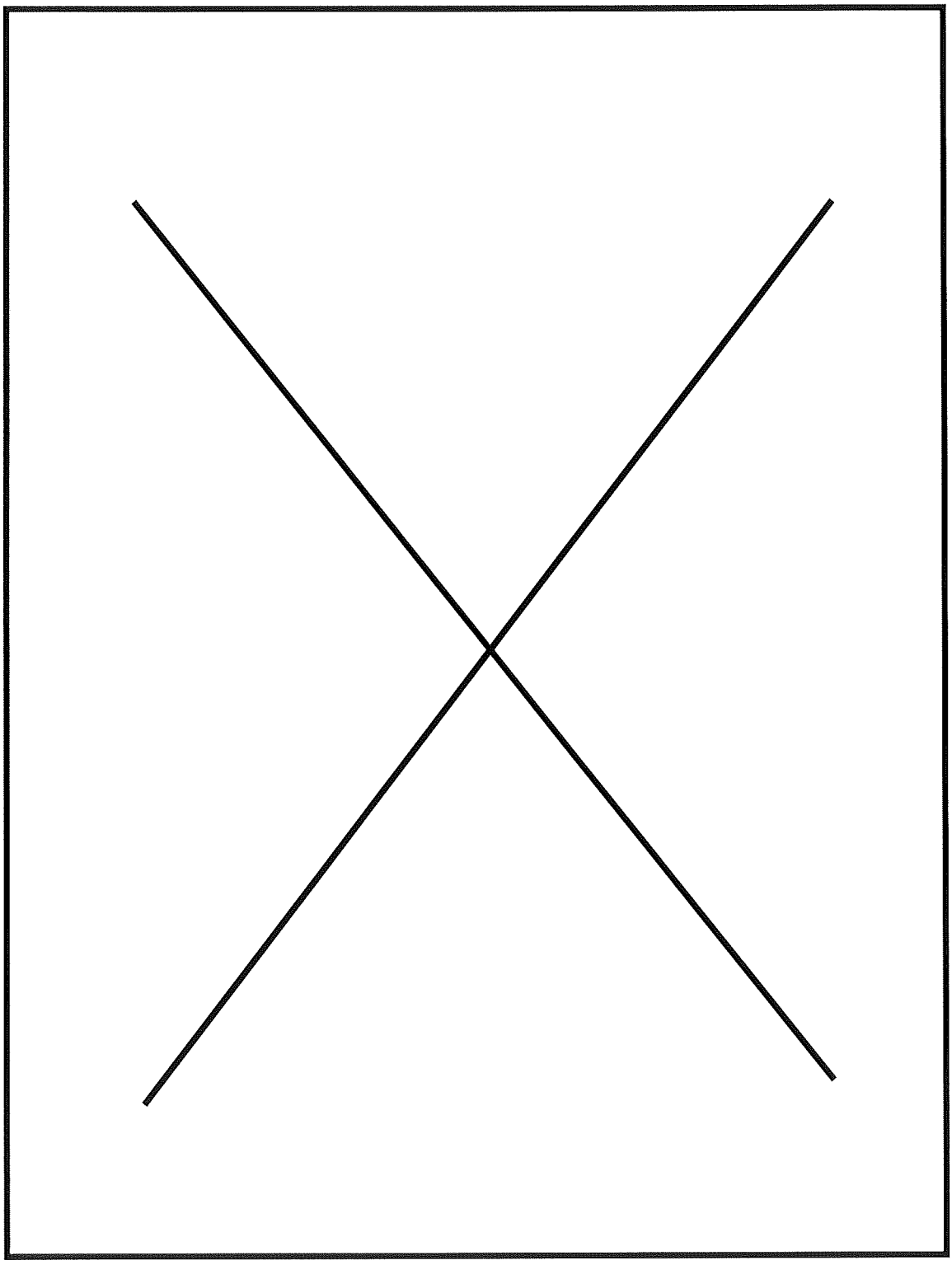
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



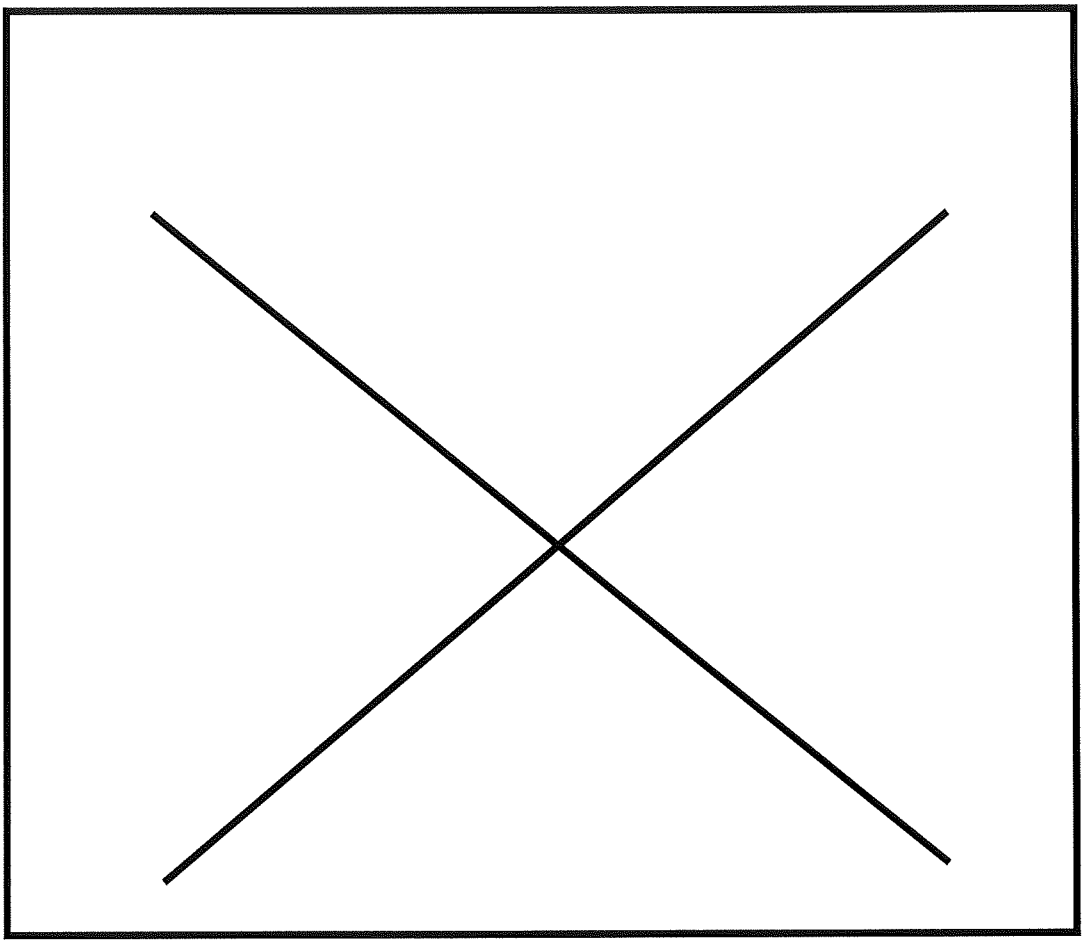
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



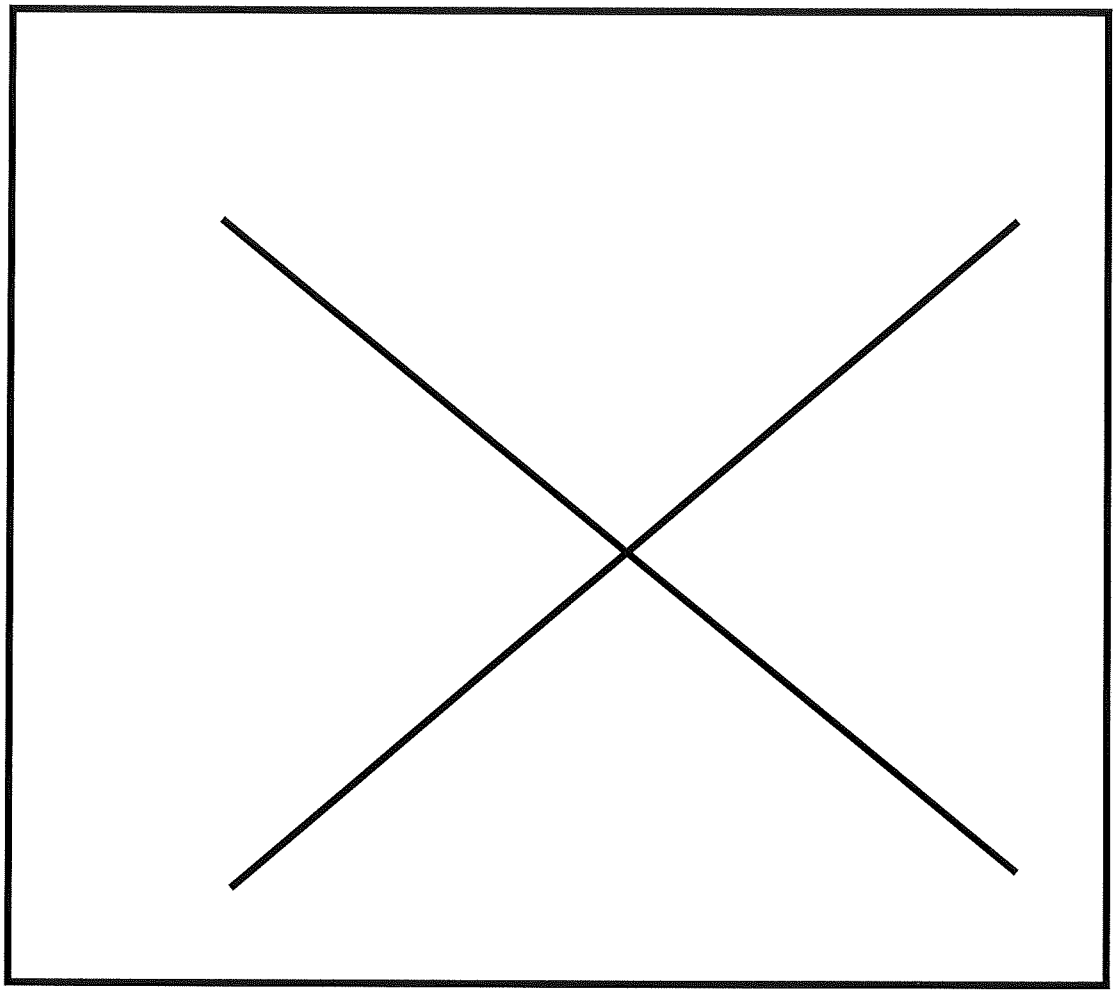
BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW



Valerie J C Fotheringham

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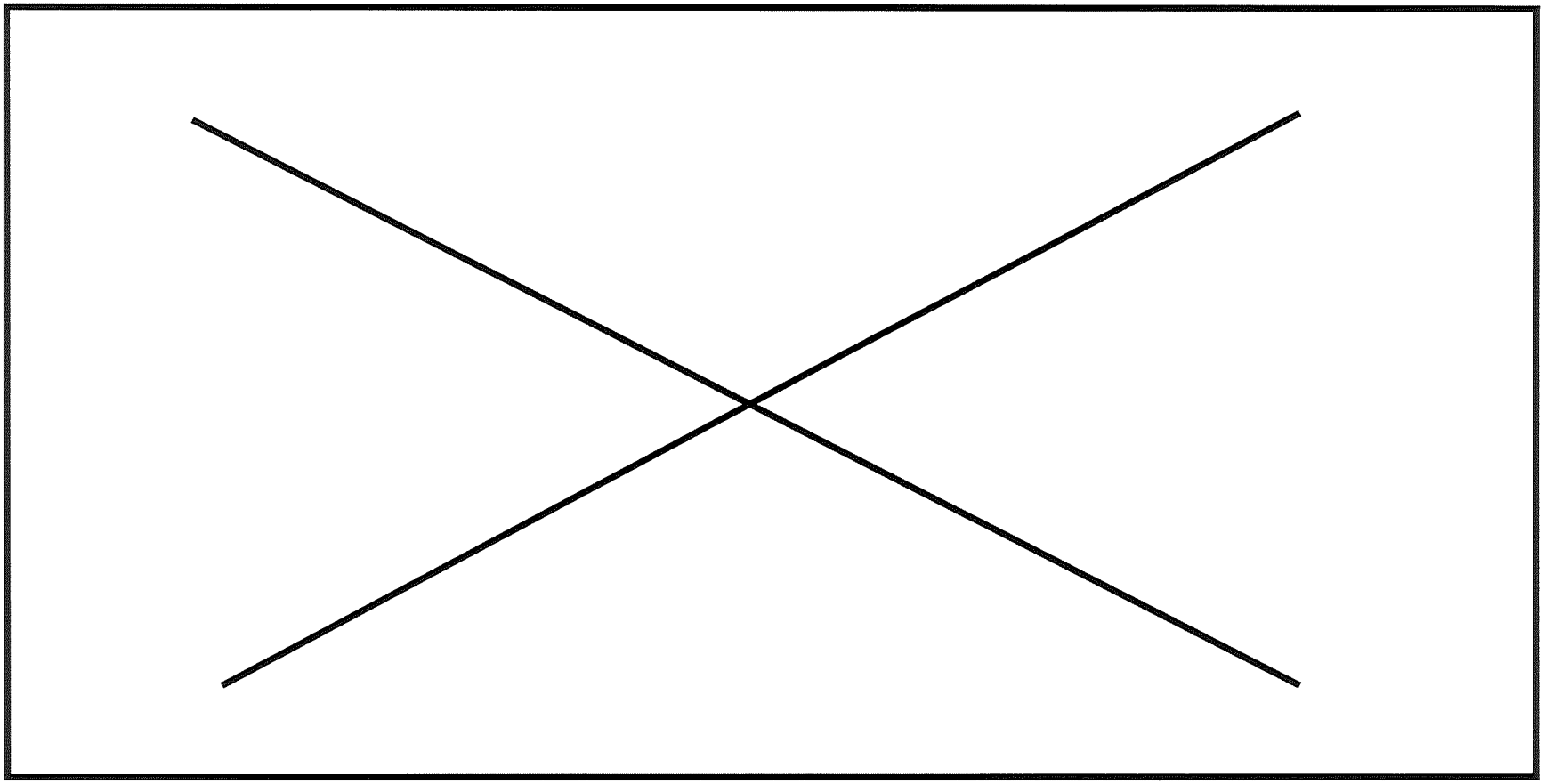
Chief Microbiologist

DATE: 30 April 2007.

BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 1: PASS DILUTIONS FOR IODOPHOR SURFACE DISINFECTANT* AGAINST A RANGE OF MICRO-ORGANISMS



BACTERIAL RESISTANCE TO IODINE BASED DISINFECTANTS

A REVIEW

TABLE 2: PASS DILUTIONS FOR IODOPHOR TEAT DISINFECTANT*** AGAINST A RANGE OF BACTERIA

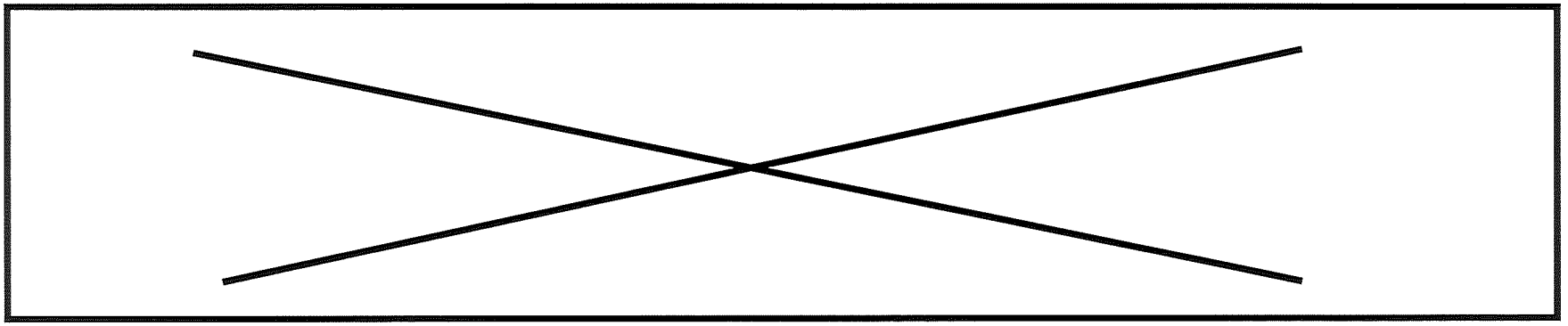


TABLE 3: PASS DILUTIONS FOR QUATERNARY AMMONIUM COMPOUND DISINFECTANT# AGAINST A RANGE OF BACTERIA