Draft Priority Existing Chemical Assessment Report

Australian Government
Department of Health and Ageing
NICNAS

Triclosan

October 2008

National Industrial Chemicals Notification and Assessment Scheme
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Preface

This assessment was carried out under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). This Scheme was established by the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act), which came into operation on 17 July 1990.

The principal aim of NICNAS is to aid in the protection of people at work, the public and the environment from the harmful effects of industrial chemicals.

NICNAS assessments are carried out in conjunction with the Australian Government Department of the Environment, Water, Heritage and the Arts, which carries out the environmental assessment for NICNAS.

NICNAS has two major assessment programs: the assessment of human health and safety and environmental effects of new industrial chemicals prior to importation or manufacture; and the other focusing on the assessment of chemicals already in use in Australia, in response to specific concerns about their health/or environmental effects.

There is an established mechanism within NICNAS for prioritising and assessing the many thousands of existing chemicals in use in Australia. Chemicals selected for assessment are referred to as Priority Existing Chemicals.

Chemicals that have been assessed as new or existing chemicals may require a reassessment of the risk of the chemical under the secondary notification provisions of the Act.

This priority existing chemical report has been prepared by the Director of NICNAS, in accordance with the Act. Under the Act, manufacturers and importers of priority existing chemicals are required to apply for assessment. Applicants for assessment are given a draft copy of the report and 28 days to advise the Director of any errors. Following the correction of any errors, the Director provides applicants and other interested parties with a copy of the draft assessment report for consideration. This is a period of public comment lasting for 28 days during which requests for variation of the report may be made. Where variations are requested, the Director's decision concerning each request is made available to each respondent and to other interested parties (for a further period of 28 days). Notices in relation to public comment and decisions made, appear in the *Commonwealth Chemical Gazette.*

In accordance with the Act, publication of this report revokes the declaration of this chemical as a Priority Existing Chemical, therefore, manufacturers and importers wishing to introduce this chemical in the future need not apply for assessment. However, manufacturers and importers need to be aware of their duty to provide any new information to NICNAS, as required under section 64 of the Act.

For the purposes of Section 78(1) of the Act, copies of assessment reports for new and existing chemical assessments are freely available from the web. Hardcopies are available from NICNAS from the following address:

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Other information about NICNAS (also available on request and on the NICNAS web site) includes:

- NICNAS Service Charter;
- Information sheets on NICNAS Company Registration;
- Information sheets on the Priority Existing Chemicals and New Chemical assessment programs;
- Safety information sheets on chemicals that have been assessed as Priority Existing Chemicals;
- Details for the NICNAS Handbook for Notifiers; and
- Details for the *Commonwealth Chemical Gazette*.

More information on NICNAS can be found at the NICNAS web site:

http://www.nicnas.gov.au

Other information on the management of workplace chemicals can be found at the web site of the Australian Safety and Compensation Council
http://www.ascc.gov.au

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Overview

Background

Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-, commonly known as triclosan (CAS No. 3380-34-5), was declared a Priority Existing Chemical for full assessment under the *Industrial Chemicals (Notification and Assessment) Act, 1989* (the Act) by notice in the *Chemical Gazette* of 6 May 2003. Triclosan was declared a Priority Existing Chemical because of environmental concerns. The widespread use of triclosan provides a number of pathways for the chemical to enter the environment, and laboratory tests have shown it to be toxic to aquatic species, with algae being the most sensitive species. The chemical properties of triclosan indicate that it may also bioaccumulate and persist in the environment. In addition, there are reports that suggest incineration of textile products containing triclosan may result in the formation of dioxin-like substances.

Scope

A full risk assessment was conducted on public health, occupational health and safety, and environmental effects of industrial uses of triclosan. Quantities of triclosan in pesticides and veterinary medicines and therapeutic products were collected for this assessment, but no further assessment of these products were conducted as they are not within the scope of the ICNA Act. This assessment considered the quantities of triclosan included in locally manufactured articles and leaching from all articles (locally manufactured or imported), but no information was provided to NICNAS on the amounts of triclosan in imported articles and leaching from articles.

Uses

Triclosan is not manufactured in Australia but is imported into Australia as the raw chemical (>99% (w/w) powder); as a liquid solution (10 - < 20% (w/v)); as plastic pellets; and as an ingredient in various products. Triclosan is included in many consumer products because of its antimicrobial activity. The main use of triclosan in Australia is in the formulation of personal care and cosmetic products, therapeutic products and cleaning agents. Other uses of triclosan are in the treatment of textiles and in plastics manufacture. It is also used in the formulation of some oil-based paints. Additionally, triclosan is imported into Australia as an ingredient in a large number of end products intended for consumer use, including cosmetic and personal care products, therapeutic products, veterinary products, pesticides, household cleaning products, and grouting material. Triclosan is reported to be used in a similar range of products overseas.

This assessment did not take into account the health or environmental effects of triclosan imported as part of finished plastic and textile articles, as no information was provided on the amounts of triclosan in imported articles.

Health effects

In humans, triclosan is rapidly and completely absorbed from the gastrointestinal tract while a lower rate of absorption occurs dermally. It is also rapidly removed from the blood, and extensive first pass metabolism occurs following oral administration. The major metabolic pathways in humans and animals involve glucuronide and sulphate conjugation, and metabolism to these conjugates has also been observed in the skin. In

humans excretion is relatively rapid; the major route of excretion being the urine, while the faeces is of secondary importance. Triclosan has also been observed in human breast milk samples. The human oral and dermal data provide no evidence of a bioaccumulation potential. Additionally, enterohepatic circulation has been demonstrated in rats, while limited evidence is available in mice and hamsters.

Triclosan has low acute oral and dermal toxicity in animals, although there is some evidence of higher acute toxicity via inhalation. A repeat dose inhalation toxicity study indicates triclosan is a respiratory irritant in rats. Both animal and human data indicate it is a skin irritant, and a study in rabbits indicates it is an eye irritant. Data from both humans and animals indicate that triclosan has at most a very weak skin sensitisation potential. No data on respiratory sensitisation are available.

Systemic toxicity was observed following repeated exposure to triclosan in oral and dermal animal studies. No reliable human data are available. Animal data indicate that the liver is the target organ following ingestion of triclosan, with hepatocyte hypertrophy and hepatocyte vacuolisation in cells observed. While the mouse is the most sensitive species, there is evidence that (unlike the rat and hamster) it is sensitive to peroxisome proliferator-type effects in the liver that are not considered relevant to humans. Similar effects on the liver are seen in dermal studies.

A number of in vitro and in vivo genotoxicity studies are available, and, although some positive results were obtained, overall, there is no evidence of an in vivo genotoxic potential. Oral carcinogenicity studies in the rat and hamster provide no evidence of a carcinogenic potential. No effects on fertility were seen in a 2-generation study in the rat, and there was no evidence of teratogenicity in developmental toxicity studies conducted in rats and rabbits.

Triclosan is listed in the Australian Safety & Compensation Council's (ASCC) *List of Designated Hazardous Substances*, contained in the Hazardous Substances Information System (HSIS). Prior to July 2008, triclosan was classified as a hazardous substance in the HSIS with the risk phrase, 'Toxic by inhalation (R23)'. ASCC updated the HSIS in July 2008 to adopt the changes in Europe's 29th Adaptation to Technical Progress (ATP) to Directive 67/548/EEC dated April 2004. With this update in July 2008, triclosan is now listed on the HSIS with the risk phrase, 'Irritating to eyes and skin (R36/38)'. Based on the current NICNAS assessment and according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), triclosan is classified as 'Toxic by inhalation (R23)' and 'Irritating to eyes, respiratory system and skin (R36/37/38)'(see recommendation 1).

Triclosan is not specifically listed in the Australian Dangerous Goods (ADG) Code. Due to its moderate inhalation toxicity, triclosan raw material (100% powder) would fall under Class 6.1 (Toxic substances), packaging class III (Substances presenting low danger) and UN number 2811 (toxic, solid, organic) (see recommendation 2a).

Occupational exposure and health risks

Workers may be potentially exposed to triclosan by skin and eye contact and inhalation. Oral exposure is not expected in occupational settings. The low vapour pressure of triclosan means inhalation exposure will be low, although there is still potential for inhalation of triclosan powder. The main route of exposure is likely to be dermal route.

No occupational monitoring data for triclosan are available in Australia or reported in the literature. Therefore, the Estimation and Assessment of Substance Exposure (EASE)

model developed by the United Kingdom Health and Safety Executive was used to estimate inhalation and dermal exposure.

It was determined that under normal occupational conditions the risk of workers being exposed to concentrations that would lead to adverse health effects such as skin and eye irritation and chronic effects is low. However, in cases of accidental spills or leaks of triclosan, the risk of skin and eye irritation would increase, especially where personal protective equipment is not used. The risk of inhalation toxicity and respiratory irritation would increase in formulation workers when using triclosan powder without local exhaust ventilation (LEV).

Public exposure and health risks

Public exposure to triclosan can occur through the use of cosmetic and personal care products, household cleaning products, paint, and textile articles containing triclosan. Given the types of triclosan-containing products available to the public, the main route of exposure is likely to be dermal. However, oral exposure may occur through accidental or incidental ingestion of lip balm, toothpaste or mouthwash formulations. Also inhalation exposure may occur through breathing aerosols generated from the use of cosmetic and personal care products or cleaning products.

Exposure data from direct measurement is limited and available only for the use of cosmetic and personal care products. Consequently, various exposure models have been used to estimate consumer exposure to triclosan-containing consumer products. No data are available on the leaching of triclosan from plastic products and therefore the potential dermal and oral exposure of babies or young children as a result of sucking or mouthing these products cannot be determined.

The risk to the public of inhalation toxicity, skin, eye or respiratory irritation is low because of the low concentrations of triclosan in cosmetic and personal care products, and in textiles and plastic products. Under normal conditions of consumer use, the risk of adults and children being exposed to levels of triclosan that would lead to chronic health effects is low. Furthermore, although there is a potential for breast-feeding babies to be exposed to triclosan via breast milk, this assessment indicates it is likely to be the lowest source of exposure to babies, and therefore the risk of an adverse health effect during lactation is very low.

Potentially, the greatest source of exposure to consumers (adults, young children and babies), and thus the risk of an adverse health effect, is from the use of cosmetic and personal care products containing triclosan. Although the chronic health risk from such products is generally considered to be low, there are exposure data from volunteer studies that suggest that repeated use of a range of triclosan-containing products could increase the exposure levels, and therefore the potential health risk (see Recommendation 4).

The available data in humans and animals provide no evidence that triclosan has the potential to cause harm to breastfed babies.

On the basis of available data, there is also no evidence that the use of triclosan is leading to an increase in triclosan-resistant bacterial populations or that there is any increased risk to humans regarding antibiotic resistance.

Environmental effects

For terrestrial organisms, triclosan is slightly toxic to birds by the oral route of exposure, based on acute data available for two standard test species. Triclosan is toxic to plants

when grown in sandy soil, though toxicity is less for plants grown in sandy loam, probably due to the higher organic matter content of the sandy loam soil binding the triclosan (see Recommendation 8a with regard to biosolids applied as soil conditioners). The only terrestrial invertebrate data available are for earthworms, for which triclosan was found to be very slightly toxic. Triclosan does not affect soil respiration or nitrification. Only limited data were available to examine the effects of triclosan on activated sewage sludge microorganisms. These data indicate that triclosan can initially reduce the ability of the sludge microorganisms to remove ammonia as well as reduce their nitrification capacity, although the effects decrease with acclimation.

In the aquatic compartment, triclosan is highly to very highly toxic to a number of freshwater aquatic organisms such as fish, plants and invertebrates. From the limited data available, freshwater algae are the most sensitive species. Algae form an important food source for numerous other organisms. In both acute and chronic tests with freshwater invertebrates, triclosan is much more toxic to freshwater invertebrates in neutral or acidic waters than in alkaline waters. Consequently, because the tests on algae were performed under alkaline pH conditions, the toxicity values for algae may under-estimate algal toxicity through the full environmental pH range. Recent research has indicated that effects on hormonally-induced metamorphosis of tadpoles can occur at concentrations around the predicted no-effect concentration (PNEC). However, the biological significance of these effects is currently unclear.

Both triclosan and a minor metabolite (methyl triclosan) have a high potential to bioaccumulate in aquatic organisms. Bioaccumulation potential is also evident from laboratory-scale bioconcentration factor (BCF) studies and field monitoring studies. The bioconcentration of triclosan is dependent on water pH (greater accumulation at lower pH) and exposure concentration.

In summary, various microbial species and algae are highly sensitive to triclosan, consistent with its antimicrobial properties. Triclosan is highly toxic to fish and daphnids, and slightly toxic to birds and earthworms. Triclosan is also very highly toxic to sediment dwelling organisms when exposed through the water column. Limited data are available for the toxicity of triclosan to marine organisms. The available data indicates that triclosan is highly toxic to grass shrimp with larvae being the most sensitive life stage. Triclosan is also very highly toxic to the marine bacterium *Vibio fischeri.* There is a lack of data for the effects of triclosan to soil organisms, with the limited data indicating that it is does not affect soil respiration or nitrification.

Environmental exposure and risks

The exposure of the environment to triclosan from accidental spills and leaks during transport should be limited by engineering controls (e.g. container specifications) and emergency clean-up procedures. Triclosan is predominantly released to the sewerage system in various cosmetic and personal care products during washing and bathing, or from the disposal of cleaning products. Triclosan can also be discharged from formulating facilities. The use of triclosan in oil-based paints is not expected to result in significant release to the aquatic compartment as the vast majority of the triclosan is expected to be contained within the cross-linked inert paint matrix and will share its fate. This is likely to be disposed of to landfill (either as paint dust resulting from sanding back the painted surface or bound to the surface) at the end of its useful lifetime. As the triclosan will be bound within the inert paint matrix, leaching from landfill is not expected, and it will slowly degrade through a mixture of biotic and abiotic processes. The use of the tile paint in shower cubicles raises the potential for release of triclosan to the environment through

leaching from the paint. However, the rate of leaching is expected to be extremely low and hence, the release from this source is expected to be insignificant.

Environmental exposure can occur through beneficial re-use of treated effluent and biosolids (sewage sludge) that may also contain triclosan. Throughout Australia, treated effluent is increasingly being utilised in a range of agriculture (irrigation), agroforestry and industrial applications, which provides a pathway for release of triclosan and its derivatives to soils. Similarly, application of biosolids to soils as a soil conditioner also provides another pathway for transfer of triclosan from the sewerage system to soils.

Consequently, triclosan largely enters the environment in Australia through discharges from Sewage Treatment Plants (STPs). Constant emission to sewer occurs, leading to ongoing environmental exposure in waters and sediments downstream of sewage outfalls.

The risk of toxicity to birds and most mammals that are not solely dependent on the freshwater aquatic environment for food is considered to be low and at an acceptable level. There is potential for indirect effects on birds and mammals to occur near STP outlets as a result of adverse effects of triclosan on their food supply. There is also potential for direct toxicity arising through triclosan residues in food resulting from the presence of triclosan in surface waters. The risk to platypus living in the vicinity of a sewage outfall is considered to be low and at an acceptable level at the triclosan concentrations reported in Queensland. However, the triclosan concentrations in the vicinity of sewage outfalls in other parts of Australia, and the subsequent risk to platypus, is unknown.

The use of triclosan and subsequent release to the Australian sewage system, at current levels of use, may likely to result in concentrations of the chemical within natural waterways which may pose risks to algae, aquatic plants and fish at all levels of wastewater treatment. If the limited data available from Queensland are representative of data for the rest of Australia, the risks of adverse impacts on fish and aquatic plants are at worst marginal. However, for algae, these limited data confirm that triclosan is present at levels that could result in adverse effects. In the absence of data on the concentrations downstream of representative STPs in Australia, it is not possible to exclude the possibility of adverse effects to certain species of algae within inland waterways (see Recommendation 7). As dilution is high in ocean outfalls, risks to marine species are considered to be low and at an acceptable level.

Studies indicate that triclosan is present in biosolids at levels which, when applied to soil, may result in adverse effects on plants. Some data are also available which point to the persistence of triclosan in treated soils. Although recent studies indicate that triclosan will degrade relatively rapidly in aerobic soils, which would mitigate potential risks, triclosan will persist if the soil is anaerobic. The continual application of triclosan to soil through use of biosolids (as soil conditioners) or effluent (for irrigation) from STPs also has the potential to disrupt microbial soil populations, but it does not appear to affect soil respiration or nitrification. Consequently, an understanding of the toxicity of triclosan to soil dwelling organisms is also important to fully determine the effects in the field of triclosan release to the soil environment and to establish the level of risk (See Recommendation 8b).

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Recommendations

This section provides recommendations arising from the priority existing chemical assessment of triclosan. Recommendations are directed principally at regulatory bodies and importers and formulators of triclosan and triclosan products. Implicit in these recommendations is that best practice is implemented to minimise occupational and public exposure, and environmental impact.

Occupational Health and Safety

Recommendation 1. Revised occupational hazard classification (ASCC)

Based on the hazard assessment of the available data and in accordance with the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), triclosan is determined to be hazardous and should be classified as:

- R23 Toxic by inhalation
- R36 Irritating to eyes
- R37 Irritating to respiratory system
- R38 Irritating to skin

It is recommended that this revised classification for triclosan be included in the Hazardous Substances Information System (HSIS) as soon as possible.

The appropriate risk phrases for mixtures containing triclosan are as follows:

Risk Phrase	Concentration Cut-off
R23, R36/37/38	≥25%
R20[1], R36/37/38	25% > conc ≥20%
R20	20% > conc ≥ 3%

The following safety phrases are also recommended for triclosan:

- S22 Do not breathe dust
- S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
- S37 Wear suitable gloves
- S38: In case of insufficient ventilation, wear suitable respiratory equipment
- S39 Wear eye/face protection
- S45: In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)
- S60: This material and its container must be disposed of as hazardous waste

[1] R20 Harmful by inhalation.

Recommendations 2a and 2b. Hazard communication (Industry)

The industry should take note of the revised hazard classification (i.e. toxic by inhalation, irritating to eyes, skin and respiratory system) and UN numbers (according to the Australian Code for the Transport of Dangerous Goods by Road & Rail, 2007) for triclosan.

Recommendation 2a. Australian Code for the Transport of Dangerous Goods by Road & Rail

It is recommended that the industry should take note of the UN numbers applicable for triclosan according to the Australian Code for the Transport of Dangerous Goods by Road & Rail (ADG Code, 2007).

According to the ADG Code, due to its moderate inhalation toxicity, triclosan powder (100%) falls under Class 6.1 (Toxic substances), packaging class III (Substances presenting low danger) and UN number 2811 (toxic, solid, organic) for road and rail transport.

The other forms of triclosan imported to Australia (liquids and pellets) should have the appropriate UN number (solid or liquid) depending on the concentration of triclosan. Class 6.1 applies only if the estimated LC50 value (1 hour) falls within the ADG Code (2007) classification range for inhalation toxicity (1 hour LC50 $\leq$ 4.0 mg/L).

Triclosan is highly toxic (acute and chronic) to some aquatic species. If the LC50 value (1 hour) of triclosan liquids or solids falls outside the Class 6.1 classification range for inhalation toxicity (1 hour LC50 > 4 mg/L), Class 9 (Miscellaneous dangerous substances and articles) and UN number 3077 (environmentally hazardous substance, liquid, not otherwise specified) or 3082 (environmentally hazardous substance, solid, not otherwise specified) is applicable to triclosan (ADG Code, 2007).

Recommendation 2b. MSDS and label amendments

It is recommended that suppliers and employers take note of the revised hazard classification (i.e. toxic by inhalation, irritating to eyes, skin and respiratory system) and UN numbers and, amend Material Safety Data Sheets (MSDS), labels and training material accordingly.

MSDS (see Sample MSDS, Appendix I):

Under the *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC, 1994c) and the Commonwealth State and Territory regulations introduced in accordance with these National Model Regulations, employees shall have ready access to MSDS for hazardous substances at their workplace.

In accordance with the *National Code of Practice for the Preparation of Material* Safety *Data Sheets 2nd Edition* (NOHSC, 2003), it is recommended that all manufacturers, suppliers and employers review their hazard communication, paying particular attention to the following points:

(i) correct identification of health hazards and risk phrases as contained in Recommendation 1;

(ii) correct information on the concentration cut-offs for mixtures containing triclosan as provided in Recommendation 1;

(iii) inclusion of safety phrases as noted in Recommendation 1; and

(iv) inclusion of ADG Code Class and UN number for transport by Road & Rail as provided in Recommendation 2a.

Labels:

In accordance with the *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994a), it is recommended that importers and suppliers review their hazard communication paying particular attention to the following points:

(i) correct signal word; and

(ii) correct risk and safety phrases as contained in Recommendation 1.

Recommendation 3. Compliance with state and territory legislation (Government)

It is recommended that the State and Territory Occupational Health and Safety authorities review compliance in the workplace with the revised MSDS and labels which take into consideration the above information.

Public Health and Safety

Recommendation 4. Poison scheduling (Government)

Given the acute toxicity profile (inhalation toxicity and irritation effects) of triclosan and the potential for human exposure, it is recommended that the National Drugs and Poisons Schedule Committee (NDPSC) consider scheduling triclosan in the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP).

The levels of triclosan and its metabolites in some volunteer studies following repeated use of a cosmetic or personal care product containing triclosan raise a concern. The plasma levels may have increased in some individuals through combined use of many products containing triclosan, and/or using products containing relatively high concentrations of triclosan.

The major source of exposure of the public to triclosan comes from cosmetics and personal care products with about 15 tonnes per year being used in these products. Consequently it is also recommended that NDPSC consider establishing a maximum level for triclosan as a preservative in cosmetic and personal care products.

The EU maximum concentration level for triclosan in cosmetic and personal care products is provided below as being protective to public health and promotes international harmonisation:

Triclosan (as a preservative) for cosmetic use:
0.3% or less in all cosmetic preparations

The public can also be exposed to triclosan used in cleaning products. Currently the level of exposure from this source is relatively low with less than 1 tonne/year being used in industrial cleaning products that may also be available to the general public through retail outlets. NICNAS will monitor the use of triclosan in cleaning products and consider the need for a maximum level in these products based on the potential public health risk. Further recommendations may be made to the NDPSC.

The final report will be forwarded to the NDPSC for their consideration.

Recommendation 5. Utilisation of the health hazard assessment (Government)

It is recommended that other government organisations, such as Australian Pesticides and Veterinary Medicines Authority (APVMA) and Therapeutic Good Administration (TGA), take the findings of the human health hazard assessment into consideration in future work on triclosan or products containing triclosan, noting use of triclosan in therapeutic and agricultural and veterinary products.

It is recommended that the APVMA should also take note of Recommendation 4 of this report regarding the poison scheduling of triclosan, which may have impact on currently registered Agricultural and Veterinary products containing triclosan.

It is also recommended that the National Health and Medical Research Council (NHMRC) take the findings of the hazard assessment of antimicrobial resistance discussed in this report into consideration in any future advice being provided on triclosan. Noting that this report recognizes that there is presently limited information available on the following:

- The prevalence of triclosan resistant organisms in clinical environments;
- The exact mechanisms of antibacterial action of triclosan;
- The kinetics of triclosan antibacterial resistance mechanisms and their possible transferability; and
- The fate of triclosan in the environment, the rate and extent of degradation of triclosan and the anti-microbial activity of degradates or low concentrations in the environment.

Recommendations 6a and 6b. Impurities in triclosan (Government and Industry)

Australia ratified the Stockholm Convention on Persistent Organic Pollutants (POPs), whose aim is to protect human health and the environment from the effects of POPs, on 20 May 2004. Dioxins and dibenzofurans, which are found in varying low-level amounts as synthesis impurities in triclosan, were included in the first 12 POPs identified by the Stockholm Convention. Annex C of the Stockholm Convention on POPs dealing with unintentional production of POPs provides general prevention measures relating to both best available techniques and best environmental practices, that includes "minimisation of these chemicals [i.e. dioxins and dibenzofurans] as contaminants in products" (UNEP, 2002).

For Australia to meet its obligations under the Stockholm Convention for POPs, the levels of dioxins and dibenzofurans in triclosan imported into Australia should be kept as low as possible.

Recommendation 6a. Impurities in triclosan (TGA)

It is recommended that the Therapeutic Good Administration particularly note that the U.S. Pharmacopoeia[2] have set limits for dioxins and dibenzofurans as impurities in triclosan used in therapeutics.

[2] The U.S limits are set by the U.S. Pharmacopoeia (USP) and these recommendations form the basis of enforcement actions by the U.S. Food and Drug Agency. In the US, impurities in triclosan were first regulated in 2000 when the chemical was included in USP Volume XXIV.

This assessment of triclosan notes the following:

1. It is possible that several polychlorodibenzo-p-dioxins (dioxins) and polychloro-dibenzofurans (dibenzofurans) can be found in varying low-level amounts as synthesis impurities in triclosan. Their presence or absence is dependent upon the type and purity of the starting materials used to synthesize triclosan as well as reaction conditions such as temperature and pressure. If present, their relative concentrations as impurities can vary from batch to batch.

2. As guidance, the limits of dioxins and dibenzofurans as impurities in the U.S. Pharamacopoeia (USP) are as below:

- less than 10 µg/g for monochlorophenols;
- less than 10 µg/g for 2,4-dichlorophenol;
- less than 0.25 µg/g for 1,3,7-trichlorodibenzo-p-dioxin;
- less than 0.5 µg/g for 2,8-dichlorodibenzo-p-dioxin;
- less than 0.25 µg/g for 2,8-dichlorodibenzofuran;
- less than 0.5 µg/g for 2,4,8-trichlorodibenzofuran;
- less than 1 pg/g for 2,3,7,8-tetrachlorodibenzo-p-dioxin; and
- less than 1 pg/g for 2,3,7,8-tetra chlorodibenzofuran

3. Evidence is available in the literature that some grades of triclosan may not meet USP specifications. This assessment could not conclusively determine from the data submitted that all the triclosan imported into Australia met the specifications of the current edition of the USP.

4. Limiting the amount of dioxin and dibenzofuran impurities in triclosan is consistent with the Australian Government National Action Plan for addressing dioxins in Australia under the National Dioxins Program[3]. The National Action Plan sets out a range of actions that will be taken by Australian governments to minimise, and where feasible, eliminate sources of dioxin release.

5. The basis for the US (or the Canadian) limits cannot be determined. Though NICNAS has been informed by the USP that such documents may not be available or may be confidential, it is assumed that these limits have a health basis. It is known that industry overseas has met the US regulations indicating that it is practically feasible to achieve these limits.

Recommendation 6b. Impurities in triclosan (Industry)

It is recommended that importers of triclosan, as a voluntary measure, ensure that triclosan imported into Australia meets the concentration limits specified in Recommendation 6a for dioxins and dibenzofurans as impurities. These limits are based on those in the U.S. Pharamacopoeia (USP) and are technically achievable.

[3] The recent Australian National Dioxins Program concluded that the Australian Tolerable Monthly Intake (TMI) "should be adequately protective of the general population with respect to effects of dioxin-like compounds" (National Dioxins Program Technical Report No. 12, 2005). The Australian TMI value for dioxins and furans combined is 70 pg TEQ/kg bw/month as recommended by the NHMRC and the Office of Chemical Safety in 2002, and is equivalent to that set by the Joint Expert Committee on Food Additives, a committee of the United Nations Food and Agriculture Organization and the World Health Organization (Environment Protection and Heritage Council, 2005).

Environmental Safety

Recommendation 7. Releases from sewage treatment plants (Federal, State and Territory agencies through Environment Protection and Heritage Council (EPHC) Chemicals Working Group)

The major route by which triclosan is released to the environment is through the sewer. Constant discharge occurs, leading to ongoing environmental exposure. The rate of removal of triclosan by wastewater treatment varies substantially, depending on whether anaerobic or aerobic processes are used, acclimation of the sludge microbes and the concentrations in the influent. The measured levels are at the lower end of internationally observed values for sewage effluent, biosolids and surface water, however, the limited available data do not cover the full range of urban plants in Australia.

Based on the uncertainty in the available data, there is sufficient cause to recommend the conduct of targeted short term sampling of the levels of triclosan in sewage effluent and receiving freshwater in order to determine the extent of release to, and levels in the environment, together with impacts on biota. Freshwater environments with larger quantities of receiving waters will lead to dilution of the effluent, indicating that any monitoring should be focused on areas with limited flow in receiving waters, such as in smaller rivers and creeks.

It is recommended that:

- A targeted sampling study of the levels of triclosan in sewage effluent and receiving freshwaters, focused on areas of highest potential risk of adverse effects, should be conducted in order to clarify risks in the field associated with representative conditions. Federal, state and territory agencies, through the EPHC Chemicals Working Group, should consider how to design and implement the study, including the associated funding sources.
- The targeted sampling study should also focus on plants that have large urban catchments to ensure that there is good coverage of the possible upper range triclosan levels. Areas where only primary treatment occurs should also be monitored for a limited period, and the data provided to DEWHA.
- Triclosan levels above the predicted-no-effect concentration (PNEC) detected in effluent as a result of sampling will require toxicity tests of the effluent to most sensitive algal species to be conducted. Federal, state and territory agencies, through the EPHC working group, should develop mechanisms to facilitate any such testing according to OECD or equivalent guidelines and consider the associated funding sources.

Recommendations 8a, 8b and 8c. Biosolids applied as soil conditioners (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

Re-use of biosolids for soil improvement, and as a fertiliser substitute has a number of benefits, and reduces the need to dispose of biosolids at landfill sites. Several states have biosolids guidelines that detail acceptable uses of biosolids. Triclosan has been measured in samples of biosolids from 19 waste water treatment plants around Australia (19 out of about 900, excluding New South Wales and Northern Territory). The measured levels were similar to those recorded overseas and similar to those predicted by modelling.

It is recommended that the maximum concentrations of triclosan present in the biosolids and/or maximum application rate of biosolids should be measured in a targeted and short-term sampling strategy. The toxicity of triclosan to soil dwelling organisms is also important to fully determine the effects in the field of triclosan release to the environment in Australia.

Recommendation 8a. Targeted study of triclosan in biosolids (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

It is recommended that a targeted study of the level of triclosan in biosolids used as a soil conditioner should be conducted in order to clarify risks in the field associated with common use practices. Federal, state and territory agencies, through the EPHC Chemicals Working Group, should consider possible mechanisms to design, develop and implement the study, including the associated funding sources and any relevant industry input or support that may be required.

Recommendation 8b. Toxicity tests for soil dwelling organisms (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

In addition to the above study, it is further recommended that toxicity tests for soil dwelling organisms, potentially in conjunction with the sampling strategy outlined above, should also be conducted. Federal, state and territory agencies, through the EPHC Chemicals Working Group, should also consider how to design and implement this testing, including the associated funding sources.

Recommendation 8c. Proactive management actions to reduce risks (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

Given the uncertainty regarding the persistence and effects of triclosan in soils, it is recommended that proactive management actions to reduce risks should be developed. Such actions to ameliorate risks include further ageing of biosolids prior to incorporation into soil, or incorporation in smaller proportions. Federal, state and territory agencies, through the EPHC chemicals working group, should collaborate on the development and implementation of such actions, including the associated funding sources.

Secondary Notification

Under section 64 of the *Industrial Chemicals (Notification and Assessment) Act 1989*, the secondary notification of a chemical that has been assessed under the Act may be required where an applicant or other introducer (importer) of a chemical becomes aware of any circumstances which may warrant a reassessment of its hazards and risks. In the case of triclosan, specific circumstances include:

- The function or use of triclosan has increased, or is likely to change, significantly;
- The amount of triclosan introduced into Australia has increased, or is likely to increase significantly;
- Manufacture of triclosan in Australia is proposed;
- Significant new information has become available to the applicant/notifier as to adverse environmental effects of triclosan such as those identified in this assessment (e.g. methyl-triclosan and 2,8-dichlorodibenzo-p-dioxine);
- Additional data has become available to the applicant/notifier to confirm and clarify the biological significance of the observed effects of triclosan on the development of tadpoles of the North American bullfrog, *Rana catesbeiana*.
- Recommended environmental monitoring detects the presence of triclosan in the Australian aquatic environment above levels of concern (i.e. 0.05 µg/L);
- Additional information has become available to the applicant/notifier as to the adverse health effects of triclosan, including development of antimicrobial resistance to triclosan in clinical or natural settings; or
- Additional information has become available on the amount of triclosan that may be leached from textile and plastic articles under normal conditions of use, or from the sucking or mouthing of such (i.e. extraction into saliva).

The Director (Chemicals Notification and Assessment) must be notified within 28 days of the introducer becoming aware of any of the above or other circumstances prescribed under section 64(2) of the Act.

Acronyms and Abbreviations

ACT	Australian Capital Territory
ADG Code	Australian Code for the Transport of Dangerous Goods by Road and Rail
AE	atomic emission
AICS	Australian Inventory of Chemical Substances
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARTG	Australian Register of Therapeutic Goods
AS	activated sludge
ASCC	Australian Safety and Compensation Council
AUC	area under the curve
BCF	bio-concentration factor
BOD	biological oxygen demand
BTEB	basic transcription element binding protein
CAS	Chemical Abstracts Service, OR continuous activated sludge
cfu	colony-forming units
cm^2	square centimeter
cm^3	cubic centimetre
CO_2	carbon dioxide
COD	chemical oxygen demand
d	day
dh^o	Deutsche Härte (German degree of hardness)
DEWHA	Australian Government Department of the Environment, Water, Heritage and the Arts
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
DOM	dissolved organic matter

DPV	differential pulse voltametry
EAR	enoyl-ACP reductase
EASE	Estimation and Assessment of Substance Exposure
EbC0	concentration at which the biomass of 50% of the test population is impacted (*OR median effective concentration in terms of reduction of biomass)*
EC	European Commission
EC50	median effective concentration
EHD	estimated or measured human dose or exposure
EPA	environmental protection agency
EPHC	Environment Protection and Heritage Council
ErC50	concentration at which the rate of growth of 50 percent of the test population is impacted (*OR median effective concentration in terms of reduction of growth rate*
EU	European Union
g	gram
GC	gas chromatography
GC/AE	gas chromatography with atomic emission detection
GC/EC	gas chromatography with electron capture
GC/MS	gas chromatography/mass spectrometry
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GLC	gas liquid chromatography
GLC/EC	gas liquid chromatography with electron capture
h	hour
HPLC	high performance liquid chromatography
HPLC/MS	high performance liquid chromatography/mass spectrometry
HPLC/VD	high performance liquid chromatography/voltametric detection
HSIS	Hazardous Substances Information System
IC50	median inhibition concentration

ip	intraperitoneal
iv	intravenous
kg	kilogram
L	litre
LC	liquid chromatography
LC/MS	lIquid chromatography/mass spectrometry (LC/MS).
LC50	median lethal concentration
LD50	median lethal dose
L(E)C50	LC50 or EC50
LEV	local exhaust ventilation
LOAEL	lowest-observed-adverse-effect level
LOEC	lowest-observed-effect concentration
LSC	liquid scintillation counting
M	Molar
MATC	maximum acceptable toxicant concentration
MBC	minimal bacterial concentration
MIC	minimum inhibitory concentration
µg	micrograms
mg	milligram
mg/cm^2/day	milligrams per square centimetre per day
mg/kg bw	milligrams per kilogram body weight
mg/kg bw/day	milligrams per kilogram bodyweight per day
mg/m^3	milligrams per cubic meter
MIC	minimum inhibitory concentration
min	minute
mL	millilitre
MOE	margin of exposure
MRSA	multi (methicillin) resistant *Staphylococcus aureus*

MRSE	multi (methicillin) resistant *Staphylococcus epidermidis*
MS	mass spectrometry
MSDS	Material Safety Data Sheet
MSSA	multi (methicillin) sensitive *Staphylococcus aureus*
MTCS	methyl-triclosan
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NMR	Nuclear magnetic resonance
NOAEC	no-observed-adverse-effect-concentration
NOAEL	no-observed-adverse-effect-level
NOEC	no-observed-effect concentration
NOHSC	National Occupational Health and Safety Commission
NSW	New South Wales
NT	Northern Territory
OECD	Organisation for Economic Cooperation and Development
PCNA	proliferating nuclear cell antigen
PEC	predicted environmental concentration
pg	picogram
PNEC	predicted-no-effect concentration
POPs	persistent organic pollutants
ppb	parts per billion
PPE	personal protective equipment
ppm	part per million
QLD	Queensland
RF	retention factor

RQ	risk quotient
S	spectrophotometer
+S9	with rat liver microsome preparations
-S9	without rat liver microsome preparations
SIDS	Screening Information Data Set
SPE	solid phase extraction
SSC	Scientific Steering Committee (European Commission)
STP	sewage treatment plant
SUSDP	Standard for Uniform Scheduling of Drugs and Poisons
TCS	triclosan
TGA	Therapeutic Goods Administration
TLC	thin layer chromatography
TF	trickling filter
TR	thyroid hormone receptor
TRV	toxicity reference value
TWA	time-weighted average
UDS	unscheduled DNA synthesis
UN	United Nations
US EPA	United States Environmental Protection Agency
USP	United States Pharmacopoeia
V	volume
VD	voltametric detection
WHO	World Health Organization
w/o	wash-off
wt	weight
WWTP	wastewater treatment plants