Government of Canada / Gouvernement du Canada

RISK MANAGEMENT SCOPE

for

Chlorhexidine and its salts

Environment and Climate Change Canada

Health Canada

August 2017

Canada

Summary of Proposed Risk Management

This document outlines the proposed risk management options for chlorhexidine and its salts, with a focus on specific sources of exposure to the chlorhexidine moiety. In particular, the Government of Canada is considering the implementation of certain risk management instruments (such as, but not limited to, pollution prevention planning notices, guidelines and codes of practice or environmental performance agreements) to prevent or minimize the release of the chlorhexidine moiety to the environment from the industrial use of these substances.

Interested stakeholders are invited to provide information regarding best management practices in place at product formulating facilities using chlorhexidine and its salts and efficiency of treatment methods in removing these substances from wastewater. This information should be provided on or before October 18, 2017 to the contact details identified in section 8 of this document.

Note: The above summary is an abridged list of options proposed to manage chlorhexidine and its salts and of information sought to inform the risk management decision-making process. Refer to section 3 of this document for more complete details in this regard. It should be noted that the proposed risk management options may evolve through consideration of additional information obtained from the public comment period, from other sources, and from the information presented herein.

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1. Context

The *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999) provides the authority for the Minister of the Environment and the Minister of Health (the ministers) to conduct assessments to determine if substances are toxic[1] to the environment and/or harmful to human health[2], and if so to manage the associated risks.

In December 2006, 193 chemical substances were identified as high priorities for assessment due to their hazardous properties and their potential to pose risks to human health and the environment. In February 2007, the ministers began publishing, for industry and stakeholder comments, profiles of batches containing 12 to 19 high-priority substances. New batches were released for comments every three months and information-gathering authority in section 71 of CEPA was used to collect specific information on these substances, where required, as part of the Challenge initiative under the Government of Canada's Chemicals Management Plan (CMP).

A substance, chlorhexidine acetate (also known as chlorhexidine diacetate), Chemical Abstracts Service Registry Number (CAS RN)[3] 56-95-1, was identified as a priority for assessment and included in Batch 12 of the Challenge initiative under the CMP. In July 2013, Health Canada and Environment and Climate Change Canada (ECCC) published a draft Screening Assessment Report (SAR) and Risk Management (RM) Scope for chlorhexidine diacetate (Canada 2013a, 2013b). At the time, chlorhexidine diacetate was proposed to be toxic under section 64 of CEPA. It was also noted that chlorhexidine diacetate is a salt, and dissociates in water to produce the acetate counterion and chlorhexidine. This

[1] Section 64 [of CEPA]: *For the purposes of* [Parts 5 and 6 of CEPA]*, except where the expression "inherently toxic" appears, a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that*

- *(a) have or may have an immediate or long-term harmful effect on the environment or its biological diversity;*
- *(b) constitute or may constitute a danger to the environment on which life depends; or*
- *(c) constitute or may constitute a danger in Canada to human life or health.*

[2] A determination of whether one or more of the criteria of section 64 of CEPA are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and products used by consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations,* which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other Acts.

[3] [CAS RN] Chemical Abstracts Service Registry Number. The Chemical Abstracts Service information is the property of the American Chemical Society, and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the Government of Canada when the information and the reports are required by law or administrative policy, is not permitted without the prior, written permission of the American Chemical Society.

dissociated chlorhexidine moiety has the potential to cause acute harm to aquatic organisms at low concentrations (Canada 2013a).

Subsequent to the publications for chlorhexidine diacetate, significant new information became available regarding other potential sources of exposure to the chlorhexidine moiety. This information included quantities of chlorhexidine and its salts in commerce, presence in products sold in Canada, and industry details related to the formulation of chlorhexidine-based products. As a result, the scope of the chlorhexidine diacetate assessment was expanded to consider potential impacts on the environment and human health with respect to combined exposure from other potential sources of chlorhexidine.

The updated draft screening assessment includes, chlorhexidine (CAS RN 55-56-1), chlorhexidine diacetate (CAS RN 56-95-1), chlorhexidine digluconate (CAS RN 18472-51-0), and chlorhexidine dihydrochloride (CAS RN 3697-42-5) (Canada 2017a). All of these substances are on the *Domestic Substances List* (DSL) (ECCC 2015a), with the exception of chlorhexidine dihydrochloride, which is on the *Revised In Commerce List* (ICL) (Health Canada 2016a) of the *Food and Drugs Act* (F&DA) (Canada 1978).

2. Issue

Health Canada and ECCC conducted a joint scientific assessment relevant to the evaluation of chlorhexidine and its salts in Canada. A notice summarizing the scientific considerations of the draft SAR for chlorhexidine and its salts was published by Health Canada and ECCC in the *Canada Gazette*, Part I, on August 19, 2017 (Canada 2017a, 2017b). For further information on the proposed screening assessment conclusion for chlorhexidine and its salts, refer to the draft SAR, available from: http://www.chemicalsubstanceschimiques.gc.ca/plan/approach-approche/chlorhexidine-eng.php.

2.1 Draft Screening Assessment Report Conclusion

Based on the information available, the draft SAR proposes to conclude that chlorhexidine and its salts meet the criteria under paragraph 64(*a*) of CEPA as they are or may be entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity (Canada 2017a). The proposed assessment conclusion is applicable to chlorhexidine and its salts (but not limited to the salts listed in the report) (Canada 2017b). The chlorhexidine moiety is proposed to meet the persistence criteria, but it does not meet the bioaccumulation criteria, as defined in the *Persistence and Bioaccumulation Regulations* of CEPA (Canada 2000, 2017a).

2.2 Proposed Recommendation under CEPA

When a substance is found to meet one or more of the criteria under section 64 of CEPA, the ministers can (1) take no further action with respect to the substance, (2) recommend the addition of the substance to the Priority Substances List for further assessment, or (3) recommend the addition of the substance to the List of Toxic Substances in Schedule 1 of the Act.

Based on the findings of the draft assessment conducted under CEPA, the ministers propose to recommend adding “chlorhexidine and its salts” to the List of Toxic Substances in Schedule 1 of the Act (Canada 2017b). The ministers will take into consideration comments made by stakeholders during the 60-day public comment period on the draft SAR and RM Scope. If the ministers finalize the recommendation to add “chlorhexidine and its salts” to Schedule 1 of the Act, risk management instrument(s) must be proposed and finalized within a set period of time, as outlined in sections 91 and 92 of CEPA (refer to section 8 of this document for targeted publication timelines applicable to these substances).

3. Proposed Risk Management

3.1 Proposed Environmental Objective

Proposed environmental objectives are quantitative or qualitative statements of what should be achieved to address environmental concerns.

In this case, the proposed environmental objective would be to prevent or minimize the presence of the chlorhexidine moiety in the aquatic environment to the greatest extent practicable. This objective may be quantitatively defined to achieve and maintain the lowest environmental levels possible. Predicted no-effect concentrations (PNECs) may be used as ultimate goals to work towards but interim levels may also be set, for the media of interest (e.g., water, soil or sediment compartments) or for the affected biota (e.g., aquatic organisms).

Measured environmental concentrations in water, soil, sediment and biota for the chlorhexidine substances assessed have not been identified in Canada. ECCC is currently involved with the development of an analytical method starting with the wastewater compartment, considering methods reported in literature. ECCC is also preparing preliminary sampling activities for the summer 2017 to determine the levels of chlorhexidine moiety that may be released to the environment. Analytical results will be considered, when available, to inform risk management decision-making regarding chlorhexidine and its salts, as the case may be and may help establish a baseline for environmental presence. Stakeholders that may have analytical methods or results to share, or who may be interested in participating in the 2017 sampling campaign, are encouraged to contact ECCC

on or before October 18, 2017 (via the contact details identified in section 8 of this document).

3.2 Proposed Risk Management Objective

Proposed risk management objectives set quantitative or qualitative targets to be achieved by the implementation of risk management regulations, instrument(s) and/or tool(s) for given substance(s) to work towards meeting the proposed environmental objective.

In this case, the proposed risk management objective would be to achieve the lowest total concentration or quantity of chlorhexidine in wastewater released from the formulation of chlorhexidine-based products (the activity identified as being of concern in Canada 2017a). This objective may be quantitatively defined to ensure that practices in place are protective of the environment at existing and new facilities that may be manufacturing or repackaging products containing these substances (e.g., using specific quantity or concentration levels of chlorhexidine found in wastewater released as a result of the activity of concern).

3.3 Proposed Risk Management Options

To meet the proposed risk management objective and work towards achieving the proposed environmental objective, risk management is proposed to prevent or minimize the release of chlorhexidine and its salts to the environment from the industrial use of these substances. To do so, the Government of Canada may select from a number of risk management instruments[4], which may be used alone or in combination. These include, for example:

- **Pollution prevention planning notices** (section 56 of CEPA)

  Pollution prevention (P2) planning is a process to examine current operations and develop a plan to eliminate or reduce pollution at the source. By developing a P2 plan facilities are able to identify options according to the environmental protection hierarchy (prevention, reuse/recycle, treatment, control, waste disposal), evaluate these options and implement them within a specified time frame. P2 planning places emphasis on identifying the most cost-effective options, including those where facilities can see a return on investment (ECCC 2015b). In this case, a P2 planning notice could be used to help ensure that practices in place are sufficient to prevent or minimize the release of chlorhexidine and its salts to the environment. Such a notice could be limited to existing facilities that may be of concern or more broadly apply to certain activities (chlorhexidine-based products manufacturing and repackaging) or related industry sectors (noted in section 4.1 of this

[4] More details as to instruments available under CEPA may be found on the CEPA Registry website at: https://www.ec.gc.ca/lcpe-cepa/

document) so as to also capture new facilities. The use of triggers (such as use quantities) and factors to encourage the use of best management practices may also be considered in the development of a P2 planning notice on chlorhexidine and its salts, if ultimately selected.

- **Guidelines and Codes of practice** (section 54 of CEPA)

  Guidance instruments may be developed to give industries and regulators clear direction on how to reduce emissions, effluents, and wastes. ECCC consults with interested parties to develop such tools. As a result, they reflect a shared, national view of environmental measures. Such tools are not enforceable instruments, but may form the basis for enforceable instruments to be made in the future (ECCC 2013). In this case, a code of practice or technical guidelines could be developed and used, alone or in combination with other tools, to help industrial facilities reduce their impact on the environment through non-regulatory means.

- **Environmental performance agreements** (non-statutory instrument)

  An environmental performance agreement (EPA) is an agreement negotiated among parties to achieve specified environmental results. ECCC may negotiate an EPA with a single company, multiple companies or one or more industry associations. Other government agencies (federal, provincial, territorial or municipal) and third parties (non-government organizations) may also be parties to such agreements. EPAs are voluntary instruments, which may have similar objectives as those of other risk management instruments (such as regulations, codes of practice, or P2 planning notices) under CEPA and can be used as a complement to any of them (ECCC 2016). In this case, it may be that an EPA is used with existing facilities that may be of concern to require the use of certain pollution controls, identify opportunities for environmental improvements or set specific performance targets to limit/prevent their release. Alternatively, an EPA could also be used more broadly with the related industry sectors (e.g., via their industry associations) if an EPA is ultimately selected.

Other Considerations

Depending on the results of the 2017 or subsequent sampling activities, regulatory controls may be needed to establish release limits. If this is the case, the use of regulations could be recommended, instead of the options outlined above, to control the release of chlorhexidine and its salts to the environment. However, given the limited number of facilities that may be of concern, the uncertainties with respect to removal during wastewater treatment, and considering socio-economic and technical factors (noted in section 6 of this document), these other instrument may be more appropriate to meet the risk management objective.

Future Activities

The manufacture or import of substances that are not listed on the DSL (ECCC 2015a,c) are subject to the *New Substances Notifications Regulations (Chemicals and Polymers)* (NSNR (Chemicals and Polymers)) (Canada 2005). This may be the case for chlorhexidine substances that may not be in commerce in Canada above notification thresholds (ECCC 2014a). For chlorhexidine substances listed on the DSL, the Government of Canada may also consider the application of the Significant New Activity (SNAc)[5] provisions of CEPA, in order to require them to be notified prior to any new activities being undertaken in respect to these substances, if such new activities are not captured with the proposed risk management instruments that may eventually be developed.

Of note, beyond the update of information on substances on the Domestic Substances List, which is currently underway and which includes chlorhexidine dihydrochloride (Canada 2017), other activities to track changes in exposure or commercial use patterns associated with chlorhexidine substances may be considered in the future.

3.4 Risk Management Information Gaps

No comments were made by stakeholders during the 60-day public comment period on the draft SAR or RM Scope for chlorhexidine diacetate published in 2013 (Canada 2013a, 2013b). Stakeholders are currently invited to provide information, such as outlined below, to inform decision-making regarding chlorhexidine and its salts:

1. Presence of chlorhexidine and its salts in wastewater and in the Canadian environment;
2. Efficiency of treatment methods in removing chlorhexidine and its salts from wastewater;
3. Best management practices in place at facilities manufacturing or repackaging chlorhexidine-based products;
4. Socio-economic and technical impacts and benefits associated with the proposed risk management for these substances; and

[5] A significant new activity can include an activity that is not currently occurring or an existing activity involving a different quantity or occurring in different circumstances that could affect the exposure pattern of the substance. The SNAc provisions trigger an obligation for a person (individual or corporation) to provide, and for the Government to assess, information about a substance when a person proposes to use the substance in a significant new activity. The provisions are used to assess the risks associated with the proposed new activity before the new activity is undertaken. The ministers assess the information provided by the notifier and other information available to them to determine whether the substance, if used in the proposed new activity, could pose a risk to the environment or human health, and if so, whether risk management is required. For more information on SNAc orders and notices, refer to: http://www.ec.gc.ca/lcpe-cepa/default.asp?Lang=En&n=9EFCCB36-1#q1. Similar tools exist for the risk assessment and risk management of substances subject to the NSNR.

5. Changes in use patterns from data collection initiatives (noted in section 4.1 of this document).

Stakeholders are invited to provide this information on or before October 18, 2017 to the contact identified in section 8 of this document.

4. Background

Chlorhexidine and its salts are broad-spectrum antiseptics used for sterilization, cleaning skin and hands, disinfecting wounds, and oral health, and are generally effective against a wide variety of bacteria, viruses and yeasts (Chemicalland21 2010, Cheminfo Services Inc. 2014). Chlorhexidine and its salts are also used as antimicrobial preservative in cosmetics and pharmaceuticals (Block 2001). Products containing chlorhexidine salts are also used as disinfectant products in hospitals, health care facilities, food premises, and farms; a subset of these products is available for consumer use (human and/or veterinary). Chlorhexidine and its salts are used in similar applications worldwide (PCPC 2013, ECHA 2016, European Commission 2016). Refer to the draft SAR for more details as to chlorhexidine-based product types and applications in Canada (Canada 2017a).

4.1 Current Uses and Identified Sectors

Surveys have been conducted under section 71 of CEPA for chlorhexidine (reporting year 2011), chlorhexidine diacetate (reporting years 2005, 2006 and 2011), and chlorhexidine digluconate (reporting year 2011) (Canada 2006, 2009, 2012a). Additional information was also obtained voluntarily (Study Submissions 2010, 2014, 2015a,b), as a result of follow-up on the past RM Scope for chlorhexidine diacetate and on the survey initiatives, or derived from other sources.

Based on this information, chlorhexidine, chlorhexidine diacetate and chlorhexidine digluconate were not manufactured in Canada for the years reported. However, the diacetate, digluconate and dihydrochloride salts were imported into Canada during one or more of these reporting years, and were also identified as being used in products available to consumers in the Canadian marketplace (Cheminfo Services Inc. 2014, Health Canada 2015a, 2016a-d).

Overall, total quantity imported into Canada (in a product or as a pure salt for processing/formulation) is estimated to be less than 50 tonnes (or 50 000 kg) per year, on a chlorhexidine-equivalent basis[6]. Of the total quantity imported into Canada, approximately one third is expected to be used in the manufacturing of chlorhexidine-based products (ECCC 2015d).

[6] Since chlorhexidine is the moiety of concern, total quantity estimates have been expressed in chlorhexidine equivalent values, through application of a molecular weight ratio with the associated salts.

The primary industry sectors relevant to these substances include:

- Pharmaceutical and medicine manufacturing, North American Industry Classification System (NAICS) 3254; and
- Soap, cleaning compound and toilet preparation manufacturing, NAICS 3256.

5. Exposure Sources and Identified Risks

Chlorhexidine and its salts are expected to persist in water, soil and sediment. They have a low potential to bioaccumulate but have the potential to cause acute and chronic adverse effects to aquatic and benthic organisms at low concentrations. The quantity of these substances imported into Canada, along with information on their uses, indicate potential for release into the Canadian environment. Chlorhexidine salts released to the aquatic environment will dissociate to release chlorhexidine, the moiety of concern. Chlorhexidine will partition to negatively-charged, dissolved and suspended solids in the aquatic environment, may settle in bed sediment, or be transported far from source releases. In soil, chlorhexidine may or may not be mobile, but could be transported via soil erosion or runoff (Canada 2017a).

5.1 Environmental Presence

Chlorhexidine and its salts do not naturally occur in the environment. No information on concentrations of chlorhexidine and its salts in wastewater and the environment in Canada have been identified (Canada 2017a, Study Submission 2015b), and very few data from other countries have been obtained (Yamayoshi et al. 1981, Matsushima and Sakurai 1984, Kido et al. 1988, Kodama et al. 1988, SWECO Environment 2011).

5.2 Releases and Exposure of Concern in Canada

The exposure assessment estimated releases for two scenarios: from the industrial formulation of chlorhexidine-based products and the down-the-drain releases from the use of such products in Canada (Canada 2017a).

For the industrial exposure scenario, concentrations released via wastewater treatment systems[7] were estimated (as predicted environmental concentrations

[7] In the assessment, the term “wastewater treatment system” refers to a system that collects domestic, commercial and/or institutional wastewater and possibly industrial wastewater (following discharge to the sewer), typically for treatment and eventual discharge to the environment. Unless otherwise stated, the term wastewater treatment system makes no distinction of ownership or operator type (municipal, provincial, federal, aboriginal, private, partnerships). Systems located at industrial operations and specifically designed to treat industrial effluents are identified by the term “industrial wastewater treatment system”.

or PECs) based on annual quantity of chlorhexidine salts used in Canada at select formulation sites (Canada 2017a).

For the down-the-drain exposure scenario from the use of chlorhexidine-based products, PECs were estimated based on the total mass of chlorhexidine found in products (excluding products used on farms[8]), and assumed as completely released down-the-drain (Canada 2017a).

Risk quotient analyses were performed in the screening assessment by integrating the realistic worst-case estimates of exposure (PECs) with ecological toxicity information (PNECs) to determine whether there is a potential for ecological harm in Canada. Risk quotients were calculated by dividing the PEC by the PNEC for the associated environmental compartment. Table 1 shows resulting risk quotients (RQs) for exposure scenarios developed for the industrial use (including aquatic, sediment and soil from the application of biosolids) and down-the-drain releases from products use. Consequently, it was determined that there is potential for ecological harm in Canada from the release of chlorhexidine and its salts as a result of their industrial use, but not from down-the-drain releases as a result of the use of products containing these substances (Canada 2017a).

Table 1. Summary of risk quotients calculated for different media and exposure scenarios for chlorhexidine (from Canada 2017a)

PEC exposure scenario[b]	PEC range	PNEC	PEC and PNEC units	RQ range
$PEC_{aquatic:\ industrial}$	0.0200 – 2.63	0.21	µg/L	0.1 – 13
$PEC_{sediment}$	0.0134 – 2.88	0.049	mg/kg dw	0.3 – 59
$PEC_{soil\ biosolids}$	0.377 (maximum)	0.93	mg/kg dw	≤0.4
$PEC_{aquatic:\ down\ the\ drain}$	0.126 (95^{th} percentile)	0.21	µg/L	0.6

[a] $PEC_{aquatic\ industrial}$, $PEC_{sediment}$, and $PEC_{soil\ biosolids}$ have been estimated from the scenario for industrial formulation of chlorhexidine-based products.

In Canada, a number of companies that are manufacturing or repackaging chlorhexidine-based products may be contributing to the release of chlorhexidine to the environment. Most known or potential product formulators are located within or in the vicinity of the Toronto and Montreal metropolitan areas but not exclusively (ECCC 2015d).

[8] Releases as a result of veterinary applications were not considered, as total concentrations of chlorhexidine used and released during any given period at a farm are expected to be lower than those considered in the above-noted key exposure scenarios.

Industrial activities of concern are expected to be the result of wastewater generated from equipment, container and facility cleaning. Such activities may also involve the release of off-specification products. From Tekin et al. (2006), the majority of pharmaceutical wastewaters that originate from equipment cleaning typically amounts to about 2 – 3 m^3/day while container cleaning increases this flow rate to approximately 6 – 7 m^3/day. Limited on-site wastewater treatment practices (e.g., pH control) were reported from a few chlorhexidine-based product formulators in Canada (ECCC 2015d, Study Submission 2015b).

6. Risk Management Considerations

6.1 Alternatives

Although chlorhexidine-based products may be favoured for their broad-spectrum efficacy (McDonnell and Russell 1999), several antiseptics, antimicrobials and disinfectants not containing chlorhexidine salts are commercially available in Canada for both hard-surface disinfection and skin antisepsis (Atiyeh et al. 2009). Several preservatives may also be used in cosmetics, natural health products, and non-prescription drugs for product preservation; some with applicable restrictions (Steinberg 2010, Health Canada 2016d). More information on substances assessed as part of the CMP is available on the Chemical Substances website at: http://www.chemicalsubstanceschimiques.gc.ca/.

6.2 Technical Considerations

Guidance on good manufacturing practices has been found in literature for the drugs and cosmetics manufacturing sectors although they focus on product quality assurance and offers little in terms of environmental controls (Health Canada 2009, 2014).

In terms of wastewater treatment efficiencies, the characteristics of the wastewater treatment system and chlorhexidine's affinity for negatively-charged suspended solids will determine the degree to which chlorhexidine is associated with suspended solids or biological matter and removed from wastewater (Canada 2017a). Otherwise, pharmaceuticals and other personal care products[9] are generally resistant to conventional wastewater treatment as they are structurally complex and non-biodegradable under standard wastewater treatment conditions, as may be the case for chlorhexidine (Kodama et al. 1988,

[9] For the purpose of this document, a personal care product is defined as a substance or mixture of substances which is generally recognized by the public for use in daily cleansing or grooming. Depending on how the product is represented for sale and its composition, personal care products may fall into one of three regulatory categories in Canada: cosmetics, drugs or natural health products.

Sugio and Kojima 1992, Study Submission 2010). This may create the need for pre-treatment or more advanced removal techniques (e.g., activated carbon filtration, advanced oxidation pre-treatments, reverse osmosis, nanofiltration, or membrane bioreactors) (Boxall et al. 2003, Clara et al. 2005, Dolar et al. 2012, Radjenovic et al. 2007, Tekin et al. 2006). But, it does not prevent the use of other best management practices in lieu of or in addition to wastewater treatment (such as, but not limited to, recycling and re-use of water used for equipment, container and facility cleaning, where possible).

6.3 Socio-economic Context

Socio-economic factors have been considered in the selection process for the instrument respecting preventive or control actions, and in the development of the risk management objective. Socio-economic factors as identified in the *Cabinet Directive on Regulatory Management* (TBS 2012a), Red Tape Reduction Action Plan (TBS 2012b) and the *Red Tape Reduction Act* (Canada 2015a) will be considered in the development of the instrument.

Most establishments involved in pharmaceutical and medicine manufacturing (NAICS 3254) in Canada are either micro (less than 5 employees) or small and medium enterprises (5 to 499 employees) (SMEs). Pharmaceutical sales in Canada have a 2.5% global market-share, making Canada the 9th largest world market. Total pharmaceutical sales in Canada were $22 billion in 2013, with 89% sold to retail drug stores and 11% sold to hospitals. As of about mid-2014, the pharmaceutical manufacturing portion of the sector was valued at $7.7 billion and employed 26 300 people, although growth and employment rates have been declining. More than half of Canada's pharmaceutical production is exported and a significant portion of the Canadian market is supplied by foreign imports (ISEDC 2015, 2016a).

The soap, cleaning compound and toilet preparation manufacturing industry (NAICS 3256) is also predominantly comprised of micro or SMEs. For this sector, total number of production employees was 6 386 and manufacturing revenues were $3.0 billion in 2012, although recent trends show this may be increasing (ISEDC 2016b).

7. Overview of Existing Risk Management

7.1 Related Canadian Risk Management Context

There are no existing Canadian risk management measures identified that are specific to controlling the releases of chlorhexidine and its salts to the environment.

A number of instruments exist under the *Food and Drugs Act* (F&DA), administered by Health Canada, to limit the presence of chlorhexidine and its salts found in prescription and non-prescription drugs, natural health products and cosmetics (Health Canada 2008, 2013, 2015b, 2016c, 2016d). Higher levels may be permitted but companies are required to submit safety and efficacy data to Health Canada for evaluation. Canadian drug manufacturers also have regulatory responsibilities and obligations when it comes to conducting licensable activities in compliance with regulations under the F&DA to meet safety, efficacy, and quality requirements (Health Canada 2016e). None of these requirements impose environmental conditions.

Furthermore, while not specific to releases of chlorhexidine and its salts, the management of wastewater systems, including biosolids, is subject to various federal, provincial, territorial and municipal legislations in Canada. At the federal level, ECCC administers the *Wastewater Systems Effluent Regulations* (WSER) under the *Fisheries Act* (Canada 1985b; Canada 2012b; ECCC 2012). The WSER require wastewater systems to achieve and maintain at least a level of secondary wastewater treatment. For wastewater systems discharging untreated and undertreated wastewater, timelines to upgrade these systems are established within the regulatory framework. Chlorhexidine and its salts are not explicitly regulated in the WSER, and the efficiency in removing these substances from wastewater is not known at this time.

Of note, the transportation of chlorhexidine and its salts are subject to the *Transportation of Dangerous Goods Act* and regulations, administered by Transport Canada (Canada 1992, 2011) and, if intended to be disposed of or recycled, to the *Export and Import of Hazardous Waste and Hazardous Recyclable Material Regulations* (Canada 2005) and *Interprovincial Movement of Hazardous Waste Regulations*, administered by ECCC (Canada 2002b).

7.2 Pertinent International Risk Management Context

Although similar health controls also exist in other jurisdictions (EU 2008, 2009, ECHA 2014, European Commission 2014, US FDA 2016), no existing international risk management measures were identified for controlling the releases of chlorhexidine or its salts to the environment.

Chlorhexidine is included on the 2007 Organisation for Economic Co-operation and Development's list of High Production Volume chemicals (OECD 2009), indicating that it is produced or imported at levels greater than 1000 tonnes per year in at least one member country or region. The United States Environmental Protection Agency completed a Reregistration Eligibility Decision for chlorhexidine diacetate (as a pesticide active ingredient) in 1996 (US EPA 1996) and the substance, along with chlorhexidine digluconate, is currently under a registration review (US EPA 2011). Chlorhexidine and its digluconate salt have since been registered as part of the Registration, Evaluation, Authorisation and

Restriction of Chemicals program in Europe. In particular, chlorhexidine (EC 200-238-7) has been registered for intermediate use only, and the digluconate salt (EC 242-354-0) has been registered for the manufacturing and/or importation in the European Economic Area in the 10 – 100 tonnes per year range (ECHA 2016).

8. Next Steps

Stakeholders are invited to submit comments on the content of this RM Scope or other information (such as outlined in section 3.4 of this document) that would help to inform decision-making for these substances. Please submit additional information and comments on or prior to October 18, 2017. If needed, the RM Approach, which will outline and seek input on the proposed risk management instrument(s) moving forward, will be published at the same time as the final SAR. At that time, there will be a further opportunity for public comment on the RM Approach only. Comments and information submissions on the RM Scope should be submitted to the address provided below:

Environment and Climate Change Canada
Chemicals Management Division
Gatineau (Quebec) K1A 0H3
Tel: 1-800-567-1999 | 819-938-3232
Fax: 819-938-3231
E-mail: eccc.substances.eccc@canada.ca

Companies that have a business interest in chlorhexidine and its salts are encouraged to identify themselves as stakeholders. Stakeholders will be informed of future decisions regarding chlorhexidine and its salts and may be contacted for further information.

Actions	Date
Electronic consultation on the draft SAR and RM Scope for chlorhexidine and its salts	August 19 to October 18, 2017
Submission of public comments and additional information on chlorhexidine and its salts	On or before October 18, 2017
Publication of responses to comments on the draft SAR and RM Scope for chlorhexidine and its salts	No later than the time of publication of the final SAR
Publication of the final SAR and, if required, the RM Approach for chlorhexidine and its salts	August 2018 (tentative)
Publication of responses to public comments on the RM Approach for chlorhexidine and its salts, if applicable	No later than the time of publication of the proposed instrument
If required, consultation and publication of the proposed instrument(s) in accordance with section 91 of CEPA	Within 24-month from the publication of the final SAR and RM Approach

Publication of the final instrument(s), if required, in accordance with section 92 of CEPA	Within 18-month from the publication of the proposed instrument

9. References

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