Cleaning and disinfection in the poultry, eggs, leafy greens and sprouts supply chains

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Summary

Cleaning and disinfection are used in several steps of the food supply chain to prevent cross-contamination and microbial contamination of the end product. However, the use of cleaning and disinfection agents may result in chemical residues in food products. Therefore, the aim of this research was to gain insight into the active ingredients used as cleaning agents and disinfectants, their efficacy and whether potential residues may result in human health risks. During phase I of this research insights were gained on the active ingredients used in cleaning agents and disinfectants applied in poultry, eggs, leafy vegetables, and sprouts supply chains as example food chains, making use of a literature study, monitoring data, questionnaires and interviews. After this first phase, the second phase of this study focused on the poultry supply chain. An expert study, using questionnaires and interviews, was held in order to get more information on the use and the most important active ingredients for human health risks in cleaning agents. Furthermore, with a literature study, the efficacy of active ingredients (log reduction of pathogens), the possible by-products, and the toxicity of active ingredients was established for disinfectant.

Phase I: Legislation

Only chemicals that are registered under Registration, Evaluation, Authorization and restriction of Chemicals (REACH) can be used in cleaning and disinfection products. The regulation of disinfectants within the European Union (EU) is more extensive compared to cleaning agents, as additional safety assessments are explicitly needed for the intended use of the disinfectants(Regulation (EU) No 528/2012 – Biocidal Products Regulation (BPR)). First, European Chemicals Agency (ECHA) performs a safety assessment on the level of solely the active ingredients. Secondly, another safety assessment has to be performed on the complete biocidal product under the responsibility of the Member States. In the Netherlands, the Board for the Authorisation of Plant Protection Products and Biocides (College voor de toelating van gewasbeschermingsmiddelen en biociden - Ctgb) is responsible for the authorisation of disinfectants. The Ctgb evaluates whether the intended use of the product is safe for humans, animals and the environment.

Phase I: Cleaning and disinfection in poultry, egg, leafy vegetables and sprouts chains

A literature study, questionnaires and interviews, as well as the Ctgb database were used to establish a long-list of cleaning agents consisting of 37 active ingredients and of disinfection agents consisting of 42 active ingredients possible used for cleaning and disinfection in the Netherlands in poultry, egg, leafy vegetables and sprouts chains. Although a prioritisation of active ingredients in cleaning agents on risk of possible residues in food products was not possible, a long-list of disinfection agents was prioritised into a so-called intermediate list of 18 active ingredients. Disinfectants that were authorised by Ctgb but for which human health risks could not be excluded were included on the intermediate list. This intermediate list consists of: eight chlorine-containing compounds, two quaternary ammonium compounds, one acid, iodine, ozone and five other compounds.

During the interviews and questionnaires, information on actual use of cleaning and disinfection agents was gathered. Proper use of products, rinsing, availability of effective products, cleaning and disinfection by external companies were important topics that were discussed. This information was used to indicate possible risks on residues in food products of active ingredients.

Phase II: Cleaning in the poultry chain

The second phase of this research further explored cleaning and disinfection agents used in the poultry chain. Cleaning is an important step before disinfection because, during this step, most dirt will be removed, which makes the disinfection afterwards more efficient and effective. There are many cleaning and disinfection products available. Experts confirmed the long-list of active ingredients used for cleaning in the poultry chain. Sodium hydroxide was identified as the most frequently used cleaning agent in the poultry chain. At the farm level, the products that are used depend on farmers own preferences and the suppliers of the products. Compared to disinfection, it is less likely that

rinsing after cleaning will be skipped, because of the visual need to remove the product or foam. Around half of the cleaning of the poultry farms is performed by farmers and half is performed by external cleaning companies.

Phase II: Disinfection in the poultry chain
Thirteen active ingredients were concluded to be relevant in the poultry supply chain (intermediate list). These included seven chlorine-containing compounds, iodine, two quaternary ammonium compounds and three other substances. For each of these ingredients, the efficacy was evaluated. However, the efficacy of these active ingredients is difficult to compare since it depends on many factors, and their interactions, such as concentration, temperature, contact time, soil type, type of equipment, water properties, pH, and the microbial population and attachment to surfaces.

Furthermore, possible production of by-products and toxicological characteristics were evaluated for the thirteen active ingredients in disinfectants. By-products that may be of a concern to human health, such as chlorite, chlorate, chlorine dioxide, and semicarbazide, can be formed depending on the type of chlorine-containing product used. Dutch monitoring data (2017 and 2018) showed residues of chlorate in vegetables; however, information on residues of these by-products in food products (including poultry) is limited. Iodine can be used for disinfection, but it can also enter the food chain via other sources. The origin of iodine in food is difficult to trace back. Therefore, monitoring iodine contamination because of disinfection is challenging. Monitoring data showed that quaternary ammonium compounds residues (benzalkonium chloride (BAC) and didecyldimethylammonium chloride (DDAC)) are sometimes detected in milk and milk products above the EU Maximum Residue Limit (MRL). The European Food Safety Authority (EFSA) indicated that there is a large uncertainty in the risk assessment of BAC and DDAC because of limited available data. Formaldehyde is a substance which is under discussion for use as a disinfectant, because of its reclassification as carcinogen and mutagen. For the other substances, no safety concerns are expected for the general consumer in case of proper use of the products. Exposure through food for many substances is not expected. However, for some substances, residues in food can occur but are likely to be low, as stated by Ctgb.

Conclusion
Overall, this study showed that there are many cleaning and disinfection products available, with a range of active ingredients. Cleaning agents are intended to remove dirt, and a rinsing-step is generally applied after its application. Therefore, residues are not expected to come into contact with food, and no safety issues are expected in case of proper use of the products. Disinfectants have to be authorised by Ctgb and as such, are evaluated for their safety. Proper use of disinfectants will not lead to human health problems. However, the expert study did indicate that incorrect cleaning and disinfection occurs due to a lack of knowledge or time constraints. Furthermore, unauthorised products could be used, or products could be used for applications for which they are not authorized. These activities may lead to residues of disinfection agents in food products.

1 Introduction

Cleaning and disinfection are used in several steps of the food supply chain in order to prevent food safety problems and to control animal health and welfare.

The aim of the use of cleaning and disinfection agents is to safeguard product quality, enhance the shelf-life, and secure food safety. In primary production, cleaning and disinfection includes that of stables, but also of hands or boots from employees. In secondary production such products are used for, for example, cleaning of lines in slaughterhouses or vegetable cutters. Also at retail, products are used for cleaning and disinfection of surfaces and for personal hygiene. Hygiene codes are available for various food sectors that indicate which hygiene measures should be used where and when in the supply chain. Hygiene codes also give guidance on cleaning and disinfection.

As a result of the use of cleaning agents and disinfectants, residues of these products may be present in food products. For example, animals could be exposed to cleaning agents and disinfectants via materials in the stables, transport crates and at the later stages, the meat could come into contact via cleaning and disinfection during slaughtering and further processing.

The extent to which consumers are exposed to residues of cleaning agents and disinfectants (via food consumption) is largely unknown. Scientific literature does not provide much information about this. Furthermore, whether there are subsequent food safety risks for consumers is also unknown. Therefore, the aim of this research was to gain insight into the active ingredients used as cleaning agents and disinfectants, their efficacy and whether potential residues may result in human health risks. The following research questions were put forward to contribute to this aim:

1. Which active ingredients of cleaning agents and disinfectants are authorised and used in the Netherlands and in which steps of the supply chain?
2. What is the efficacy of the most relevant active ingredients in inactivating human pathogens?
3. Can residues of these active ingredients lead to human health risks via food consumption?

The research was performed in two phases. In phase I of this research, the poultry and egg supply chains was chosen as two relevant but significantly different animal supply chains, while the leafy greens and sprouts were chosen as two relevant but significantly different vegetable supply chains. Authorisation of cleaning and disinfection was investigated. Furthermore, a list of active ingredients used in cleaning and disinfection products and possible residues and related human health risks for these supply chains were obtained. In phase II, the focus was only on the poultry supply chain. The efficacy, chemical safety and possible by-products of the active ingredients in disinfectants were investigated. Furthermore, the use of cleaning agents in the poultry supply chain was studied in more detail.

2 Materials and methods

2.1 Approach

The following approaches were used in the two phases of our research:

Phase I (applied to poultry, egg, leafy vegetables and sprouts supply chains):
1. Hygiene codes, guidelines and legislation applicable for using cleaning agents and disinfectants in the food supply chain were identified by means of literature search.
2. Lists of active ingredients possible used in the Netherlands were established the so-called long-list). This information was obtained through a literature research (see 2.3), the Board for the Authorisation of Plant Protection Products and Biocides (College voor de toelating van gewasbeschermingsmiddelen en biociden, Ctgb) website, and expert opinions (interviews and questionnaires (see 2.5.1)).
3. The long-list of active ingredients in disinfectants prioritised to an intermediate list for possible human health risks related to the active ingredients. This was done based on a discussion of the long list with NVWA-BuRO and based on Ctgb authorisations.
4. Different issues and concerns about the use of cleaning and disinfections agents which could lead to possible residues of cleaning and disinfection agents in food products were identified using expert interviews.
5. Available monitoring data of disinfection agents were analysed and used as confirmation of the intermediate list as defined in step 3 of phase I.

Phase II (applied to the poultry supply chain):
1. An expert study, using questionnaires and interviews, was held in order to get more information on the use and the most important active ingredients for human health risks in cleaning agents in the poultry supply chain.
2. The efficacy of active ingredients (log reduction of pathogens), the possible by-products, and the toxicity of active ingredients was established for the intermediate list of disinfectants as established in step 3 of phase I.

In general, the terms cleaning and disinfection are used throughout the report where possible. In Annex 1 a list of terms can be found, which includes many terms used in literature to describe or relate to cleaning and disinfection agents.

2.2 Demarcation

Exposure of employees to the use of cleaning agents and disinfectants (working conditions) was not included in this research. This study focused on the Dutch food supply chains with production and processing within the Netherlands. Import and export was not incorporated and as a result, disinfectants used for decontamination were not evaluated further since this is not allowed in the Netherlands. Eurostat data from the last 5 years (2015-2019) showed that 83% of the poultry products that were imported to the Netherlands were from European countries.

The study did not identify all cleaning agents and disinfectants used in the food industry, but focused in phase I of this research on poultry (meat and eggs), leafy greens, and sprouts. These were chosen as relevant examples for animal and vegetable production systems. In order to focus the scope of the research, the emphasis was on active chemical substances used in cleaning agents and disinfectants (for example essential oils were excluded). Other substances used, such as preservatives and auxiliary agents, and microbial cleaners were not included in the study. However, when we came across information on this during the study, the information was included in the report. In the second phase of this research, the focus was specifically on the poultry chain.

2.3 Literature study

A scientific literature search was performed to identify active ingredients from cleaning and disinfection agents used in the poultry (meat and eggs), leafy greens, and sprout chains. A general search for each of the supply chains, including filters like language (English) and years (2008-2018) was performed. This search was performed in two scientific databases: Scopus and Web of Science (WoS).

Since multiple food chains were included in the study, it was relevant to use search terms for the food chain in question (#1). These results were then combined with search terms for cleaning agents and disinfectants (#2). When filter #1 and #2, along with the language and date filters, obtained too many hits (>500), the search was refined by 'Document type(s)' to reviews and book chapters. For the poultry chain, the filter (#1) was based only on title given the high number of records (>500). For the sprout chain, all the document types were included due to the limited hits obtained. All references were downloaded and extracted to Endnote by including complete citation information (like keywords and abstracts) when available. Below are the search terms applied for each chain.

Poultry supply chain (meat and eggs)
#1 supply chain: (poultr* OR broiler* OR chick* OR egg* OR hatch* OR "laying hen*") in Title
AND
#2 cleaning agents and disinfectants: ("cleaning agent*" OR disinfect* OR sanit* OR decontaminat* OR biocide* OR hygien* OR "chemical residu*") in TI-ABS-KEY (Scopus) or Topic (WOS)

Leafy greens
#1 supply chain: ("leafy green*" OR "leafy vegetable*" OR " green leave*" OR " fresh produce" OR arugula* OR lettuce* OR kale* OR spinach* OR "mustard green*" OR "collard green*" OR chard* OR cabbage* OR rapini* OR " turnip green*") in TI-ABS-KEY (Scopus) or Topic (WOS)
AND
#2 cleaning agents and disinfectants: ("cleaning agent*" OR disinfect* OR sanit* OR decontaminat* OR biocide* OR hygien* OR " chemical residu*") in TI-ABS-KEY (Scopus) or Topic (WOS)

Sprouts
#1 supply chain: (sprout* OR "mung bean*" OR cress* OR "fenugreek seed*" OR alfalfa*) in TITLE-ABS-KEY (Scopus) or Topic (WOS)
#2 cleaning agents and disinfectants: ("cleaning agent*" OR disinfect* OR sanit* OR decontaminat* OR biocide* OR hygien* OR "chemical residu*") in TI-ABS-KEY (Scopus) or Topic (WOS)

First of all, duplicate references were removed. Then, the resulting lists of references were screened based on title for relevance. References that were not appropriate to the chain (and products) identified, based on the title, were discarded. In addition, references that were not related to cleaning agents and disinfectants were discarded. Table A2.1 (Annex 2) provides examples of the non-relevant topics based on title. Relevant titles were then screened based on the article (i.e., abstract, conclusions). The aim was to find cleaning agents and disinfectants that were chemically based, i.e. physical and biological treatments were not the focus. Table A2.2 (Annex 2) provides examples of the non-relevant topics based on abstract. The resulting list of references was further screened to identify relevant information about the aim of the study, chemical methods studied, and the main conclusions of the research.

Additional searches were performed with Scopus and Google to search for other relevant reports and guidelines, which were used by compiling general information on cleaning and disinfection (paragraph 3.1), and to compile the information on disinfection outside Europe as described in paragraph 3.9. The literature research on efficacy, by-products and toxicological profile of active ingredients of disinfectants on the intermediate list for poultry (paragraph 3.8) is described in paragraph 2.6.

2.4 Monitoring data

Monitoring data on the concentrations of biocides and residues thereof measured in several types of food groups (i.e., baby and infant foods, vegetables, dairy) were provided by the NVWA. The data supplied were from 2017 and 2018. Data related to the poultry supply chain (meat and eggs), as well as those related to sprouts, were not available. Data related to vegetables such as lettuce, endive, and spinach were available. These results will be elaborated upon in more detail.

2.5 Expert elicitation (Phase I and II)

2.5.1 Phase I: Identification of active ingredients

In order to gain insight into the active ingredients used for cleaning and disinfection in the poultry (meat and eggs) and horticulture supply chain in practice, a predefined questionnaire was established (Annex 3). Specific questionnaires were drafted for horticulture primary production, horticulture processing, poultry farms, poultry processing, retail, and a general questionnaire was established for producers of cleaning and disinfection agents. Organisations and companies were identified that produce cleaning agents and disinfectants for these supply chains or companies providing cleaning and disinfection services using popular journals such as VMT, Pluimveeweb, Pluimveehouderij, Boerderij, Nieuwe oogst, Groenten & fruit, and Vleesmagazine. Furthermore, branch organisations and companies producing poultry meat, eggs, leafy vegetables or sprouts were identified. These organisations were sent the appropriate questionnaire. For example, the Dutch branch organisation for egg producers and egg traders was sent part 1 of the poultry questionnaire. Organisations and companies were contacted via email and sent a specified questionnaire depending on their expertise or were interviewed based on the questionnaire. In total, 76 questionnaires were sent and 16 people were invited for an interview using the predefined questionnaire. People invited for the interviews were experts from branch organisations, large cleaning and disinfection companies, NVWA and Ctgb.

2.5.2 Phase II: Cleaning in the poultry chain

In order to gain more insight on cleaning agents, which are used in the poultry chain, questionnaires were disseminated and interviews were conducted in the second phase of this research. In total, 72 persons were contacted by e-mail for a short questionnaire, of which 47 persons were involved in poultry stables, 20 in poultry processing and 5 in both. A questionnaire was made for each subgroup using the program Qualtrics. A direct link to the questionnaire was included in the message of the e-mail. The questionnaires can be found in the Annex 4.

Seven persons were contacted to be interviewed about the use of cleaning agent in the poultry chain. These persons were connected the poultry chain in general, one person specifically to the primary production and one to secondary production. The outline of questions used during the interviews can be found in Annex 5. Additionally, RIVM was invited for an interview in relation to their report on a database of the use of biocides in various economic sectors, this information is added to chapter 3.3, because it is about disinfection agents.

2.6 Efficacy, by-products and toxicological profile of active ingredients on intermediate list of disinfectants used in the poultry supply chain (Phase II)

In order to gain insight into the active ingredients on the intermediate list of disinfectants, we performed a short review. The result of which provides information on the active ingredients' (i) efficacy in terms of their potential log reduction of pathogens, (ii) possible formation of by-products or residues, and (iii) the toxicological profile concerning human health effects.

First, we evaluated the following websites in August 2019 to retrieve articles to support the three aforementioned points:

- European Chemicals Agency (ECHA): https://echa.europa.eu
- Federal Institute for Risk Assessment (BfR): https://www.bfr.bund.de/en/home.html
- European Food Safety Authority (EFSA): http://www.efsa.europa.eu/
- EFSA OpenFoodTox database: http://www.efsa.europa.eu/en/microstrategy/openfoodtox

The resulting articles were extracted and reviewed. For instance, from ECHA, the scientific brief profiles were first consulted. Additional information for active ingredients that have a Biocidal Product Committee (BRC) opinion was provided for:

- Sodium hypochlorite for the following product types (PT, as specified in the Biocidal Product Regulation (EU) No 528/2012): PT 1 (human hygiene), PT 3 (veterinary hygiene), and PT 4 (food and feed area)
- Chlorocresol for PT 1 and PT 3
- Formaldehyde for PT 3
- Glutaral for PT 3 and PT 4

When no results were retrieved from EFSA, a separate advanced google search was performed via https://www.google.com/advanced_search to access articles that may have already been archived on the EFSA website, meaning they will not have shown up in the initial search. An example for chlorine dioxide is provided below:

1. Search for EFSA via advanced google search: https://www.google.com/advanced_search
2. Find pages with "this exact word or phrase": "chlorine dioxide"
3. Then narrow your results by "site or domain": https://www.efsa.europa.eu
4. Output: 200 results, of which the first 40 were reviewed. (With this search, Google has narrowed down the results: "*In order to show you the most relevant results, we have omitted some entries very similar to the 40 already displayed.*")
5. Results reviewed: 3 hits

Second, we screened the Ctgb authorisation database in October 2019 to provide further insight into the use of active ingredients on the Dutch market. An example of the search performed is provided below:

1. Access the English version of the Ctgb authorisation database: https://pesticidesdatabase.ctgb.nl/en/authorisations
2. Enter 'active substance' name (including synonyms when required)
3. Filter based on 'authorised' status
4. Filter with the advanced search for the product types: PT 1 – Human hygiene biocidal products; PT 3 – Veterinary hygiene biocidal products; and PT 4 – Food and feed area disinfectants
5. Sort resulting hits based on 'newest decision first'

An example product for each active ingredient is provided in section 3.8 unless stated otherwise.

3 Results

3.1 General background on cleaning and disinfection

Food hygiene implies the necessary controls and measures to ensure the safe production of food from production to consumption (Codex Alimentarius Commission, 2003). Cleaning and disinfection are important parts of hygiene in food supply chains. Procedures on how this should be done need to be well documented to motivate compliance. The Codex has a Code of Practice and General Principles of Food Hygiene (CAC/RCP 1-1969) in which general principles about food hygiene are outlined from primary production through to the consumer. This document recommends using a Hazard Analysis and Critical Control Points (HACCP)-based approach. Moreover, in the code of practice, cleaning and disinfection are defined. Cleaning is defined as "the removal of soil, food residue, dirt, grease or other objectionable matter". Disinfection is defined as "the reduction, by means of chemical agents and/or physical methods, of the number of micro-organisms in the environment, to a level that does not compromise food safety or suitability" (Codex Alimentarius Commission, 2003). Next to cleaning and disinfection, sterilisation is a process that completely destroys all microorganisms, including spores.

Cleaning should take place before disinfection to remove soil and dust. The order for cleaning and disinfection procedures for food product contact surfaces can be generalised: 1. Rinse, 2. Clean, 3. Rinse, and 4. Disinfect (Schmidt, 2015), in most cases followed by another rinsing step depending on the chemical agent and the application.

In general, there are three cleaning and disinfection methods: thermal, physical, and chemical methods. Thermal methods can include treatments like steam, hot air, and hot water. These are generally energy-intensive, and their efficiency depends on other variables like humidity, temperature, and length of treatment (contact time) (Fraser, 2012; Marriott, Schilling, & Gravani, 2018b). For example, in food establishments, the use of hot water is a common method, e.g., for immersion of small components like knives and utensils (Fraser, 2012). An example of a physical method is ultraviolet (UV) light or high-energy cathode or gamma rays that can be used to destroy micro-organisms. The advantage is that it is pH and temperature-independent and produces no off-tastes or odour, e.g. in treated water. Besides these, there are also other physical treatments like high hydrostatic pressure (HPP) and vacuum/steam-vacuum, which are applied to food products, causing (pathogenic) microorganisms to be inactivated (Marriott et al., 2018b). A third method is a chemical method, in which chemical agents are used to reduce microbial loads. The latter chemical method used for cleaning and disinfection is the focus of this report.

There are several ways in which pathogenic and spoilage microorganisms can be destroyed using chemical agents. Furthermore, there are also a lot of different terms used to describe cleaning or disinfection agents or ingredients. In this report, we have chosen to use the terms cleaning and disinfection, following the Codex definitions as described above. In the term list (Annex 1) also other terms and their definition can be found. In the legal sections (3.2), we have used the terms as used in the legislation. In this report, decontamination is a term used for disinfection of food products or seeds, which is a process that is not allowed in Europe, and therefore out of the scope of this research (some additional information can be found in 3.9).

3.1.1 Cleaning

Cleaning is imperative in food hygiene for each stage of the (food) chain. It helps to remove soil, dust and food residues, e.g. fats and proteins, from tools, equipment, walls, floors and surfaces that are in direct or indirect contact with food. Generally, cleaning serves to remove microorganisms present on surfaces by about 90% (Heinz & Hautzinger, 2007). This, in turn, helps to remove the potential for bacterial growth. However, microorganisms may stick to each other and remain firmly attached to surfaces, in layers of organic materials called biofilms. They may not be removed solely by cleaning, meaning they can persist and multiply; hence, they usually require cleaners and disinfectants with strong oxidizing properties (Heinz & Hautzinger, 2007; Schmidt, 2015).

In general, it is important to define the type and frequency of cleaning, so that the purpose thereof is identified for each step in the (food) chain. Thereby, the procedure by which cleaning is performed can be evaluated, monitored, and recorded for compliance purposes by, e.g., auditors or quality managers. Equipment cleaning can be categorised based on mechanical cleaning, cleaning in place (CIP), cleaning out of place (COP), and manual cleaning. These types of cleaning relate to the need for equipment disassembly, ranging from none to partial to complete disassembly (Schmidt, 2015).

Different types of cleaning agents can be used depending, e.g., on the type of food soil to be removed. Food soils can be defined as an unwanted matter on food contact surfaces or can be recognised as "matter out of place" (Marriott, Schilling, & Gravani, 2018a; Schmidt, 2015). The solubility of soils can relate to how easily it can be removed during cleaning. Soils can be classified as follows:

- Soluble in water (sugars, most salts, some starches)
- Soluble in acid (mineral deposits)
- Soluble in alkali (protein, fat emulsions)

Water-soluble soils are easier to remove than fats and proteins, which are water-insoluble. Proteins that have been, e.g., heat-denatured, can be even more difficult than fats to remove (Schmidt, 2015). Table 1 provides an overview of soil type, its solubility, and recommended cleaning agent (modified from Holah, Lelieveld, Holah, and Napper (2014); Marriott et al. (2018a)).

Table 1 *Solubility characteristics and recommended cleaning agents of various soil types*

Type of soil	Solubility	Recommended cleaning agent
Sugars, organic acids, salts	water soluble	mild alkali
High protein foods (e.g., meat, poultry, fish, eggs)	water insoluble (water soluble when denatured) alkali soluble	alkali
Starchy foods (e.g., potatoes)	partly water soluble alkali soluble	mild alkali
Fatty foods (e.g., butter, oil, meat fats)	water insoluble alkali soluble	mild-strong alkali
Minerals (e.g., milk stone, protein scale, beer stone)	water insoluble alkali soluble acid soluble	acid

The efficacy of each cleaning agent is associated with the solubility of the type of soil. For example, acidic cleaning is effective in removing inorganic deposits (e.g., hard water deposits, alkali deposits - from films left after using a cleaner); an alkaline cleaner for non-petroleum organic soils (e.g., food residues, vegetable oils), and a solvent-type cleaner for petroleum oils (e.g., lubrication grease) (Marriott et al., 2018a). However, no single cleaning agent can facilitate all the needs during a cleaning regime, so it is made up of a blend of components: water, surfactants, inorganic alkalis, inorganic and organic acid, and sequestrants (Holah et al., 2014).

3.1.1.1 Alkaline cleaning agents

These cleaning agents contain strong bases (pH >7). Alkaline cleaners can range from mild alkaline cleaners to heavy-duty alkaline cleaners to strongly alkaline cleaners. They can dissolve fats, oils, and protein-based substances (Table 1). Mild alkaline cleaners are used, e.g., for hand cleaning or in lightly soiled areas. For example, in the meat industry, they can be used as general-purpose cleaners for washing equipment (made of rubber or plastic), walls, and floors (Allen, Wang, Dikeman, & Devine, 2014). Examples of mild alkaline cleaners include sodium bicarbonate, sodium sesqui-carbonate, and tetrasodium pyrophosphate (Marriott et al., 2018a). Heavy-duty alkaline cleaners have a moderate dissolving capacity and are generally slightly or non-corrosive. Examples of active ingredients included in such cleaners are sodium metasilicate, sodium hexametaphosphate, sodium pyrophosphate, sodium carbonate, and trisodium phosphate (Marriott et al., 2018a). Strongly alkaline cleaners have a strong dissolving capacity and are very corrosive; hence, they can burn or scar skin and with prolonged contact can damage tissue. Examples include sodium hydroxide (caustic soda) or caustic potash (potassium hydroxide) and silicates with high N_2O:SiO_2 ratios (Marriott et al., 2018a; Schmidt, 2015). They can be used in CIP systems or machines for washing bottles (Schmidt, 2015). In addition, alkaline cleaners can also be chlorinated, e.g., hypochlorite is added to peptize proteins; these are used for CIP (Marriott et al., 2018a).

3.1.1.2 Acid cleaning agents

These cleaning agents have a pH <7 in diluted water and are used to remove inorganic deposits. They are not used as frequently as alkalis in food operations and are used more for periodic cleaning because of their corrosive action (Holah et al., 2014). Active ingredients include mineral acids and sequestrants. Surfactants (compounds that lower the surface tension) are corrosion inhibitors that can be added to the acid. Mild acidic cleaners are mildly corrosive and may cause allergic reactions. Examples include levulinic, hydroxyacetic, acetic, and gluconic acids (Marriott et al., 2018a). Strongly acidic cleaners are corrosive to concrete, fabrics, and most metals. They are used during cleaning to remove caked-on surface matter and mineral scale. Examples of common strongly acid agents include hydrochloric, hydrofluoric, sulfamic, sulfuric, and phosphoric acids (Marriott et al., 2018a; Schmidt, 2015).

3.1.1.3 Solvent cleaners

These cleaners (also called degreasers) are used for removal of petroleum-based soils (Fraser, 2012). They are ether -or alcohol- type cleaners capable of dissolving, e.g. lubricant oils and greases. These cleaners break down or melt compounds (Marriott et al., 2018b).

3.1.2 Disinfection

Compounds used during disinfection should ideally (Marriott et al., 2018b; Schmidt, 2015):

- have a broad-spectrum activity or wide range of scope;
- tolerate (or resist) to environmental conditions: e.g. the presence of organic matter or residues of cleaning agents, and varying water hardness;
- be low in toxicity or non-toxic, have non-irritating properties, and be non-corrosive;
- be stable in both concentrated and applied dilutions;
- have an acceptable odour or no odour;
- be fast-acting;
- be easy to use and readily available; and
- be cost-effective.

No one (chemical) agent meets all the criteria mentioned above, meaning the advantages and disadvantages for each needs to be elucidated on a case-by-case basis. In general, the concentration, temperature, and contact time (exposure) are three factors that should be considered when evaluating the efficacy (Fraser, 2012; Marriott et al., 2018b; Schmidt, 2015). The soil type (e.g. presence of organic matter) is a very important factor that should also be taken into consideration when considering efficacy (Schmidt, 2015). Besides these, other factors that can influence the efficacy include the pH, cleanliness and type of equipment, water properties (e.g., hardness), microbial population and attachment (Marriott et al., 2018b).

The following paragraphs indicate compounds that are used in the food supply chain during disinfection. These were seen as the main categories reported in the literature.

3.1.2.1 Chlorine containing compounds

Chlorine-based compounds can include several types of compounds such as aqueous chlorine, hypochlorite, chlorine gas, inorganic and organic chloramine, and chlorine dioxide. The antimicrobial capacity of these varies (Holah et al., 2014). Generally, the efficacy of chlorine increases with decreasing pH; however, with a pH below 4.0, there is the risk of forming toxic and corrosive chlorine gas (Marriott et al., 2018b). A disadvantage is that it is inactivated by organic matter, which is problematic if (food) soil has not been cleaned from surfaces. Another disadvantage is that it has an adverse effect on the environment (Holah et al., 2014; Olmez & Kretzschmar, 2009) as the formation of disinfectant residuals in wastewater effluent can have deleterious effects on the environment (van Haute, Sampers, Jacxsens, & Uyttendaele, 2015). Moreover, with the undiluted form of chlorine, it can be corrosive to equipment and a hazard to human health (Holah et al., 2014). Concerns related to the formation of carcinogenic, halogenated disinfection by-products such as trihalomethanes and haloacetic acids have been raised, as reviewed by (Banach, Sampers, Van Haute, & van der Fels-Klerx, 2015). Hypochlorous acid (HOCl) is produced when chlorine is added to the water. An advantage is that it has a wide spectrum, including that against spores and it is inexpensive compared to iodine compounds.

3.1.2.2 Iodine compounds

Iodine compounds that can be used during disinfection include iodophors, alcohol-iodine solutions, and aqueous iodine solutions. Iodophors are reported to be used for disinfection of equipment (e.g., food handling equipment), and as a skin antiseptic (non-irritant).They are also used during water treatment (Marriott et al., 2018b). Iodophors are a common form of iodine compounds. Hypoiodous acid and diatonic iodine are the active antimicrobial forms of iodophors (Marriott et al., 2018b).

Advantages of iodine-type compounds are that they are less reactive to organic matter compared to chlorine compounds, more effective than other chemicals on viruses, are stable at low pHs and can be used at low concentrations, and they are less irritating to the skin compare to chlorine compounds (Fraser, 2012; Marriott et al., 2018b). A disadvantage is their lower efficacy (versus chlorine) in spore inactivation and against bacteriophages (Fraser, 2012; Marriott et al., 2018b). Other disadvantages are the higher costs – versus that of chlorine, potential off-flavours in products (e.g., iodine-based disinfectants can react with food to form iodophenols, which generate off-flavours), poor low-temperature efficacy, sensitivity to pH, and their ability to stain porous and plastic materials (Marriott et al., 2018b).

3.1.2.3 Bromine compounds

Bromine compounds are used alone or in combination with other compounds (e.g. with chlorine compounds). They can be used on processing equipment and utensils but are more commonly used for water treatment. However, bromine is more expensive than chlorine. Examples include hydrogen bromide as well as the combination of hydrogen bromide with sodium hypochlorite (bleach) to form hypobromous acid. A disadvantage is that bromine is very reactive. However, bromine compounds can be very effective to destroy bacteria and viruses. Hydrogen bromide has been applied to destroy pathogens and other microbes on carcasses (Marriott et al., 2018b), which is not allowed in the EU, according to Regulation (EU) No 528/2012, article 2.5.

3.1.2.4 Quaternary ammonium compounds

Quaternary ammonium compounds (quats) are positively charged polyatomic ions that act by disrupting cell membranes. Examples include alkyldimethylbenzylammonium chloride (syn. benzalkonium chloride, BZK, BKC, BAC, ADBAC) and alkyldimethylethylbenzylammonium chloride (syn. ADEBAC). They are used on equipment, walls, floors, etc., as they can penetrate surfaces, including porous surfaces, which are more difficult to clean (Marriott et al., 2018b). In general, advantages of quats are that they are non-corrosive, non-irritating (skin), and have low toxicity. They have no odour or taste in dilution (Marriott et al., 2018b). They are stable in concentrated form and have long shelf-lives (Holah et al., 2014). Quats are generally more effective with alkaline pH but are active over a wide pH (Fraser, 2012; Marriott et al., 2018b). Disadvantages include their decreased (bactericidal) efficacy in the presence of organic matter (Holah et al., 2014), as well as their limited efficacy against Gram-negative bacteria and bacteriophages (Fraser, 2012; Holah et al., 2014). Their lack of tolerance to hard water is considered a major disadvantage (Schmidt, 2015). Also, they should not be combined with cleaning compounds, since they can be neutralised or inactivated with anionic detergents (Marriott et al., 2018b).

3.1.2.5 Amphoteric (ampholytic) compounds

These compounds are basically alkyl or acyl amino acids (Skaarup, 1985). They are used for manual cleaning and are not recommended for CIP, given their high foaming characteristics (Holah et al., 2014). Advantages are that they are non-corrosive, non-irritating (skin), have low toxicity, and are effective against Gram-positive and Gram-negative bacteria (Holah et al., 2014; Skaarup, 1985). A disadvantage is their costs (Skaarup, 1985).

3.1.2.6 Alcohols

Alcohol-based compounds such as ethyl alcohol (ethanol) and isopropyl alcohol (isopropanol or propan-2-ol) are used in the food industry, particularly during cleaning and disinfection in high-risk areas. The antimicrobial activity of alcohols are most active between 60% and 70%. Advantages include their bactericidal and virucidal properties. Disadvantages include their non-sporicidal properties, inactivity in the presence of organic matter, and health and safety issues (Holah et al., 2014), such as localised irritation with inhalation or dermal exposure (ANSES, 2016) (ECA, 2019a) (ECA, 2019b).

3.1.2.7 Acids

Acid disinfectants are often used for rinsing and disinfecting. Organic acids, such as acetic, peroxyacetic, lactic, propionic, and formic acid, among others, are frequently used. Acid disinfectants destroy microorganisms by penetrating and destroying cell membranes; treatment is dose-dependent for spoilage and pathogenic microorganisms. Advantages include their rapid action and effectivity against yeasts and viruses. Disadvantages include their decreased efficacy with increasing pH and decreased efficacy against thermoduric organisms. Also, at high concentrations, they may cause discolouration on food and odour (Marriott et al., 2018b).

Acid anionic compounds can be formulated with acids (e.g., phosphoric acid, organic acids) and anionic surfactants. The advantages include their rapid action and broad-spectrum against bacteria. They are stable, non-staining, have a minimal odour, and are effective at a wide temperature range. Also, they are not affected by water hardness. Disadvantages include their corrosiveness (certain metals) and irritation (skin). They are also less effective at higher pH and more expensive than halogen disinfectants, such as chlorine, bromine and iodine. They should not be used for CIP, given their tendency to foam (Marriott et al., 2018b).

Peracetic acid (PAA) is more commonly found in the food-industry applications (e.g. as chlorine replacement), including that for CIP (Holah et al., 2014; Marriott et al., 2018b). Advantages include its rapid action, broad-spectrum kill (bacteria, yeasts, moulds), stability against heat and organic matter, activity at broad temperature ranges, pH tolerance, tolerance to hard water, efficacy against biofilm, among others. Disadvantages include the costs, slightly corrosive properties, and lower efficacy against yeasts and moulds compared to other chemicals (Holah et al., 2014; Marriott et al., 2018b; Schmidt, 2015).

Fatty acid (also known as carboxylic acid) disinfectants are used for mechanical or CIP applications, given their low foaming potential. Advantages include their broad bactericidal activity; stability in dilution, in the presence of organic matter, and at high temperatures; non-corrosive properties (stainless steel); shelf-life; and cost-effectivity. Disadvantages include their decreased activity against yeasts and moulds; that they are negatively affected by cationic surfactants; and that they are corrosive to non-stainless steel metals, plastics, and some rubbers (Marriott et al., 2018b).

3.1.2.8 Ozone

Ozone is an activated form of oxygen, consisting of three oxygen atoms of oxygen (i.e. ozone is oxygen (O_2) with an extra oxygen atom). It has been used for many decades for water treatment (Holah et al., 2014). It is a broad-spectrum disinfectant, which is effective against bacteria (including spores), yeasts, moulds, viruses, and protozoa. It is a colourless, tasteless, odourless gas (Marriott et al., 2018b). Advantages include its high reactivity, penetrability, and spontaneous decomposition to non-toxic products. A disadvantage is possible safety issues for people working with ozone upon inhalation (Fatica & Schneider, 2009). Another disadvantage is its decreased efficacy, owning to its decreased stability, with increasing temperature (Holah et al., 2014).

3.1.2.9 Hydrogen peroxide

In the food industry, hydrogen peroxide can be used on several surfaces like equipment, walls, gloves, belts etc. Fumigation with vapour-phase hydrogen peroxide is one application. It displays antimicrobial activity against bacteria, viruses, fungi and bacterial spores. Another application is foaming hydrogen peroxide (quat hybrid), which is used to remove biofilms from drains. The use of hydrogen peroxide with or without peracetic acid is increasing given its advantageous reduced corrosive nature (on stainless steel) versus that of, e.g. active chlorine (Marriott et al., 2018b). A disadvantage is its eye and skin irritation, meaning concentrations above. e.g. 5%, should be handled carefully (Schmidt, 2015).

3.1.2.10 Electrolyzed water

Electrolyzed water (syn. electrolyzed oxidizing water (EOW)) is produced from the electrolysis of water containing an electrolyte (e.g. sodium chloride, potassium chloride, dilute hydrochloric acid). Advantages over traditional cleaning agents include the efficacy of the disinfection, ease of operation, relatively low costs, environmental friendliness, and safety (Huang, Hung, Hsu, Huang, & Hwang, 2008). The main disadvantage is that it loses its antimicrobial activity without continuous electrolysis (Huang et al., 2008; Marriott et al., 2018b).

3.2 Legislation related to cleaning agents and disinfectants

The European law prescribes that food produced within the EU should comply with the hygienic rules outlined in Regulation (EC) No 852/2004 on the hygiene of foodstuffs and Regulation (EC) No 853/2004 laying down specific hygiene rules for food of animal origin. Provisions outlined in the regulation apply to the entire supply chain from production, processing to distribution, and include exports, but excludes, inter alia, private domestic production/non-commercial production, since this production is not meant to be sold but used for personal consumption. Food business operators (e.g. companies) have the primary responsibility to ensure that the food under their control complies with the hygiene requirements as outlined in those regulations. Such requirements concern the hygienic design of food premises and procedures in the food chain. With regard to cleaning and disinfection, both regulations prescribe general rules and among others specific provisions for food premises, rooms where food is prepared, treated or processed, transportation, equipment and personal hygiene to ensure food hygiene. Cleaning and disinfection play an important role in achieving the overall goal, being hygiene and is, therefore, mentioned several times in these regulations. One can think of provisions, that describe that cleaning and/or disinfection shall take place in other areas or in separate rooms than where food is handled. However, these regulations do not list authorised cleaning and disinfection products to be used in the food sector. A solely referral to cleaning and disinfection products is made in the context of storage, namely those products must not be stored where food is handled.

To understand the use of cleaning agents and disinfectants, other regulations related to chemicals have to be consulted. These regulations can be divided into regulations applicable to cleaning agents and disinfectants (basic for all chemicals) and regulations specific to the end-user (Detergent regulation for cleaning agents; Biocidal Products regulation for disinfectants). The former is explained in the next section 3.2.1, whereas the latter is outlined in sections 3.2.2 and 3.2.3.

3.2.1 Generic regulations on chemicals – REACH and CLP

Regulation (EC) No 1907/2006 concerning Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and Regulation (EC) No 1272/2008 on Classification, labelling and packaging of substances and mixtures (CLP) apply to manufacturers of substances, as well as downstream users who use these substances in course of their industrial or professional activities, in all industrial sectors. Both regulations aim at a high level of human health and environmental protection. REACH requires that all chemical substances need to be registered before they are manufactured or placed on the market within the EU. The registration requires a technical report, which includes the results of a chemical safety assessment of the substance. The chemical safety assessment shall include a human health hazard assessment, a physicochemical hazard assessment, an environmental hazard assessment (including environmental fate assessment), a persistent, bioaccumulative and toxic (PBT) assessment, and a very persistent and very bioaccumulative (vPvB) assessment. According to the results of the chemical safety assessment, as discussed above, the substances should be classified into hazard classes as set out in the CLP Regulation. The CLP Regulation ensures that the chemical substances are classified, labelled and packaged according to the properties of the substances that may lead to a hazard. If the characteristics of a substance correspond with defined classification criteria, the substances are assigned to a hazard class (physical, health, environmental or other hazard). Before the chemicals are put on the market, the hazards need to be communicated to the clients in the next step of the supply chain, who are going to use the substances to produce cleaning agents and disinfectants.

Concluding this section, only chemicals that are registered within REACH, and thus have undergone a safety evaluation and data thereon is available, have the potential to be used in cleaning agents and disinfectants. More detailed information on the application of substances as cleaning and disinfection agents are discussed below.

3.2.2 Cleaning

In this report we use the term cleaning agents for all substances used to remove soil, like food residues, grease or other objectionable matter. In legislation, the term detergent is used (Regulation (EC) No 648/2004). The overall aim of this regulation is to ensure a high level of protection of human health and the environment. The regulation prescribes inter alia provisions on labelling of detergents and that an ultimate aerobic biodegradation test shall be conducted on the surfactants used in detergents. The requirement for the detergent is that the surfactant should be biodegraded with at least 60% within 28 days. Besides that, this regulation does not prescribe any additional safety assessment (e.g. toxicological studies) for cleaning agents. Cleaning agents are not prone to pre-market approval. Nevertheless, like all chemical substances (i.e. active ingredients and other chemical substances), they should still be registered in REACH.

3.2.3 Disinfection

3.2.3.1 EU regulation

The regulation of disinfectants within the EU is more sophisticated compared to the cleaning agents, as it involves additional safety assessments. Disinfectants is one main group of biocidal products, which are covered by the Biocidal Products Regulation (Regulation (EU) No 528/2012 - BPR). This regulation aims at the protection of human and animal health and the environment. Besides the fact that the substances are registered, as required by REACH, biocidal products are subject to safety assessments specifically for their intended use. This shall first be executed on the level of solely the active substance in the biocidal product, which shall be followed by a safety assessment of the complete biocidal product.

The first step requires that companies assess the active substances. Toxicological, eco-toxicological and environmental studies have to be conducted and included in a dossier, which is evaluated by the ECHA. Based on the information in the dossiers, ECHA advises on whether to approve or disapprove the use of the active substances on the European market. This step is conducted on supranational level by ECHA. A Union list of active substances (approved and non-approved) is published on the ECHA-website. As a second step, the whole biocidal products, which contain these approved active substances, have to undergo another safety assessment. This step is conducted on national level by the authorities of the Member States. This also requires the manufacturer of disinfectants to conduct toxicological, eco-toxicological and environmental studies. These additional safety evaluations are necessary as products are intended to kill microorganism so that these products pose a greater danger to human health and environment than cleaning agents. Cleaning agents are intended to merely remove dirt and a rinsing-step is generally applied after its application so that residues are not expected to come into contact with food.

The Member States are responsible to evaluate and authorise disinfectants (the biocidal product as a whole) on their own territory before they are placed on the market. Once the biocidal product is authorised, it can be placed on the market within the EU. However, notifications to each Member State shall be given at least 30 days prior to marketing of the biocidal product in the respective Member State by the authorisation holder.

3.2.3.2 Authorisation in the Netherlands by the Ctgb

In the Netherlands, the Board for the Authorisation of Plant Protection Products and Biocides (College voor de toelating van gewasbeschermingsmiddelen en biociden - Ctgb) is responsible for the authorisation of disinfectants. Ctgb assesses whether the products are safe for humans, animals and the environment with their intended uses based on the dossiers provided by the manufacturer. The Ctgb website contains a database that indicates the authorised biocides in the Netherlands (https://pesticidesdatabase.ctgb.nl/). Cleaning agents may contain active substances that are also used in biocides. Nevertheless, these active substances of cleaning agents do not require authorisation by the Ctgb. This applies when:

- The concentration of the active substance is very low in the final concentration in which the product should be used. The substance is not added for disinfection purposes and it will not significantly contribute to the cleaning effect of the product. For example sodium hydroxide is only considered as an active substance for disinfection when the concentration is higher than 0.1 M or a pH>13. Another example, didecyldimethylammonium chloride (DDAC) is an active substance from use concentrations of 0.04%.
- The product is explicitly intended for other applications than disinfection (for example bleaching).
- The active substance is used as an additive to preserve the stability in the cleaning product.

The Biocidal Product Regulation prescribes in its Annex V 22 product types (PT), which are grouped into four main areas (disinfectants, preservatives, pest control, other biocidal products). Within the disinfectants group, five product types are classified (Table 2). For the purpose of this study, product types 1 (human hygiene), 3 (veterinary hygiene) and 4 (food and feed area) are of interest. The other two categories are not relevant for the application in the food chain.

3.2.3.3 Brexit consequences on the use of active substances and biocidal products

Substances and products authorised in the UK after the Brexit will no longer be recognised in the EU. New authorisation for biocidal products within the EU are no longer possible, provided that the inherent active substances are based on a UK authorisation. Besides new decisions taken by the UK after withdrawing as EU Member State, also previous authorisations for biocidal products prior to the Brexit will no longer be recognised (Ctgb, 2018).

As a UK based manufacturer, in order to be able to continue to sell substances or products to the EU market, an EU-based representative (European Economic Area (EEA) countries) needs to be appointed as a new authorisation holder under the BPR (ECHA, 2018d). Substances registered under REACH by a UK-based company, are not legally registered anymore after the Brexit takes place. Therefore, EU-based companies, in order to legally use these substances, have to either apply for an authorisation of those substances themselves or the UK-based company is required to appoint for their authorisation a representative in the EU or EEA countries (ECHA, 2018b, 2018c).

Evaluations of active substances currently under review by the UK as part of the EU review programme for biocides, will be reclassified by the European Commission to other Member States, EEA country or Switzerland (ECHA, 2018a).

3.2.3.4 Disinfectants in agriculture versus Plant Protection Products

The Biocidal Products Regulation explicitly mentions in Art. 2 (2) (i) that a product is not a biocide if it falls within the scope of the plant protection products (PPP) regulation. Similarly, the Plant Protection Regulation (Regulation (EC) No 1107/2009 excludes products outside the scope of its regulation if they are not specifically aimed at the protection of plants or plant products, but have the main purpose of hygiene instead (Art. 2 (1) (a)). Therefore, the criteria to distinguish these two categories is whether the intended use is on plant pathogens specifically or on general hygiene. In earlier days, in some cases, the actual use has been different from the described intended use for which it was authorised. For example, authorised plant protection products were used for the purpose of disinfection, not for the protection of any plant material. In order to be in line with the earlier published European Borderline Guidance of 2001 (Ctgb, 2017d) and a European Agreement of 2004 (Manual of Decisions for Implementation of Directive 98/8/EC concerning the Placing on the Market of Biocidal Products, issue 2.1.1.5), the Ctgb elaborated its policy (approved on 28 June 2017) on biocides with crop protection applications. The policy will be applied to new biocides or existing biocides which are re-registered with the aim to clarify the classification of biocides applied in agriculture and plant protection products and the interface between these products. In the future, a product cannot be authorised as a biocide if it already has an application as a plant protection product. In case a product solely aims at the protection of plants or plant products, it is seen as a plant protection product and in case a product aims at the general hygiene, it is seen as a biocidal product.

Table 2 *Product types (PT) related to disinfectants as specified in the Biocidal Product Regulation ((EU) No 528/2012)*

Number	Product-type	Description
PT 1	Human hygiene	Products in this group are biocidal products used for human hygiene purposes, applied on or in contact with human skin or scalps for the primary purpose of disinfecting the skin or scalp.
PT 2	Disinfectants and algaecides not intended for direct application to humans or animals	Used for the disinfection of surfaces, materials, equipment and furniture that are not used for direct contact with food or feeding stuffs. Usage areas include, inter alia, swimming pools, aquariums, bathing and other waters; air conditioning systems; and walls and floors in private, public, and industrial areas and in other areas for professional activities. Used for disinfection of air, water not used for human or animal consumption, chemical toilets, wastewater, hospital waste and soil. Used as algaecides for treatment of swimming pools, aquariums and other waters and for remedial treatment of construction materials. Used to be incorporated in textiles, tissues, masks, paints and other articles or materials with the purpose of producing treated articles with disinfecting properties.
PT 3	Veterinary hygiene	Used for veterinary hygiene purposes such as disinfectants, disinfecting soaps, oral or corporal hygiene products or with anti-microbial function. Used to disinfect the materials and surfaces associated with the housing or transportation of animals.
PT 4	Food and feed area	Used for the disinfection of equipment, containers, consumption utensils, surfaces or pipework associated with the production, transport, storage or consumption of food or feed (including drinking water) for humans and animals. Used to impregnate materials that may enter into contact with food.
PT 5	Drinking water	Used for the disinfection of drinking water for both humans and animals.

3.2.3.5 MRLs for disinfectants

The concept of MRLs for biocides has been introduced with the new Biocidal Products Regulation in force since 2013. In order to authorise new biocidal products, an MRL for food and feed needs to be set, provided that it is appropriate (Regulation (EU) No 528/2012 Art. 19 (1) (e)). It is the applicant’s responsibility to apply for an MRL for the active substances in the biocidal product. The conditions and the context of what is considered ‘appropriate’ is, however, not prescribed.

In practice, active substances with MRLs up to now are rare. In 2014, MRLs were established for two quats, i.e. benzalkonium chloride (BAC) and didecyldimethylammonium chloride (DDAC), in Regulation (EC) No 396/2005. These new MRLs entered into force from 12th August, 2015. Before the regulation was amended by Commission Regulation (EU) No 1119/2014, the two compounds were not subject to specific MRLs, and therefore, a default MRL of 0.01 mg/kg applied to these compounds. However, many Member States noticed that residues of these compounds were often found in levels exceeding the default MRL. As a consequence, EFSA and BfR performed risk assessments and new MRLs were set at 0.1 mg/kg (Regulation (EU) No 1119/2014). Even so, there are limited data to support the proposed MRLs (0.1 mg/kg), meaning that the risk assessment has a high degree of uncertainty (EFSA, 2014c). Concerns, regarding the validity of these new MRLs proposed by EFSA, were raised by the biocides industry due to an incomplete DDAC and BAC evaluation under the Biocidal Products Regulation and absence of an agreement on an unanimous methodology to evaluate MRLs for biocides (ChemicalWatch, 2014). A revision of the MRL for DDAC was planned in 2019 with The Netherlands as Rapporteur Member State. Nevertheless, no start date for data collection, nor a deadline, are established (EFSA 2019).

Since 2008, chlorate is withdrawn from the positive list of active substances to be used in plant protection products. Plant protection products, which contain chlorate and were already authorised are prohibited as of 10^{th} May 2009 (Commission Decision 2008/865). Therefore the default MRL of 0.01 mg/kg currently applies for chlorate. In May 2017, the Commission announced to establish a MRL for chlorate in food based on occurrence data, whereas a MRL of 0.01 mg/kg is intended to remain for infants and young children foods. Moreover, the Commission had planned to establish a guidance on good food hygiene practices for Mid-November 2017 in order to reduce the formation of chlorate from disinfectants. Proposed MRLs range from 0.02 mg/kg for eggs and several fruits, for example up to 0.7 mg/kg for table olives (SANTE 10684 2015 Rev. 3). However, chlorate can also occur for example as by-product from chlorine disinfectants used in the food industry and is in many cases not a residue of a pesticide. For that reason, there is more resistance from industry on the approach of chlorate as a pesticide. So, although new MRLs for chlorate in foodstuffs are drafted, none of these are adopted yet (European Commission, n.d.).

Further work on the establishment of MRLs for biocides in general is in progress. EFSA has already notified that it will not consider the substances hydrogen peroxide and peracetic acid, since they are rapidly degraded and therefore residues of these substances cannot be detected (Christeyns Food Hygiene, 2016).

For perchlorate, which can, inter alia, occur via degradation of the disinfectant sodium hypochlorite, the European Commission published a recommendation for the monitoring in food (Commission Recommendation (EU) 2015/682). Maximum levels (MLs) of perchlorate in food are set as a reference for intra-Union trade, and Member States can decide to which extent they enforce these levels on their market. MLs are set at 0.1 mg/kg for perchlorate in fruits and vegetables in general (some deviations for specific products), 0.5 mg/kg for perchlorate in dried spices in general (some deviations for specific products), 0.02 mg/kg for perchlorate in food for infants and young children and 0.05 mg/kg for other food (European Commission, 2015).

In 2014, a European Conference on MRL Setting for Biocides was organised by the European Commission and BfR. The Commission stressed that the establishment of MRLs for biocides should be targeted and focused, because of the high number of biocidal products and the limited resources to set MRLs. The Commission outlined a total number of 300 active substances that are affected by MRL setting, of which

- about 150 potentially lead to relevant residues (e.g., PT 3, 4, 5)
- 75 have specific MRLs in Plant Protection Products (PPP) and/or Veterinary Medicinal Products (VMP) legislation
- 14 have a default MRL from PPP legislation
- 61 have no MRL so far

According to the monitoring experiences in The Netherlands, it was found that residues of biocides for some product types (PTs) are detected at levels above the LOQ and that adequate measures should be taken to mitigate the presence of these residual biocides. (BfR, 2014).

3.3 Inventory of active ingredients used for cleaning and disinfection in the poultry and eggs, leafy greens and sprouts chains (Phase I)

Review of the literature, the Ctgb website, and expert elicitation were used to derive a long-list of active ingredients used as cleaning agents or disinfectants.

3.3.1 Literature

In total, 96 papers were seen as relevant based on title, keywords and abstract since they contained information on cleaning agents and disinfectants (13 for poultry, 37 for leafy greens, and 46 for sprouts).

However, a large part of the references described the use of disinfectants for decontamination of products, which was not the focus of this study. These are presented in Annex 6 as additional information. Decontamination is not allowed in the EU according to Regulation (EC) No 528/2012, article 2.5, while e.g. in the US it is allowed.

3.3.1.1 Poultry and eggs

With regards to cleaning agents, limited information on compounds used in practice was found. Only alkaline solutions were mentioned, such as sodium hydroxide and alkaline phosphates.

Several papers specifically outlined disinfectants that are used in the poultry sector and in the egg sector. Some of the substances were mentioned to potentially be of human health concern for consumers (formaldehyde, sodium hypochlorite, acidified sodium chlorite, benzalkonium chloride, citric acid, lactic acid, and copper sulphate, and trisodium phosphate) while others may lead to allergic contact dermatitis for personnel in the poultry processing industry (chlorhexidine, formaldehyde, glutaraldehyde).

Table 3 outlines the disinfectants found in the literature for the poultry meat sector. The disinfectants were divided into categories corresponding with section 3.1.2. Most of these disinfectants were used in poultry processing only, whereas hypochlorite and formaldehyde are also used on farms. Iodine, copper sulphate and quats were specifically indicated to be used on poultry farms.

For the egg industry, several disinfectants were mentioned in the literature. The chemical agents noted in these articles are reflected in Annex 6. However, these encompassed washing and disinfection of the eggshell surface referring to practices in the USA. Regulation (EC) No 589/2008 prohibits the washing and cleaning of eggs in the EU.

Table 3 *Active ingredients to be used for disinfection in the poultry chain as found in literature*

Group	Type of disinfectant	References
Chlorine-containing compounds	Acidified sodium chlorite	(Alter, 2016; Johnson, 2014; Loretz, Stephan, & Zweifel, 2010; Sarjit & Dykes, 2015; Umaraw, Prajapati, Verma, Pathak, & Singh, 2017)
	Alkyl dimethylbenzylammonium chloride (benzalkonium chloride)	(Sarjit & Dykes, 2015)
	Chlorine	(Alter, 2016; Barbut & Pronk, 2014; Bucher, Farrar, et al., 2012; Loretz et al., 2010; Umaraw et al., 2017)
	Chlorine dioxide	(Alter, 2016; Bucher, Farrar, et al., 2012; Johnson, 2014; Loretz et al., 2010; Umaraw et al., 2017)
	Chlorhexidine digluconate	(GonÇalo, 2012)
	Sodium hypochlorite	(Loretz et al., 2010; Sarjit & Dykes, 2015)
Iodine compounds	Iodine	(Arnold, 2009)
Quaternary ammonium compounds	Quaternary ammonium compounds	(Arnold, 2009)
Acids	Acetic acid	(Alter, 2016; Loretz et al., 2010; Umaraw et al., 2017)
	Citric acid	(Loretz et al., 2010; Sarjit & Dykes, 2015)
	Lactic acid	(Alter, 2016; Barbut & Pronk, 2014; Bucher, Farrar, et al., 2012; Bucher, Rajic, Waddell, Greig, & McEwen, 2012; Loretz et al., 2010; Sarjit & Dykes, 2015; Umaraw et al., 2017)
	Peroxyacids	(Alter, 2016; Johnson, 2014; Umaraw et al., 2017)
	Propionic acid	(Bucher, Farrar, et al., 2012; Ducatelle & Van Immerseel, 2011)
Others	Copper sulphate	(Ducatelle & Van Immerseel, 2011)
	Formaldehyde	(GonÇalo, 2012)
	Glutaraldehyde	(Bucher, Farrar, et al., 2012; GonÇalo, 2012)
	Phenolic compounds (phenols, cresols)	(Ducatelle & Van Immerseel, 2011)
	Triphenylphosphate (TPP)	(Barbut & Pronk, 2014)
	Trisodium phosphate (TSP)	(Alter, 2016; Barbut & Pronk, 2014; Bucher, Rajic, et al., 2012; Johnson, 2014; Loretz et al., 2010; Sarjit & Dykes, 2015; Umaraw et al., 2017)

3.3.1.2 Horticulture: leafy vegetables and sprouts

Several active ingredients were reported in the literature to be used for leafy vegetables and sprouts. With regard to cleaning agents, no information on compounds used were specified; articles only provided information on the scope of cleaning and disinfection. Disinfection can include disinfection of the environment (walls, floors, equipment, etc.), disinfection of products or seeds (i.*e.* decontamination), the latter being a common practice in the sprout chain. Some chemical agents are used for both purposes.

Table 4 illustrates several disinfectants reported to be used in the leafy green chain. According to the literature study, of the 37 relevant articles, 19 specified decontamination of the product as the main purpose; the chemical agents noted in these articles are reflected in Annex 6. Of the remaining 18 articles, 1 study focused on disinfecting the wash water rather than product decontamination (Banach et al., 2015). This shift in philosophy from decontaminating the produce to preventing cross-contamination from the wash water has been pointed out (Murray, Wu, Shi, Xue, & Warriner, 2017). This being so, the remaining 17 of the 18 articles referred to multiple purposes for the use of chemical agents; these agents are represented in Table 4. Most of the substances were indicated to be used during processing. However, sodium hypochlorite, chlorine, and chlorine dioxide were also indicated to be used pre-harvest. Chlorine based compounds could generate hazardous by-products (Chaidez et al., 2012; Fatica & Schneider, 2009; Lee, 2013).

In this literature search, the use of essential oils such as oregano oil and thyme oil were noted. Moreover, the use of surfactants (compounds that help lower the surface tension) and disinfection agents during washing of produce was mentioned (Sapers, 2009; Warriner & Namvar, 2013). These compounds are outlined in Annex 6.

In the sprout chain, the literature study resulted only in chemical agents that are used for decontamination, whether it be of the seeds (or mung beans) or of the sprouts itself. Of the 46 studies, 31 concerned seeds or beans, 12 on sprouts, and 3 on both seeds and sprouts. Annex 6 illustrates several chemical agents reported to be used in the sprout chain for decontamination.

Table 4 *Active ingredients to be used for disinfection in the leafy green chain as found in literature*

Group	Type of disinfectant	References
Chlorine containing compounds	Acidified sodium chlorite (ASC)	(Doona et al., 2015; Fatica & Schneider, 2009; Sapers, 2009; Warriner & Namvar, 2013)
	Calcium hypochlorite	(Delaquis & Bach, 2012; Sapers, 2009)
	Chlorinated trisodium phosphate	(Doona et al., 2015)
	Chlorine (free)	(Alvaro et al., 2009; Banach et al., 2015; Chaidez et al., 2012; Cook, Bertrand, Gantzer, Pinto, & Bosch, 2018; D'Acunzo, Del Cimmuto, Marinelli, Aurigemma, & De Giusti, 2012; Doona et al., 2015; Lee, 2013; Sapers, 2009; Warriner & Namvar, 2013)
	Chlorine (gas)	(Sapers, 2009)
	Chlorine dioxide (aq. or gas)	(Banach et al., 2015; Cook et al., 2018; Delaquis & Bach, 2012; Doona et al., 2015; Fatica & Schneider, 2009; Lee, 2013; Meireles, Giaouris, & Simões, 2016; Praeger, Herppich, & Hassenberg, 2018; Sapers, 2009; Warriner & Namvar, 2013)
	Sodium hypochlorite	(Alvaro et al., 2009; Cook et al., 2018; Delaquis & Bach, 2012; Doona et al., 2015; Sapers, 2009)
Bromine compounds	Potassium bromide	(Warriner & Namvar, 2013)
Iodine compounds	Iodine	(Delaquis & Bach, 2012)
Quaternary ammonium compounds	Quaternary ammonium compounds	(Delaquis & Bach, 2012; Doona et al., 2015; Meireles et al., 2016; Warriner & Namvar, 2013)
Acids	Acetic acid	(Fatica & Schneider, 2009; Lee, 2013; Meireles et al., 2016; Warriner & Namvar, 2013)
	Aliphatic acids	(Warriner & Namvar, 2013)
	Citric acid	(Doona et al., 2015; Fatica & Schneider, 2009; Lee, 2013; Meireles et al., 2016; Warriner & Namvar, 2013)
	Hydroxyethylidene diphosphonic acid	(Warriner & Namvar, 2013)
	Lactic acid	(Doona et al., 2015; Fatica & Schneider, 2009; Meireles et al., 2016; Warriner & Namvar, 2013)
	Malic acid	(Doona et al., 2015; Lee, 2013; Warriner & Namvar, 2013)
	Peracetic acid or peroxyacetic acid	(Alvaro et al., 2009; Banach et al., 2015; Delaquis & Bach, 2012; Doona et al., 2015; Fatica & Schneider, 2009; Lee, 2013; Meireles et al., 2016; Sapers, 2009; Warriner & Namvar, 2013)
Ozone	Ozone (aq. or gas)	(Banach et al., 2015; Cook et al., 2018; Delaquis & Bach, 2012; Doona et al., 2015; Fatica & Schneider, 2009; Horvitz & Cantalejo, 2014; Meireles et al., 2016; Sapers, 2009; Tzortzakis, 2016; Tzortzakis & Chrysargyris, 2017; Warriner & Namvar, 2013)
Hydrogen peroxide	Hydrogen peroxide	(Delaquis & Bach, 2012; Doona et al., 2015; Fatica & Schneider, 2009; Meireles et al., 2016; Warriner & Namvar, 2013)

Group	Type of disinfectant	References
Electrolyzed water	Sodium chloride in electrolyzed oxidizing water	(Doona et al., 2015; Huang et al., 2008; Lee, 2013; Meireles et al., 2016; Sapers, 2009; Turantas, Ersus-Bilek, Sömek, & Kusçu, 2018; Warriner & Namvar, 2013)
Others	Alkylene oxide adducts	(Warriner & Namvar, 2013)
	Naphthalene sulfonates	(Sapers, 2009; Warriner & Namvar, 2013)
	Polyacrylamide	(Warriner & Namvar, 2013)
	Silver nitrate	(Gopal, Coventry, Wan, Roginski, & Ajlouni, 2010) as cited by (Doona et al., 2015)
	Trisodium phosphate (TSP)	(Warriner & Namvar, 2013)

3.3.2 Ctgb website

Disinfectants for the product types 1, 3 and 4 were subtracted from the Ctgb Database. From that database, all biocidal products that are authorised under these product types were downloaded and the inherent active ingredient extracted. With these data, a list of all active ingredients authorised under that PT code and the number of biocidal products containing these ingredients was established (Annex 7). PT 1 contains 86 biocides, which contain 22 different combinations of active ingredients, PT 3 has 225 biocides composed of 48 combinations of active ingredients and PT 4 475 biocides with 46 active ingredients. In total, 85 different combinations of active ingredients are authorised for either of these three PT codes. The most frequently used active ingredient in biocidal products is sodium hypochlorite (148 products), followed by didecyldimethylammoniumchloride (DDAC; 132 products), the combination of hydrogen peroxide and peracetic acid (106 products), ethanol (71 products), hydrogen peroxide alone (51 products), iodine (31 products), sodium dichloroisocyanurate (24 products) and the combination hydrogen peroxide and lactic acid (15 products). Per PT code, the active ingredient most frequently used in biocidal products differed. For PT 1 (human hygiene), ethanol was the most frequently used active ingredient (38 products), whereas for PT 3 (veterinary hygiene), sodium hypochlorite (37 products), iodine (31 products), and the combination hydrogen peroxide and peracetic acid (29 products) were most frequently used and for PT 4 (food and feed area), DDAC (127 products) and sodium hypochlorite (102 products) were most frequently applied in biocidal products.

3.3.3 Questionnaires (Phase I)

The list of active ingredients in authorised products in Annex 7 indicates which active ingredients are most often applied in disinfectants. However, this information does not allow concluding which active ingredients are actually used most often in practice. In order to get more information on this, questionnaires were used and experts were interviewed. The information from the questionnaires and interviews was also used to give an overview of possible issues with cleaning and disinfectants (section 3.6).

In total, 92 emails were sent to invite people to fill in the questionnaire or to invite them for an interview. Forty-two persons responded to this invitation (46%). However, not all of these persons filled in the questionnaire, some people indicating they did not have the expertise or they referred to a colleague or they mentioned to fill it in later. In total, 20 people (22%) answered the questionnaire, 10 people responded by email and filled in the questionnaire, additionally, 10 people were interviewed using the questionnaire. There were 4 responses for horticulture primary production, 2 responses for horticulture processing, 3 responses for poultry farms, 3 responses for poultry processing, 2 responses for retail and 6 general responses. The outcome of the questionnaires was used to draft a list of active ingredients used for cleaning and disinfection (see Table 5 and Table 6, respectively). Because relatively more general responses were obtained, it was not possible to indicate more specifically if products were used at the farms or during processing, most substances being used both at farms and during processing. Ingredients were often used for floors and walls and other materials, further specification on the purpose of the ingredients were not provided (e.g. which ingredients were specifically used for floors).

Experts who were consulted on the use of chemical agents in arable crops indicated that farmers only use water or steam to clean their premises.

The output from the experts showed that cleaning agents and disinfectants were sometimes mixed up. For example, sodium hypochlorite, ethanol and penta-potassium phosphate were mentioned as being used in cleaning agents, whereas these are authorised as disinfectants. The other way around also occurred, some active substances were mentioned as being used as disinfectant, whereas these were cleaning agents. This was for example the case for potassium and sodium hydroxide. In those cases, the active ingredients were put under the right classification by the project team.

Table 5 *Active ingredients mentioned by experts as used for cleaning in horticulture, poultry, retail or general use in food supply chains*

Name	Horticulture	Poultry	Retail	General
1-dodecanaminium, n-(2-hydroxy-3-sulfopropyl)-n,n-dimethyl-, inner salt			x	
1-tetradecanol (also known as myristyl alcohol)				x
2-(2-butoxyethoxy)ethanol	x	x		
2-(2-dodecoxyethoxy)acetic acid	x			
3-butoxy-2-propanol		x		
alcohol, C10-16, ethoxylated	x			
alcohols, C13-15, ethoxylated (p.e isotridecanol)	x			
alcohols, C12-14 ethoxylated sulphates	x	x		
alkyl amidopropyl betaines/ C12-C14 pareth-4, cocamidopropylbetaine		x	x	
alkylamine oxides (Amines, C12-14 alkyldimethyl, N-oxides)	x	x		x
amines, C8-C18 (even numbered) and C18 unsaturated, N, N-bishydroxyethyl		x		x
aryl sulfonates (e.g. cumene sulfonate)	x	x		
benzenesulfonic acid, C10-13 alkyl derivation, sodium salts	x			
C14-16 (even numbered)-alkane hydroxy and C14-16 (even numbered)-alkene sodium salts			x	
D-glucopyranose, oligomeric, decyl octyl glycoside		x		x
disodium metasilicate	x			
ethanolamines		x		
ethoxylates of alkylamines	x			
ethylenediaminetetraacetic acid (EDTA)	x	x		
fatty alcohol ethoxylate (toxylated)	x	x	x	
lauryl ether sulphates (toxylated)			x	
methanesulfonic acid	x			
N-C8-22-alkyltrimethylenedi- acrylated sodium salts		x		
N-dodecylpropane-1,3-diamine	x			
nitric acid		x		
nitrillotriacetic acid (sodium-salt)	x			
phosphate esters		x		
phosphoric acid	x	x	x	x
potassium hydroxide	x	x		
sodium carbonate			x	
sodium hydroxide	x	x	x	x
sulfamic acid, aminosulfonic acid		x		
sulfonic acids (sodium C12-C14, olefin sulfonate)		x	x	
sulphuric acid	x			
tetradecanol				x
secondary alkane sulphonate	x			

Table 6 *Active ingredients mentioned by experts as used for disinfection in horticulture, poultry, retail, or general use in food supply chains*

Name	Horticulture	Poultry	Retail	General
1-propanol	x			x
2-Hydroxypropanoic acid, lactic acid		x	x	
4-chloro-3-methylphenol (also known as chlorocresol)		x		
acetic acid	x	x		x
alkyl (C8-18) dimethylbenzylammoniumchloride		x	x	x
chlorhexidine diglyconate		x		
didecyldimethylammonium chloride (DDAC)	x	x		
ethanol, alcohol, ethyl alcohol, etc. (EtOH)	x	x	x	
formaldehyde		x		
glutaraldehyde	x	x		
hydrogen peroxide	x	x		x
iodine		x		
isopropyl alcohol	x	x		x
peracetic acid	x	x		x
potassium peroxymonosulphate (also known as MPS, potassium monopersulphate, potassium caroate)		x		
sodium dichloroisocyanurate (NADCC)		x		
sodium hypochlorite (NaOCl, NaClO)	x	x	x	x
tosylchloramide or N-chloro tosylamide; sold as chloraime-T	x	x		

3.4 Long-list and intermediate list of cleaning agents and disinfectants

The output from the literature search and expert elicitation was put on a long-list of 37 active ingredients in cleaning agents (Table 7) and a long-list of active ingredients in disinfectants (Table 8). Additionally, the Ctgb database was used to establish the long-list of disinfectants that can be used in the production of poultry, leafy greens and sprouts. Furthermore, a policy document from Ctgb was used, which contains an inventory from LTO on the active ingredients used in horticulture (Ctgb, 2017c). The only active ingredient used in arable farming is Tosylchloramide (N-Chloro 4-methylbenzenesulfonamide / chloramine-T), which was included in the long-list. Additionally, a protocol from the Animal Health Service (GD) was used, indicating active ingredients used in disinfecting poultry stables (GD, n.d.).

Table 7 *Long-list of active ingredients in cleaning agents*

Name	Horticulture	Poultry	Retail	General
1-dodecanaminium, n-(2-hydroxy-3-sulfopropyl)-n,n-dimethyl-, inner salt		x		
1-tetradecanol (also known as myristyl alcohol)				x
2-(2-butoxyethoxy)ethanol	x	x		
2-(2-dodecoxyethoxy) acetic acid	x			
3-butoxy-2-propanol		x		
alcohol, C10-16, ethoxylated	x			
alcohols, C13-15, ethoxylated (p.e isotridecanol)	x			
alcohols, C12-14 ethoxylated sulphates	x	x		
alkaline phosphates		d		
alkyl amidopropyl betaines/ C12-C14 pareth-4, cocamidopropylbetaine		x	x	
alkylamine oxides (Amines, C12-14 alkyldimethyl, N-oxides)	x	x		x
amines, C8-C18 (even numbered) and C18 unsaturated, N, N-bishydroxyethyl		x		x
aryl sulfonates (eg cumene sulfonate)	x	x		
benzenesulfonic acid, C10-13 alkyl derivation, sodium salts	x			
C14-16 (even numbered)-alkane hydroxy and C14-16 (even numbered)-alkene sodium salts		x		
D-glucopyranose, oligomeric, decyl octyl glycoside		x		x
disodium metasilicate	x			
ethanolamines		x		
ethoxylates of alkylamines	x			
ethylenediaminetetraacetic acid (EDTA)	x	x		
fatty alcohol ethoxylate (toxylated)	x	x	x	
lauryl ether sulphates (toxylated)			x	
methanesulfonic acid	x			
N-C8-22-alkyltrimethylenedi- acrylated sodium salts		x		
N-dodecylpropane-1,3-diamine	x			
nitric acid		x		
nitrillotriacetic acid (sodium-salt)	x			
phosphate esters		x		
phosphoric acid	x	x	x	x
Potassium hydroxide	x	x		
secondary alkane sulphonate	x			
sodium carbonate			x	
sodium hydroxide	x	x,d	x	x
sulfonic acids (sodium C12-C14, olefin sulfonate)		x	x	
sulfamic acid, aminosulfonic acid		x		
sulphuric acid	x			
tetradecanol				x

x: mentioned by experts

d: found in literature

Table 8 *Long-list of active ingredients used as disinfectants with reasoning of presence on intermediate list*

Long list of active ingredients used as disinfectants	Used in				Authorised by Ctgb	Number of authorised products				Mentioned by experts (interview/ questionnaire) as potential concerning substances	Residues possible that might cause health problems?	Intermediate list
	Horticulture	Poultry	Retail	General		PT 1	PT 3	PT 4	Total			
1-propanol	a			a	Yes	15	0	15	30	No	No, residues in food not expected	No
4-chloro-3-methylphenol (also known as chlorocresol)		a			Yes	0	1	0	1	No		Yes
Acetic acid	a, d	a		a	No					No	No, see peracetic acid	No
Acidified sodium chlorite (ASC)	d	d			Yes	0	7	7	14	No		Yes
Aliphatic acids	d				Unknown[e]					Yes		Yes
Alkyl (C8-18) dimethylbenzylammoniumchloride (syn. benzalkonium chloride, BAC)		a,c,d	A	a	Yes	1	28	27	56	No		Yes
Alkylene oxide adducts	d				Unknown[e]					No		Yes
Calcium hypochlorite	d				No (17 in PT 2)					No		No
Chlorhexidine digluconate		a,d			Yes	14	9	0	23	No		Yes
Chlorinated trisodium phosphate	d				No					No		No
Chlorine (free chlorine)	d	d			No					No		No
Chlorine (gas)	d				No					No		No
Chlorine dioxide	d	d			Yes/No[f]					No		Yes
Copper sulphate		d			No					No		No
Citric acid	d	d			No					No		
Didecyldimethylammonium chloride (DDAC)	a	a			Yes	0	27	134	161	No		Yes
Ethanol, alcohol, ethyl alcohol, etc. (EtOH)	a	a	A		Yes	54	0	44	98	No	No, quickly evaporates	No
Formaldehyde		a,c,d			Yes	0	13	0	13	No		Yes
Glutaraldehyde	a	a,c,d			Yes	0	31	8	39	No		Yes
Hydrogen peroxide	a, d	a,c		a	Yes	3	49	125	177	No	No, not persistant, no residual hydrogen	No

Long list of active ingredients used as disinfectants	Used in				Authorised by Ctgb	Number of authorised products				Mentioned by experts (interview/ questionnaire) as potential concerning substances	Residues possible that might cause health problems?	Intermediate list
	Horticulture	Poultry	Retail	General		PT 1	PT 3	PT 4	Total			
											peroxide will appear in food.	
Hydroxyethylidene diphosphonic acid	d				No					No		No
Iodine	d	a,d			Yes	0	31	0	31	No		Yes
Isopropyl alcohol	a	a		a	Yes	19	0	5	24	No	No, residues in food are not expected	No
Lactic acid (2-Hydroxypropanoic acid)	d	a, d	A		Yes	0	27	14	41	Yes	No, residues in food are expected to be low compared to naturally occurring levels in food.	No
Malic acid	d				No					No		No
Naphthalene sulfonates	d				Unknown[e]					No		Yes
Ozone	d				Yes/No[f]					No	Yes, directly or indirectly reacts with bromide to form brominated ozone DBPS, including bromate ion (BrO3-).	Yes
Peracetic acid or peroxyacetic acid	a,d	a,c		a	Yes	0	41	68	109	No	No, no residual peracetic acid will appear in food.	No
Peroxyacids (probably peracetic acid)		d			No					No		No
Phenolic compounds (probably 4-chloro-3-methylphenol)		d			Unknown[e]					No		Yes, 4-chloro-3-

Long list of active ingredients used as disinfectants	Used in				Authorised by Ctgb	Number of authorised products				Mentioned by experts (interview/ questionnaire) as potential concerning substances	Residues possible that might cause health problems?	Intermediate list
	Horticulture	Poultry	Retail	General		PT 1	PT 3	PT 4	Total			
												methylphenol is included
polyacrylamide	d				No					No		No
Potassium bromide	d				No							No
potassium peroxymonosulphate (also known as MPS, potassium monopersulphate, potassium caroate)		a			Yes	0	5	4	9	No		Yes
Propionic acid		d			No					No		No
Qquaternary ammonium compounds	d				Unknown[e]					No		Yes, BAC and DDAC are included
Silver nitrate	d				No					No		No
Sodium chloride (used in electrolyzed oxidizing water)	d				Yes/No[f] (1 in PT 5)					No		Yes
Sodium dichloroisocyanurate (NADCC)		a			Yes	0	15	22	37	No		Yes
Sodium hypochlorite (NaOCl, NaClO)	a,d	a,d	a	a	Yes	9	37	102	148	No		Yes
Tosylchloramide (N-Chloro 4-methylbenzenesulfonamide / chloramine-T)	a,b	a,c			Yes	0	2	2	4	No		Yes
TPP (Triphenylphosphate)		d			No					No		No
Trisodium phosphate (TSP)	d	d			No					No		No

a. mentioned by experts

b. (Ctgb, 2017c)

c. (GD, n.d.)

d. literature

e. authorisations unknown, since groups of compounds were mentioned rather than individual substances

f. the active ingredient itself is not authorsed, but precursors used to generate the active ingredient in-situ are authorised.

For disinfectants, several criteria were established to come to an intermediate list of active ingredients (Table 8). For cleaning agents, this proved more difficult, since no authorisation by the Ctgb is needed and no further information was available to downsize the list.

Some disinfectants mentioned in the literature, are not used in the Netherlands. Only products authorised by Ctgb are allowed to be used. No unauthorised products were indicated to be used in the Netherlands based on the interviews and questionnaires. Therefore, disinfectants that were mentioned in literature, but were not authorised by the Ctgb in PT 1, 3 and 4 (no products were found in the Ctgb database) were excluded from the intermediate list, because there were no indications of use for the Netherlands.

When residues of active ingredients are not to be expected in food products, the active ingredients were excluded from the intermediate list (based on Biocidal Product Committee (BPC) opinions and Ctgb authorisation reports). For example, some active ingredients quickly evaporate, such as ethanol, or degrade into non-harmful substances, such as peracetic acid (Gezondheidsraad 2016 rapport).

Furthermore, for some active ingredients, experts indicated that there might be human health effects related to the substance. These substances were also included in the intermediate list. In some cases, groups of substances were mentioned to be used. These groups were also placed on the intermediate list. In the next stage, the individual substances of these groups were evaluated.

The approach to include or exclude active ingredients on the intermediate list is depicted below:
1. Is the active ingredient authorised in the Netherlands?
    a. Yes -> question 3
    b. No/unknown -> question 2
2. Is there an indication that the product is used in the Netherlands (based on interviews and questionnaires)?
    a. Yes -> question 3
    b. No -> substance is not included on the intermediate list
3. Residues possible that might cause health problems?
    a. No (e.g. substance rapidly degrades into un-harmful break-down products or evaporates) -> substance is not included on the intermediate list
    b. Yes/Unknown -> substance is included on the intermediate list

The final list of active ingredients and the rationale for inclusion on the intermediate list is indicated in Table 9.

Table 9 *Intermediate list of active ingredients used for disinfection*

Group	Active ingredients used as disinfectants	Used in				Authorised by Ctgb?	Nr of products authorised in PT 1, 3 or 4	Residues possible?
		Horticulture	Poultry	Retail	General			
Chlorine-containing compounds	4-chloro-3-methylphenol (also known as chlorocresol)		a, d			Yes	1	Yes
	Acidified sodium chlorite (ASC)	d	d			Yes	14	Yes
	Chlorhexidine digluconate		a,d			Yes	23	Yes
	Chlorine dioxide	d	d			Yes[f]	Unknown[f]	Yes
	Sodium chloride	d				Yes[f]	Unknown[f]	Yes
	Sodium dichloroisocyanurate (NADCC)		a			Yes	37	Yes
	Sodium hypochlorite (NaOCl, NaClO)	a, d	a,d	a	a	Yes	148	Yes
	Tosylchloramide/N-chloro tosylamide (sold as chloramine-T)	a,b	a,c			Yes	4	Yes
Iodine	Iodine	d	a,d			Yes	31	Yes
Quaternary ammonium compounds	Alkyl (C8-18) dimethylbenzylammoniumchloride (syn. benzalkonium chloride, BAC)		a,c,d	a	a	Yes	56	Yes
	Didecyldimethylammonium chloride (DDAC)	a, d	a,d			Yes	161	Yes
Acids	Aliphatic acids	d				Unknown[e]	Unknown[e]	Unknown[e]
Ozone	Ozone	d				Yes[f]	Unknown[f]	Yes
	Alkylene oxide adducts	d				Unknown[e]	Unknown[e]	Unknown[e]
	Formaldehyde	a	a,c,d			Yes	13	Yes
	Glutaraldehyde	a	a,c,d			Yes	39	Yes
	Naphthalene sulfonates	d				Unknown[e]	Unknown[e]	Unknown[e]
	Potassium peroxymonosulphate (also known as MPS, potassium monopersulphate, potassium caroate)		a			Yes	9	Yes

a. mentioned by experts

b. (Ctgb, 2017c)

c. (GD, n.d.)

d. literature research (section 3.3.1)

e. a group of compounds was mentioned instead of individual substances

f. the active ingredient itself is not authorised, but precursors used to generate the active ingredient in-situ are authorised.

3.5 NVWA Monitoring data

The available 2017 monitoring data of disinfectants showed that quaternary ammonium compounds were measured in several foodstuffs, including, among others, milk-based products, fish products, and meat products (no chicken). Benzalkonium chloride (BAC) -12, -14, and -16, the sum of BAC, didecyldimethylammonium chloride (DDAC), chlorate, and perchlorate were measured in milk powders. From the supplied dataset, it was not possible to extract the number of samples measured and reported for each compound.

The available 2018 data showed that the following biocides were reported to be measured in vegetables such as spinach, eggplant, and green beans: the sum of BAC, chlorate, perchlorate, and quaternary ammonium compounds. Samples were taken from February - May. All results reported for the sum of BACs (n = 52) were shown to be below the LOD of 0.01 mg/kg. The total number of samples analysed and reported for the other compounds is unknown. Seven measurements were reported above the LOD for either chlorate or perchlorate. For chlorate, these were in a mixed trio salad (0.038 mg/kg) and in spinach (0.320 mg/kg). For perchlorate, the reported concentrations in spinach (n = 3) ranged from 0.038 - 0.126 mg/kg. Also, one sample of endive showed a perchlorate concentration of 0.062 mg/kg and one sample of arugula (rocket) 0.108 mg/kg. These same four residues were also reported to be measured in foodstuffs like baby and infant foods (e.g. milk or grain-based), as well as in paprika/chilli/cayenne powders.

Overall, the following compounds were reported to be tested for 2017 – 2018 by the NVWA in foodstuffs:
- Benzalkonium chloride (BAC) (sum);
- Benzalkonium chloride (BAC) -12, -14, and -16;
- Chlorate;
- Didecyldimethylammonium chloride (DDAC);
- Perchlorate; and
- Quaternary ammonium compounds.

Chlorate and perchlorate were reported above the LOD in vegetables. These could be present due to several reasons, such as from the use of chlorine-based disinfectants. However, they can also be present due to the use of chlorinated water, contaminated process additives or perchlorate can also be from the use of fertilisers. Chlorine-based disinfectants have been included on the intermediate list of disinfectants (chlorine dioxide, sodium hypochlorite, etc.). BAC, DDAC, and quaternary ammonium compounds were also included in the intermediate list of disinfectants.

The substances that were included in the monitoring were already included in the intermediate list of disinfectants. Analysis of these monitoring data did not result in additional substances to be added on the intermediate list for disinfectants.

3.6 Questionnaire and interview results on issues and concerns with cleaning agents and disinfectants used (Phase I)

Next to questions on the active ingredients used in cleaning and disinfectants as described in 3.3.3, the questionnaire of phase I also included a question regarding difficulties encountered in cleaning and disinfection, a question on possible human health problems related to cleaning and disinfection, a question on preventing the use of unauthorised products, and a question on the practical application of chemical agents. The outcome of these questions as indicated by the experts is summarised below.

3.6.1 Persistent problems in cleaning and disinfection

The horticulture sector mentioned that biofilm formation on machines and conveyor belts hampers cleaning and disinfection.

In the poultry sector, *Salmonella* spp., *Campylobacter* spp., bird flu and chicken mites were mentioned as persistent problems. In relation to bird flu, chloride products were mentioned to be effective towards viruses and bacteria. It is recommended to disinfect regularly with a mild product and once per week with a more aggressive product to prevent resistance. Resistance was also mentioned with respect to the use of low concentrations of quats. However, in practice, people rather use high concentrations of chemical agents than too low concentrations, so resistance is not likely to occur. With respect to mites, experts indicated that there is no method or product to tackle this problem. This could promote the use of unauthorised products.

Furthermore, one expert indicated that aging of stables and surfaces makes cleaning or disinfection more difficult, as surfaces are then no longer smooth but contain cracks and crevices that are difficult to reach with cleaning agents and disinfectants. Therefore, often formaldehyde will be used, which breaks down slowly resulting in a permanent disinfection.

For the retail, challenges mentioned are places that are difficult to clean, for example, edges and cavities. Material that is not made of stainless steel is also more difficult to clean.

3.6.2 Active substances that may cause human health problems

The experts were asked which active substances potentially could cause a problem for human health in case residues end up in the final products (Annex 3). The most common reply was that there is no risk, because only authorised products are used. Experts explained that when authorised products are used in the intended way, human health problems are not expected as these products passed the risk evaluation of the Ctgb. Furthermore, rinsing will remove all potential residues and rinsing can be checked by food producers by checking the pH. However, it is unknown whether the pH is always checked. According to the experts interviewed, cleaning agents and disinfectants are not always used as intended. For example, experts indicated that cleaning is not always performed before disinfection. Furthermore, rinsing after disinfections is also mentioned to be skipped in some cases.

Some substances were mentioned to potentially cause human health problems:
- Ethanol
- Didecyldimethylammoniumchloride
- Sodium hypochlorite
- Formaldehyde (formalin)
- Chlorine
- Acids

This was not further substantiated during the interviews or in the questionnaire. The information was included in the long-list of disinfectants in Table 8.

3.6.3 Prevention of unauthorised substances

Most of the persons that filled in the questionnaire or that were interviewed, mentioned that only authorised cleaning and disinfection products will be used. Furthermore, the food processing industry indicated that they have their own control system and inspections of suppliers. However, an RIVM report indicates that unauthorised products are available (RIVM, 2013). The report describes a database of the use of biocides in various economic sectors. This database distinguishes between available authorised products and available non-authorised products. PT3 products in primary production of poultry were also included in this study. Of the total number of 223 available products in this sector, 92 were unauthorised products (41%). Of these 92 unauthorised products, 32 products were previously authorised in the Netherlands, 25 products were authorised in Belgium and 35 products were available online. However, the actual use of the products was not known.

Furthermore, in 2019 there was an incident in the Netherlands with the use of a product containing chlorine dioxide for disinfection of poultry stables, the use of this product was not authorised (NieuweOogst, 2019).

The NVWA was interviewed and they explained that the NVWA periodically performs inspections on cleaning and disinfection locations at slaughterhouses and assembly centres (R&O plaats). The NVWA inspectors check whether cleaning agents are present at the R&O place and whether the disinfectants used are approved by Ctgb (PT3). In case the inspector has doubts about the disinfection procedure, this is checked using indicator paper. If cleaning and disinfection takes place during the inspection, the inspector checks the procedures followed. Sometimes, samples are taken to check if the solutions used have the right concentrations. In 2018, only once an unauthorised product was found (as indicated by an expert from the NVWA). This product was authorised in Belgium, but not in the Netherlands. These cases are reported to the 'Inspectie Leefomgeving en Transport' (ILT, human environment and transport inspectorate). Furthermore, during veterinary inspections, the NVWA occasionally finds combined products for cleaning and disinfection at farms that are not allowed for use as PT3 biocide for veterinary hygiene purposes and for use in transport equipment for animals. The Intelligence and Investigation Service of the NVWA (the IOD) works together with branch organisations in order to identify illegal use of cleaning agents and disinfectants. They monitor the trade of cleaning and disinfection agents; however, this is more difficult for internet sales. Some products are also sold via Bol.com, while these products are not meant for consumer use. Apart from information from inspections and the IOD, the NVWA can also get information from the general public in case they report unauthorised products.

3.6.4 Practical application of cleaning agents and disinfectants

In order to ensure the right application of chemical agents for cleaning and disinfection, suppliers of cleaning and disinfection agents provide hygiene plans, checklists, easy-to-read wall charts, product information and use instructions. Furthermore, some of the suppliers give trainings to users of their products; there are also online trainings and webinars. Apart from trainings and labelling, misuse of products is prevented by dosing systems and lock-and-key systems to prevent misuse of the products. These dosing systems are regularly checked by the suppliers. The food processing industry mentioned that only trained people are allowed to work with cleaning and disinfection products. Furthermore, processors indicated that they can check the pH on the presence of chemical residues and Adenosine Triphosphate (ATP) as an indicator for the presence of microorganisms to evaluate the efficacy of the cleaning and disinfection performed. Experts indicated that in slaughterhouses these checks are often performed, but in the retail this is less common. During audits, the NVWA also performs checks on the proper use of authorised products.

Experts indicated that despite all these precautionary measures, people can make mistakes and instructions cannot be followed due to time constraints. In processing and retail, experts indicated that cleaning before disinfection is sometimes skipped due to time constraints. Furthermore, several experts mentioned that some labels are very difficult to understand. Producers of cleaning agents and disinfectants should thus improve this. Experts who responded to the general questionnaire also indicated that there is a lack of knowledge on cleaning and disinfection by farmers and more training is needed on this topic. These issues were also found in a recent study performed by HAS students amongst dairy farmers (Kennisnetwerk Biociden, 2018). According to an expert interviewed, research from the GD showed that 90% of the farmers did not know the difference between cleaning and disinfection, but whether this means that the products are also not used properly is unknown. When experts were asked to name the cleaning and disinfectants used, this also showed that these substances are sometimes mixed up (see 3.3.3)

3.6.5 Conclusion

During the interviews and questionnaires, experts frequently indicated that only authorised products are used, and therefore no problems for human health are expected. However, the database of RIVM has showed that several unauthorised disinfection products were available online in 2012, but information on the actual use of these products is not available.

The large suppliers of cleaning and disinfection products provide training, product information, and advice to ensure the proper use of their products. Some experts indicated possible incorrect use of cleaning and disinfection products. Furthermore, people tend to use higher concentrations of chemical agents than recommended. For most products, it is prescribed that you have to rinse after use of the product as this will remove all potential residues. Experts indicated that sometimes cleaning before disinfection or rinsing steps can be skipped. There is also a risk that products authorised products will be wrongly used for an unauthorised application. Furthermore, the expert study showed that the terms 'cleaning' and 'disinfection' are frequently intertwined. At farm level, more training seems necessary on cleaning and disinfection. Experts indicated that when no authorised product is available for a certain contamination or problem, this will promote the use of unauthorised products.

3.7 Questionnaire and interviews on cleaning agents for poultry (Phase II)

Since a further prioritisation of the active ingredients in cleaning agents on the long-list was not possible in phase I of this study, additional interviews and questionnaires were executed during phase II. This phase focussed on the use of cleaning agents in the poultry chain using a questionnaire and interviews.

3.7.1 Questionnaire (Phase II)

From the 72 sent questionnaires on cleaning agents in the poultry chain, only experts related to poultry stables responded, 12 in total. However, six persons indicated that they could not answer the questions, because the questions did not apply to their field of work (four persons), or because they only work with disinfectants (two persons), which was out of scope of this questionnaire in phase II.

A list of 22 substances (long-list of cleaning agents for poultry, as indicated in Table 7) was included in the questionnaire, consisting of four questions in total. The respondents were asked to tick the boxes of the cleaning agents that are used in the stables, for cleaning hands or other reasons. Specification on the latter category was asked in the question following that. Out of the six respondents, four persons indicated that sodium hydroxide is used to clean the stables. One of them mentioned that this agent is also used for cleaning hands and another person answered that it is used for cleaning feeding and drinking systems. Further, chlorine, EDTA, nitric acid, and phosphoric acid were mentioned, each one time, to be used to clean stables. Hydrogen peroxide was indicated once as cleaning agent for the water pipes in the stables. One other respondent explained that the product with the commercial name Kenosan is used and another respondent only uses the product Safefoam. These products contain active ingredients, which are all listed on the long-list of active ingredients in cleaning agents.

Rinsing with water always follows after cleaning according to four respondents; one person did not answer the question. One person, who indicated that sodium hydroxide and chlorine are used in the stables and hydrogen peroxide in water pipes, explained that it is not always necessary to rinse with water afterwards. Furthermore, this person added that disinfection after cleaning is a choice of the customer. Two other respondents stated that disinfection after cleaning is always applied and the remaining respondents stated that disinfection does not always follow the cleaning.

3.7.2 Interviews (Phase II)

Seven persons were contacted for an interview (Annex 5), four responded positively and were interviewed. These persons were connected to the poultry chain in general, one person specifically to primary production. The other three persons did not respond, also not after one or two reminders. The interviews were performed to obtain more insight in the process of cleaning in the poultry chain; the type of products for different applications, concentrations, and frequency of use. Furthermore, questions were asked about the type of mistakes that could take place with cleaning, whether the performance of the cleaning and disinfection activities is checked and if residues of cleaning agents could be present in the final product. All questions were asked during the interviews; however, not all experts could answer all questions.

One expert indicated that companies need to be certified specifically for cleaning and disinfection on poultry farms, separately. It was mentioned that for farmers the differences between cleaning and disinfection are not always clear. Overall, disinfection is much faster and easier to perform than cleaning the stables which should be done prior to disinfection. One expert indicated that all active ingredients as listed in the questionnaire (long-list) are used in cleaning agents in the poultry chain.

Cleaning in the poultry stables
Experts indicated that when the animals have been transported to the slaughterhouse and the stable is empty, manure will be removed and the stable will be cleaned. In some stables, it is possible to remove all the materials before the cleaning. The cleaning is normally done by rinsing the stable and applying cleaning agents. One common techniques is foaming of the stable, followed by rinsing. It is also possible to dry-clean the stables, i.e. the stables are swept and blown clean. The dry-cleaning is often done for laying hen farms.

One of the experts estimated that 50% of the farmers use an external company to clean the stables and 70% of the farmers to disinfect them.

Choice of cleaning agents
The chemical safety of cleaning agents has to be checked by the suppliers. The farmers trust their own suppliers. The choice of the type of cleaning agents will be done by, or in consultation with the farmers. There are many different products on the market; most farmers have their own preferences depending on their own suppliers. The choice of the type of cleaning agent depends on the type of fouling in the stables. Most of the dirt is manure. Then, an alkali cleaning agent will be used (99%). Most of the cleaning agents are based on sodium hydroxide (concentrations are 2-5%). Other cleaning agents are used in case of for example *Salmonella* contamination. Then formaldehyde will be used.

The experts mentioned that cleaning of materials and trucks used for transport is well arranged by the slaughterhouses. For cleaning of hands, normal hand soap is used. Only in slaughterhouses, disinfection of hands is normal. Experts mentioned that in egg packing stations the hygiene is less. However, this is more a risk for contamination between companies than for food safety.

For most of the interviewed experts it was not possible to give an overview of the active ingredients and concentrations used for cleaning in the poultry chain.

Hygiene control
Farmers are obligated to take hygiene samples once per year. Furthermore, cleaning is normally visually checked.

Possible mistakes
It is important for farmers to clean properly in order to reduce the use of antibiotics. Therefore, cleaning is often done by external companies. The risks of mistakes are higher when farmers perform the cleaning themselves.

The concentration of cleaning agents used may vary if the dosing equipment does not work properly. In case of foam cleaning, it is important to rinse after 30-90 minutes, before the foam is completely dried.

Experts indicated that products should be available for specific problems. An active ingredient should, thus, not be prohibited when there is no alternative available as this would promote the use of unauthorised products. Formaldehyde is, for example, the only possible treatment for *Salmonella* contamination.

Possible contact with chicken
There is hardly any contact between chickens and cleaning agents, because the materials treated with cleaning agents must be rinsed after cleaning. Furthermore, the stable is normally empty for a few days to prepare the stable before new chickens will arrive. Overall, it was indicated by the experts that cleaning agents are used following the product instructions.

After disinfection you have to rinse; however, this is not always done as was stated by one of the experts. In case of cleaning, it is obvious that you have to remove the foam for instance. In case of disinfection, most products need a rinse afterwards; however, the visual need is less.

3.7.3 Conclusion

Experts indicated that they are not aware of the use on unauthorized substances. However, experts indicated again that when no authorised product is available for a certain contamination or problem, this will promote the use of unauthorised products.

Rinsing after cleaning and disinfection is often necessary. It is less likely that rinsing after cleaning will be skipped, because of the need to remove the foam. The questionnaire and interviews (phase II) confirmed the list of cleaning agents for poultry as identified in phase I of this research. Sodium hydroxide is identified as the most frequently used cleaning agent in the poultry chain.

3.8 Efficacy, by-products and toxicological profile of active ingredients of disinfectants on the intermediate list for poultry (Phase II)

Out of the 18 active ingredients for disinfections on the intermediate list for poultry, egg, leafy vegetables, and sprouts chains (Table 9), thirteen active substances were concluded to be relevant in the poultry chain. These thirteen ingredients were further assessed in phase II of the study: (i) on their efficacy in terms of their potential log reduction of pathogens, (ii) possible by-products or residues of the active ingredients, and (iii) the toxicological profile of the active ingredients concerning human health effects. For each of the active substances, unless stated otherwise, an example of a PT 1 (human hygiene), PT 3 (veterinary hygiene), or PT 4 (food and feed area) product coming from the Ctgb website, was also evaluated to provide further insight into the use of such active ingredients authorised on the Dutch market. When available, additional information from the ECHA BRC opinions on the human health risk given the exposure scenarios studied was provided. The main findings regarding toxicological profile and human health effects of the active ingredients on the intermediate list are summarised in Table 10, all detailed information can be found in the following paragraphs.

Table 10 *Summary of toxicological information, by-products and human health effects of active ingredients used as disinfectants*

Group	Active ingredients used as disinfectants	By products	Toxicological information	Human health effects
Chlorine-containing compounds	4-chloro-3-methylphenol (also known as chlorocresol)		NOAEL: 200 mg/kg bw/day (oral route - repeated dose toxicity) NOAEL: 30 mg/kg bw/day (oral route - fertility and developmental toxicity)	Exposure is acceptable or not expected in case of proper use.
	acidified sodium chlorite (ASC)	chlorite[a] chlorate[a] chlorine dioxide semicarbazide	NOAEL: 2.9 mg/kg bw/day (developmental/ teratogenicity) TDI: 0.03 mg/kg bw/day	Hazardous by-products. Chlorate residues are considered a relevant dietary exposure route from the use of chlorine disinfectants in the food area; it needs to be further investigated. No safety concern in case of proper use. However, there is some concern for semicarbazide.
	chlorine dioxide	chlorite[a] chlorate[b]	NOAEL: 200 mg/L TDI: 0.03 mg/kg bw/day	Hazardous by-products. Chlorate residues are considered a relevant dietary exposure route from the use of chlorine disinfectants in the food area; it needs to be further investigated. No safety concern in case of proper use.
	chlorhexidine digluconate		LOAEL: 8.88 mg/kg bw/day (repeated dose toxicity)	No risk is anticipated for the general population through foods such as milk or meat; exposure to residues in food is not expected
	sodium dichloroisocyanurate (NADCC)		NOAEL: 115-914 mg/kg bw/day (repeated dose toxicity)	No safety concern in case of proper use.
	sodium hypochlorite (NaOCl, NaClO)	chlorate[b]	NOAEL: 16.7-57.2 mg/kg bw/day (repeated dose toxicity)	Hazardous by-products. Chlorate residues are considered a relevant dietary exposure route from the use of chlorine disinfectants in the food area; it needs to be further investigated. No safety concern in case of proper use.
	Tosylchloramide/N-chloro tosylamide (sold as chloramine-T)		NOAEL: 214-248 mg/kg bw/day (repeated dose toxicity)	Secondary exposure cannot be excluded. No safety concern in case of proper use.
Iodine	iodine		UL: 600 µg/day (adults)	No safety concern in case of proper use.

Group	Active ingredients used as disinfectants	By products	Toxicological information	Human health effects
Quaternary ammonium compounds (Quats)	alkyl (C8-18) dimethylbenzylammoniumchloride (syn. benzalkonium chloride)		ADI: 0.1 mg/kg bw/day ARfD: 0.1 mg/kg bw	Exceedance of maximum residue levels in e.g. milk. Most food commodities were unlikely to pose an acute health risk for European consumers except for milk/milk products.
	didecyldimethylammonium chloride (DDAC)		NOAEL: 27.3–45.5 mg/kg bw/day ADI: 0.1 mg/kg bw/day ARfD: 0.1 mg/kg bw	Exceedances of maximum residue levels in e.g. milk and ice, not in poultry food products. Residues are unlikely to occur. However, there is a lack of data.
Others	formaldehyde		NOAEL: 10-25 mg/kg bw/day (repeated dose toxicity)	Formaldehyde is carcinogenic in humans. Residues of formaldehyde were found in food products. However, negligible exposure from background levels in food products.
	glutaraldehyde		NOAEL: 15-46 mg/kg bw/day (repeated dose toxicity)	Only trace amounts of glutaraldehyde may accidentally occur on the surface of food. No adverse health effects are expected for the general public
	potassium peroxymonosulphate (also known as MPS, potassium monopersulphate, potassium caroate)		NOAEL: 200 mg/ kg bw/day (repeated dose toxicity)	Data on residues is limited. Secondary exposure is expected to be limited.

NOAEL: no-observed-adverse-effect-level; TDI: tolerable daily intake; UL: tolerable upper intake level; ADI: acceptable daily intake; ARfD: acute reference dose; LOAEL: lowest-observed-adverse-effect level

a Chlorate ARfD: 36 μg/kg bw, TDI: 3 μg/kg bw/day

b Chlorite, TDI: 0.03 mg/kg bw/day

3.8.1 Chlorine-containing compounds

Chlorate is a by-product in case of use of chlorine, chlorine dioxide or hypochlorite for disinfection. It is reported that in many fruit and vegetables chlorate levels exceed the default MRL of 0.01 mg/kg. In Europe, the main contributor to dietary exposure of chlorate is drinking water. Chronic dietary exposure to chlorate in younger age groups with high exposure (P95) will exceed the tolerable daily intake (TDI) of 3 μg/kg bw/day, this is a concern for children with mild to moderate iodine deficiency. Acute exposure did not exceed the acute reference dose (ARfD) and did not indicate a concern (EFSA, 2015b).

3.8.1.1 (Acidified) sodium chlorite

According to a press release from the German Federal Institute for Risk Assessment (BfR), proposals for the use of antimicrobial substances, of which acidified sodium chlorite was included, for decontaminating poultry carcasses have been rejected by the member states (BfR, 2012d). In the EU, only the use of potable water is allowed to remove surface contamination of products of animal origin (Regulation (EC) No. 853/2004).

Microbial efficacy

For sodium chlorite, the EC_{50} for microorganisms was 100 mg/L (ECHA, 2019j). The EC_{50} is the effective concentrations that kills half of the bacterial population.

EFSA has assessed the possible effect of acidified sodium chlorite on the emergence of antimicrobial resistance. It was concluded that no published data were available to conclude that its use to remove microbial contamination of poultry carcasses, given the proposed treatments, would lead to acquired reduced susceptibility to the substance, nor would it lead to resistance to therapeutic antimicrobials (EFSA, 2008b).

Formation of residues and/or by-products
Acidified sodium chlorite can generate chlorous acid and other species like chlorite, chlorate, and chlorine dioxide. The proportion of these depends on the pH of the mixture. For instance, the formation of chlorite is about 31% at pH 2.3, 10% at pH 2.9, and 6% at pH 3.2. Moreover, semicarbazide in nitrogen-containing products, following hypochlorite treatment, has been reported. Acidified sodium hypochlorite may interact with organic matter in solution or with protein and fat compounds in the poultry carcasses, causing different reaction products (EFSA, 2006a).

According to an EFSA opinion on the treatment of poultry carcasses with products like acidified chlorite, no chlorinated organics had been found post-treatment. Semicarbazide was, moreover, not detected (LOD 1 µg/kg) following the immersion of poultry carcasses with acidified sodium chlorite. The initial health concerns about semicarbazide were no longer deemed relevant, and it was reported not to be genotoxic *in vivo*. EFSA reported that treatment with acidified sodium chlorite, given the described conditions, would not be a safety concern. Also, spraying, versus dipping or immersion treatments, would help reduce the exposure to residues and by-products that may occur (EFSA, 2006a). However, the EFSA Panel on Contaminant sin the Food Chain (CONTAM) reviewed the risks of protein-bound residues of nitrofurazone, from which semicarbazide can be released. They concluded that there is "limited evidence that semicarbazide is carcinogenic in mice, but not in rats" and "that there is sufficient evidence to conclude that semicarbazide is genotoxic *in vitro*, but that no conclusion on genotoxicity *in vivo* can be drawn" (EFSA, 2015c). Furthermore, it is possible that this hydrazine compound could cause stable protein-bound residues that can be an explanation for false-positive test results observed for nitrofurazone, which is based on release of semicarbazide from protein-bound residues (EFSA, 2015c).

Toxicological profile
In the general population, the derived no effect level (DNEL) for oral exposure of sodium chlorite, the systemic long-term systemic effects, as well as acute/short term effects, was 29 µg/kg bw/day and is based on the most sensitive developmental toxicity/teratogenicity study (ECHA, 2019j). Acute toxicity from oral exposure showed an LD_{50} range of 212 – 2,000 mg/kg bw (rat). Dermal acute toxicity showed an LD_{50} range of 100 – 2,000 mg/kg bw (rabbit) (ECHA, 2019j). Repeated dose toxicity for the oral route given systemic effects showed a no-observed-adverse-effect-level (NOAEL) of 10 mg/kg bw/day (subchronic, rat) (ECHA, 2019j). For genetic toxicity (*in vitro* and *in vivo*), test results were negative. Reproductive toxicity via the oral route was reported for effects on fertility (NOAEL 2.9 mg/kg bw/day – chronic, rat) and developmental toxicity for the oral route of exposure showed a NOAEL of 9 mg/kg bw/day (subacute, rabbit) (ECHA, 2019j). Data on carcinogenicity were not summarised for the brief profile on sodium chlorite. Data on neurotoxicity, immunotoxicity, and endocrine disruption (*in vivo*) were not provided (i.e. the registrant did not provide data) (ECHA, 2019j).

The TDI of acidified sodium chlorite for consumers is 0.03 mg/kg bw/day. From EFSA's OpenToxDatabase, no data on genotoxicity was available (Bassan et al., 2018).

For the chlorate, an ARfD for consumers was derived, being 36 µg/kg bw, while the TDI was set at 3 µg/kg bw/day (EFSA, 2015a). Chlorate inhibits the uptake of iodine by the thyroid gland and can as such cause hypothyroidy. Genotoxicity was considered negative (or ambiguous) (EFSA, 2015a). (EFSA, 2015) (Bassan et al., 2018). For chlorite, the TDI for consumers is 0.03 mg/kg bw/day. No data (or ambiguous data) on genotoxicity was available.

No information to support the hazard characterisation (e.g., of reference values) or genotoxicity of chlorous acid were available in EFSA's OpenFoodTox database on chemical hazards (Bassan et al., 2018).

3.8.1.2 Chlorine dioxide

According to a press release from the German Federal Institute for Risk Assessment (BfR), proposals for the use of antimicrobial substances, in which chlorine dioxide was included, for decontaminating poultry carcasses have been rejected by the member states (BfR, 2012d).

Microbial efficacy

Chlorine dioxide toxicity to microorganisms showed an EC_{50} (3h) of 10.7 – 1000 mg/L. Therefore the lowest EC_{50} for microorganisms is 10.7 mg/L (ECHA, 2019a).

The EFSA assessed the possible effect of chlorine dioxide on the emergence of antimicrobial resistance, finding that no published data were available to conclude that its use to remove microbial contamination of poultry carcasses, given the proposed treatments, would lead to acquired reduced susceptibility of the substance, nor would it lead to resistance to therapeutic antimicrobials (EFSA, 2008b).

An example product, from the Ctgb website, is Bello Zon Verdund, which has the active substances sodium chlorite (7.5%) and hydrochloric acid (9%) (Ctgb, 2012a). The efficacy tests were performed with "standard organisms, with the required interfering substance and the required test temperatures" (Ctgb, 2012a). For instance, for PT 4, quantitative suspension tests against bacteria were evaluated with 10 ppm chlorine dioxide with a contact time for 5 minutes and 5 ppm chlorine dioxide and a contact time of 15 minutes. Consequently, the contact time is reported on the WG/GA (in Dutch: Wettelijk Gebruiksvoorschrift en Gebruiksaanwijzing, in English: Legal Conditions for Use and the Directions for Use). Further details can be found in section 4.3 of the Ctgb evaluation. Since the efficacy tests were performed under clean conditions, surfaces must be cleaned before disinfection (Ctgb, 2012a).

Formation of residues and/or by-products

Chlorine dioxide is very reactive. Chlorate and chlorite are the primary by-products from its use. The formation of chlorate and chlorite increases (3:7 ratio) with the increased concentration of chlorine dioxide and/or treatment time. Research showed that no halomethanes were reported to form when chlorine dioxide was used to treat drinking water. Chlorine dioxide may interact with organic matter in solution or with protein and fat compounds in the poultry carcasses, causing different reaction products (EFSA, 2006a). According to an EFSA opinion on the treatment of poultry carcasses with products like chlorine dioxide, treatment with chlorine dioxide, given the described conditions, would not be a safety concern. Also, spraying, versus dipping or immersion treatments, would help reduce the levels of residues and by-products that may occur (EFSA, 2006a).

Another EFSA opinion, concerning the use of gaseous chlorine dioxide as a preservative in cold food storage, concluded that the consumption of foods treated under the conditions proposed by the applicant would not be of a safety concern (EFSA, 2016).

For Bello Zon Verdund, PT 4 applications include its use as a disinfectant for water systems in municipal buildings, for water systems in poultry and livestock industry used exclusively for animals, as well as for cleaning procedures (CIP disinfection) in the food industry. The indirect exposure to residues of chlorine dioxide could not be excluded (see evaluation Table T.1 for details). The general population may be exposed via residues in food or drinking water (Ctgb, 2012a). Secondary exposure from the use of Bello Zon Verdund of "both professionals and the general public due to treatment of systems in food industry and the poultry and livestock sector with chlorine dioxide formed using Bello Zon Verdund cannot be excluded" (Ctgb, 2012a). However, exposure of residues in food is expected to be low, while absorption into the bloodstream is unlikely and systemic availability very low (Ctgb, 2012a).

Toxicological profile

For the general population, no thresholds for systemic long-term or acute/short-term effects for oral, inhalation, dermal, or eye exposure were identified (ECHA, 2019a). Acute toxicity from oral exposure had showed an LD_{50} of 94 mg/kg bw (rat) (ECHA, 2019a). Repeated dose toxicity for the oral route showed a NOAEL (rat) of 200 mg/L drinking water (ECHA, 2019a), corresponding to 10 mg/kg bw/day (based on a default factor of 0.05 (EFSA, 2012b)). Data on genetic toxicity, carcinogenicity, toxicity to reproduction, and neurotoxicity were not considered, while data on immunotoxicity and endocrine disruption (*in vivo*) were not provided (ECHA, 2019a).

The TDI for chlorine dioxide for consumers was set at 0.03 mg/kg bw/day. No data or ambiguous data on genotoxicity were available in EFSA's OpenFoodTox database (Bassan et al., 2018).

When considering indirect exposure to chlorine dioxide from the use of Bello Zon Verdund, no adverse health effects are expected (Ctgb, 2012a).

3.8.1.3 Sodium dichloroisocyanurate (syn. troclosene sodium)

Sodium dichloroisocyanurate can also be listed as sodium dichloroisocyanurate dihydrate.

Microbial efficacy

Sodium dichloroisocyanurate toxicity to microorganisms showed an EC_{50} (3 h) of 51 – 4,500 mg/L and a no observed effects concentration (NOEC) (3 h) of 10 – 2,700 mg/L (ECHA, 2019m).

On the Ctgb website, four products containing troclosene sodium are listed for use under PT 1, PT 3, or PT 4. For instance, the product Kay-5 Sanitizer is made up of 6% (w/w) sodium dichloroisocyanurate dihydrate (3.3% active chlorine) for use in PT 4. In the efficacy evaluation, two studies were provided that were considered suitable and acceptable (Ctgb, 2013). Quantitative suspension tests (phase II, step 1) against bacteria and yeasts were evaluated, given the required interfering substances and test temperature. The dose and contact time on the WG/GA is 600 ppm (previously 180 ppm) and 1-2 min to 5 min. Since the efficacy tests were performed under clean conditions, surfaces must be cleaned before disinfection (Ctgb, 2013).

Formation of residues and/or by-products

In the Ctgb evaluation of Kay-5 Sanitizer, there is "adequate residue analytical methodology available to monitor residues of the biocide taking into account all possible exposure scenarios and the toxicity of the active substance(s)" (Ctgb, 2013), however, no further details are given. Concerning possible indirect exposure from the use of this product, exposure of food or drinks to residues is not expected, and no health effects are expected "after use of teat dip/spray formulations containing cyanuric acid, sodium chlorite and chlorine" (Ctgb, 2013). According to the instructions for use, the disinfectant is for the disinfection of hard surfaces of soft drink appliances, milkshake installations, ice machines, and kitchen tools. Before application, the surfaces and tools to be disinfected need to be thoroughly cleaned, and therefore after the use of a cleaning agent they need to be rinsed with clean water and excess water removed. Further detailed instructions are available on the application (solution), dose, and minimum contact time. Notably, the solution must be renewed after every cleaning cycle (Ctgb, 2013).

Toxicological profile

For the general population, the DNEL for oral exposure of systemic long-term and acute/short-term effects were unavailable (ECHA, 2019m). Acute toxicity from oral exposure showed an LD_{50} range of 1,671 – 2,094 mg/kg bw (rat) (ECHA, 2019m). Repeated dose toxicity for the oral route showed NOAELs of 115 - 914 mg/kg bw/day (rat) and 1,523 – 1,582 mg/kg bw/day (mouse) (ECHA, 2019m). Data on genetic toxicity, carcinogenicity, and effects on reproduction were not considered, while data on neurotoxicity, immunotoxicity, and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019m).

Overall, concerning human health, no adverse health effects are expected for the general public, given the indirect exposure to sodium dichloroisocyanurate dihydrate (cyanuric acid, active chlorine, and hypochlorite), resulting from the application of Kay-5 sanitizer as prescribed according to the WG/GA (Ctgb, 2013).

3.8.1.4 Sodium hypochlorite

Microbial efficacy
Sodium hypochlorite toxicity to microorganisms showed an EC_{50} (3 h) range of 3 – 563 mg/L, while another studied showed a NOEC (3 h) range of 41.1 – 300 mg/L and an EC_{10} (3 h) range of 46.9 – 342 mg/L (ECHA, 2019k).

On the Ctgb website, 87 products containing sodium hypochlorite are listed for use under PT 1, PT 3, or PT 4. For instance, the product AseptoSupra is made up of 7.9% (w/w) active chlorine released from sodium hypochlorite for use in PT 4. Six studies were provided and used in the assessment. The studies assessed test organisms for bacteria (excluding mycobacteria and bacterial spores), resulting in > 5 log reductions, while for yeasts, this resulted in > 4 log reductions. These studies, for phase II, steps 1 and 2, applied the most challenging test conditions resulting in the required log reduction, as mentioned (Ctgb, 2017a).

Formation of residues and/or by-products
In the BRC opinion on active chlorine released from sodium hypochlorite for PT 4, the human health scenarios evaluated made a note of an indirect exposure via food. For instance, although residues formed on surfaces from aqueous solutions of chlorine are assumed negligible, chlorate residues are considered a relevant dietary exposure route from the use of active chlorine as drinking water and/or food area disinfectant. In brief, the concern for chlorate residues in food needs to be further addressed in legislation on drinking water and/or food hygiene. Given the absence of such guidance, an assessment of disinfection by-products has not been performed (ECHA, 2016a).

In the Ctgb evaluation of AseptoSupra, residue analytical methods are required to detect residues in food or feed of plant or animal origin. These fully-validated analytical methods (for PT 4), for residues of both active chlorine and relevant metabolite chlorate, have been requested for monitoring purposes and to estimate human and animal exposures (Ctgb, 2017a). According to the instructions for use, the agent is intended for the combined cleaning and disinfection of milking installations on the farm given CIP. AseptoSupra should be applied through an automated dosing system. Further detailed instructions are available, e.g. on the operation instructions, dose (0.7%), minimal exposure time (10 min), and frequency of use (Ctgb, 2017a).

Toxicological profile
For the general population, the DNEL for oral exposure of systemic, long-term effects was 260 µg/kg bw/day, while the systemic, acute/short-term effects were considered a low hazard and, consequently, no threshold was derived (ECHA, 2019k). Acute toxicity from oral exposure showed an LD_{50} of 1,100 mg/kg bw (rat) (ECHA, 2019k). Repeated dose toxicity for the oral route showed NOAELs of 16.7 – 57.2 mg/kg bw/day (rat) and 34.4 mg/kg bw/day (mouse), while lowest-observed-adverse-effect levels (LOAELs) were 16.7 – 114.4 mg/kg bw/day (rat) and 34.4 mg/kg bw/day (mouse) (ECHA, 2019k). Data on genetic toxicity, carcinogenicity, and effects on reproduction were not considered, while data on neurotoxicity, immunotoxicity, and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019k).

An EFSA conclusion on the use of sodium hypochlorite was found; however, the focus was on irrigation water during mushroom cultivation. No significant amounts of sodium hypochlorite were expected. No specific studies evaluating sodium hypochlorite and its reaction products in mushrooms during harvest had been submitted. A quantitative consumer risk assessment through dietary intake was not requested. Other EFSA reports specific to poultry were not found. An acceptable daily intake (ADI) or ARfD for consumer exposure could not be derived (EFSA, 2012a).

BRC opinions on the approval for active chlorine released from sodium hypochlorite for PT 1, PT 3, and PT 4 are available. For PT 1, the human health and environment exposure scenarios assessed had acceptable risks identified (ECHA, 2016a). For PT 3 and PT 4, human health exposure scenarios that were assessed had acceptable risks when 'appropriate' risk mitigation measures are included, like the use of personal protective equipment or respiratory protective equipment, to prevent local effects. Details on these scenarios can be found in the BRC opinions (ECHA, 2016b, 2016c).

Concerning human health, no adverse health effects are expected for the general public given the indirect exposure to active chlorine generated from sodium hypochlorite or dietary exposure to chlorate resulting from the application of AseptoSupra as prescribed according to the WG/GA (Ctgb, 2017a).

3.8.1.5 Tosylchloramide (N-Chloro 4-methylbenzenesulfonamide)

Microbial efficacy
Tosylchloramide toxicity to microorganisms showed an EC_{50} (3 h) of 37 mg/L and an EC_{10} (3 h) of 14 mg/L, while in another study an EC_{50} (5 min) of 5 – 1,000 mg/L was reported (ECHA, 2019l).

On the Ctgb website, three products containing tosylchloramide sodium are listed for use under PT 1, PT 3, or PT 4. For instance, the product Boxclean is made up of 0.3% (w/w) tosylchloramide sodium (N-chloro-4-methylbenzenesulfonamide, sodium salt) for use in PT 3. The available information on the effects on target organisms and efficacy was 'sufficient' to evaluate the efficacy of Boxclean (Ctgb, 2012b). In brief, bactericidal and yeasticidal efficacy was demonstrated at a contact time of 30 h and a dose of 400 g/m^2. "When used in accordance with the proposed label (WG/GA), it is effective in controlling bacteria (excluding mycobacteria and bacterial spores) and yeasts on moist floor surfaces in accommodations for animals" (Ctgb, 2012b).

Formation of residues and/or by-products
In the Ctgb evaluation of Boxclean, there is "adequate residue analytical methodology available to monitor residues of the biocide taking into account all possible exposure scenarios and the toxicity of the active substance(s)" (Ctgb, 2012b), however, no further details are given. Concerning possible indirect exposure from the use of this product, secondary exposure cannot be excluded. For instance, livestock will eat granules/powders from the floor, and dermal exposure of animals lying on the stable floor is possible, meaning the presence of tosylchloramide sodium in animals cannot be excluded (Ctgb, 2012b). According to the instructions for use, Boxclean is a scattering agent used (in an undiluted form) for sit-specified disinfection of moist ground surfaces in stables, free stalls, calf sheds, and calf stables. Further detailed instructions are available, e.g. on the application dose (400 g of Boxclean per square meter), and contact time (at least 30 h).

Toxicological profile
In the general population, the DNEL for oral exposure of systemic, long-term effects was 1.6 mg/kg bw/day. A hazard for systemic, acute/short-term effects was not identified (ECHA, 2019l). Acute toxicity from oral exposure showed an LD_{50} range of 381.6 – 935 mg/kg bw (rat) (ECHA, 2019l). Repeated dose toxicity for the oral route showed NOAELs (rat) ranging from 214 – 248 mg/kg bw/day and the LOAEL (rat) ranging from 738 – 795 mg/kg bw/day (ECHA, 2019l). For genetic toxicity (*in vitro* and *in vivo*), results were negative. Effects on reproduction via the oral route were reported for fertility (NOAEL of 165 mg/kg bw/day (subchronic, rat)) and also developmental toxicity (NOAEL: 50 mg/kg bw/day (subacute, rat)) (ECHA, 2019l). Data on carcinogenicity, neurotoxicity, immunotoxicity, and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019l).

3.8.1.6 4-chloro-3-methylphenol (syn. chlorocresol)
Chlorocresol is approved for use as a biocide in the EEA and/or Switzerland for human hygiene (PT 1) and veterinary hygiene (PT 3) (ECHA, 2019b).

Microbial efficacy
Chlorocresol showed effects on microorganisms with an EC_{50} (3h) and EC_{10} (3h) of, respectively, 41.4 and 5.7 mg/L, in one study. The ECHA has summarized the EC_{50} for microorganisms as 22.86 mg/L (ECHA, 2019b).

On the Ctgb website, five products containing chlorocresol are listed for use under PT 1, 3, or 4. For instance, the product ERO MP is made up of chlorocresol (24% w/w) for use in PT 3 (veterinary hygiene). Studies assessed test organisms for bacteria (excluding mycobacteria and bacterial spores) resulting in > 5 log reductions, while for yeasts and fungi, this resulted in 3 to >4 log reductions.

Results depend on the test parameters, such as concentration, contact time, test temperature, etc. (Ctgb, 2017e).

Residues and/or by-products
Human health scenarios regarding exposure to chlorocresol residues were described during the assessment for PT 1 and PT 3 applications. For PT 1, two scenarios regarding residues were described, both related to the exposure of toddlers. The conclusion was that the primary and secondary exposure coming from either dermal and/or oral were considered acceptable (ECHA, 2016b). For PT 3, the scenario regarding residues was described for the consumption of products of animal origin contaminated with the active substance via secondary exposure (i.e. exposure via food resides) and this was also considered acceptable (ECHA, 2016c).

In the Ctgb evaluation of ERO MP (24% w/w), it is indicated that no methods are required to detect residues in food or feed of plant or animal origin, as no exposure is expected (Ctgb, 2017e).

Toxicological profile
In the general population, the derived no-effect level (DNEL) for oral exposure of systemic, long-term effects was 0.89 mg/kg bw/day (ECHA, 2019b). Acute toxicity from oral exposure showed an LD_{50} of 1,830 mg/kg bw (male rat) (ECHA, 2019b). The ECHA summarized the repeated dose toxicity for the oral route, given the most conservative of values, as having a NOAEL of 200 mg/kg bw/day (subacute, rat) (ECHA, 2019b). For genetic toxicity, the test results were negative. Effects on reproduction via the oral route were reported (reduced fertility), as well as developmental toxicity; both showed a NOAEL of 30 mg/kg bw/day (subacute, rat) (ECHA, 2019b). Data on carcinogenicity, neurotoxicity, immunotoxicity, and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019b).

According to BRC opinions on the approval for chlorocresol, they conclude that a safe use of chlorocresol for human health and environment can be applied for hand disinfection by professionals in hospital and by public in private areas (PT 1), as well as for disinfection of animal housings by spraying by professionals (PT 3) (ECHA, 2016b, 2016c, 2019b).

The Ctgb concluded that concerning human health, when used in accordance with the WG/GA, no adverse health effects are expected for the general public. Detailed instructions are available, e.g. on the dose and minimal exposure time, when used to disinfect non-porous surfaces, materials, and tools or for the disinfection of pig stables and associated spaces (Ctgb, 2017e).

3.8.1.7 Chlorhexidine digluconate (syn. D-gluconic acid)
Chlorhexidine digluconate, also referred to as D-gluconic acid, is currently being reviewed for use as a biocide for human hygiene (PT 1) and veterinary hygiene (PT 3) in the EEA and/or Switzerland (ECHA, 2019c).

Microbial efficacy
The EC_{50} of chlorhexidine digluconate for microorganisms was 25 mg/L (ECHA, 2019c).

On the Ctgb website, twenty-six products containing chlorhexidine digluconate are listed for use under PT 1, 3, or 4. For instance, the product ASJ Solution is made up of 0.4% (w/w) chlorhexidine digluconate for use in PT 3. Studies assessed test organisms for bacteria (excluding mycobacteria and bacterial spores), resulting in 4 to > 5 log reductions, while for yeasts, this resulted in >4 log reductions (Ctgb, 2017b).

Formation of residues and/or by-products
In the Ctgb evaluation of the ASJ Solution, it is indicated that methods are not relevant to detect residues in food or feed of plant origin, while for food or feed of animal origin, an HPLC/MS method with a limit of quantification (LOQ) of 100 ng/mL is described (Ctgb, 2017b).

The Ctgb also evaluated the possible indirect exposure from the use of the ASJ solution, indicating that no risk is anticipated for the general population through foods such as milk or meat; exposure to residues in food is not expected (Ctgb, 2017b).

According to the instructions, when the product ASJ Solution is used, e.g. to disinfect the teats of dairy cows after milking, the temperature of the product should be > 20 °C. Further detailed instructions are available, e.g. on the dose and minimal exposure time, when applied by dipping or spraying (e.g. manually or for milking robots) (Ctgb, 2017b).

Toxicological profile
For the general population, ECHA derived a DNEL for oral exposure of systemic acute/short-term effects of 2 mg/kg bw/day (ECHA, 2019c). Acute toxicity from oral exposure showed an LD_{50} of 2,000 – 2,270 mg/kg bw (rat) (ECHA, 2019c). Repeated dose toxicity for the oral route showed a LOAEL (rat) of 8.88 mg/kg bw/day (ECHA, 2019c). Data on genetic toxicity, carcinogenicity, effects on reproduction, and neurotoxicity were not considered, while data on immunotoxicity and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019c).

According to Ctgb, concerning human health, no adverse effects with the use of ASJ Solution 0.4% w/w chlorhexidine digluconate for the unprotected professional user or the general public (e.g. via indirect exposure) is expected given adherence to the WG/GA. Given possible resistance development and cross-resistance with antibiotics, the instructions recommend using resistance management (Ctgb, 2017b).

3.8.2 Iodine

Iodine is an essential trace element, the main source of which is food. Requirements for iodine depend on different factors such as age, environmental influences, and consumption (of vegetables) (BfR, 2012c). Iodine can enter the food chain also via sanitizing solutions and iodophors providing significant amounts. However, given its natural occurrence, the contamination via disinfectants is difficult to control (EFSA, 2014b, 2014d).

3.8.2.1 Iodine

Microbial efficacy
Iodine toxicity to microorganisms showed an EC_{50} (3 h) of 280 mg/L and an EC_{10} (3 h) of 110 mg/L (ECHA, 2019g).

On the Ctgb website, 20 products containing iodine are listed for use under PT 1, PT 3, or PT 4. For instance, the product LuxDip 50B is made up of iodine (0.5%) for use as PT 3. The evaluation concluded that it would be effective for bacteria (excluding mycobacteria and bacterial spores) and yeasts. Criteria to assess its use as a PT 3 biocide for veterinary hygiene purposes indicates ≥ 4 log reduction for bacteria and yeasts (Ctgb, 2010a).

Formation of residues and/or by-products
The LuxDip 50 is a ready to use product for disinfecting the teats of animals like dairy cows, sheep and goats after milking. In the Ctgb evaluation of LuxDip 50B, there is “adequate residue analytical methodology available to monitor residues of the biocide taking into account all possible exposure scenarios and the toxicity of the active substance(s)” (Ctgb, 2010a); however, no further details are given. Concerning indirect exposure, the possible risk of iodine residues in milk or animals treated with the teat dip/spray formulation was considered. For instance, teat dipping may increase iodine content in milk by 174 µg/mL, according to the Agency for Toxic Substances and Disease Registry (ATSDR). However, the ATSDR concluded “that the major contributor to iodine content in milk is feed supplementation rather than the use of iodine teat dip/spray and dermal absorption is only 12%”. The Ctgb evaluation did not further assess this aspect (Ctgb, 2010a).

Toxicological profile
Iodine is an essential trace element, is necessary for the synthesis of thyroid hormones. Thyroid dysfunction can be caused by iodine deficiency. While, an excessive dietary intake of iodine can also disrupt the thyroid function. Iodine deficiency disorders includes goitre, hypothyroidism, and impaired mental function (EFSA, 2010). Deficiencies are mainly a concern for infants and for women during pregnancy (EFSA, 2014e). Excessive dietary intake of iodine is particularly a concern for persons with thyroid dysfunctions and for pregnant or breastfeeding women. Excessive intake can result in goitre and other thyroid disorders (EFSA, 2006b, 2014e).

In the discussion paper of Arbeitskreis Josmangel (AKJ), the German committee on preventing iodine deficiency disorders, European minimum and maximum amounts for iodine in salt and foods supplement were discussed. Iodine deficiency is a problem in Europe. However, excessive intakes should also be prevented. In the discussion paper it was also mentioned that the use of iodine-based disinfectants could increase iodine content of animal products (AKJ).

For the general population, the DNELs for oral exposure of systemic long-term and acute/short-term effects were not available (ECHA, 2019g). There were no data summarised on the acute toxicity from oral exposure (ECHA, 2019g). Repeated dose toxicity for the oral route showed NOAELs of 10 mg/kg bw/day (rat) and 3 - 10 mg/L drinking water (rat) (ECHA, 2019g), the latter corresponding to about 0.15 – 0.5 mg/kg bw/day (based on a default factor of 0.05) (EFSA, 2012b). The LOAEL (rat) was 10 – 100 mg/L drinking water. Data on genetic toxicity, carcinogenicity, effects on reproduction, neurotoxicity, and immunotoxicity were not considered, while data on endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019g).

The tolerable upper intake level (UL) for iodine (total) is available for several populations. For human consumers, the UL as set by EFSA is indicated in Table 11. No data on genotoxicity for iodine (total) were available from EFSA's OpenToxDatabase (Bassan et al., 2018).

Table 11 *Tolerable upper intake level (UL) for iodine (total) per age group*

Age (years)	UL for iodine (total) (µg/day)	UL for iodine (mg/kg bw/day)
1 – 3	200	0.02[a]
4 – 6	250	
7 – 10	300	
11 – 14	450	
15 – 17	500	
≥ 18	600	0.01[b]

[a] Based on a 12 kg bw (EFSA, 2012b)

[b] Based on a 70 kg bw (EFSA, 2012b)

Overall, concerning human health, for the use of LuxDip 50 B, no adverse effects are expected for the general population, given indirect exposure. Further detailed instructions are available, e.g., on the dose, application, and storage instructions (Ctgb, 2010a).

No data on iodine in food products due to iodine-containing disinfection agents was available, the origin iodine in food is difficult to trace back, therefore monitoring of iodine contamination is challenging.

3.8.3 Quaternary ammonium compounds (Quats)

Two quats were further investigated. Benzalkonium chloride (BAC) and didecyldimethylammonium chloride (DDAC) are quats in the group of cationic surfactants. They can be used in disinfectants and detergents. Both are biocides and active pesticide substances. They can also be used as plant strengtheners (BfR, 2012b).

3.8.3.1 Benzalkonium chloride (BAC)

Microbial efficacy
On the Ctgb website, 38 products containing alkyl (C12-16) dimethylbenzylammonium chloride are listed for use under PT 1, PT 3, or PT 4. For instance, the product Virocid RTU is made up of alkyl (C12-16) dimethylbenzylammonium chloride (ADBAC), didecyldimethylammonium chloride (DDAC), and glutaraldehyde for use in PT 3. Studies assessed test organisms for bacteria (excluding mycobacteria and bacterial spores), yeasts, and viruses/bacteriophages, each resulting in > 4 log reductions (Ctgb, 2016c).

Formation of residues and/or by-products
During biocide evaluations of BAC at the EU-level, the following active substances were indicated: alkyl dimethyl benzyl ammonium chlorides (ADBAC; CAS 68424-85-1, C12: 39-75%, C14: 20-52%, C16: <12%) and benzalkonium chloride (BKC; CAS 68424-85-1, C12: 68%, C14: 29%, C16: 3%) (BfR, 2012a). BAC residues were reported to exceed the default maximum residue level (MRL) of 0.01 mg/kg in food. Suggested reasons for these exceedances included possible post-harvest treatment of fruits with BAC, while residues in milk and ice cream could have occurred during the disinfection of equipment. Data specific to poultry were not mentioned (BfR, 2012a).

EU monitoring data (November 2012 – April 2013) on the residues of BAC were collected and analysed. Of the 5472 food samples, 20 belonged to the category meat (swine, bovine, sheep, goat, and poultry), of which the frequency of positive detections was 0%. Milk and milk products had the highest percentage of positive detections (12%; 117 detects in 960 analysed) (EFSA, 2013).

The Ctgb evaluation of Virocid RTU (for PT 3) indicated that no methods are required to detect residues in food or feed of plant or animal origin (Ctgb, 2016c). According to the instructions for the use of Virocid RTU, the surfaces and materials to be disinfected should be cleaned thoroughly before disinfection. Further detailed instructions are available on, e.g. minimal exposure time and concentration to be used. Notably, the treated surfaces should not be rinsed after disinfection (Ctgb, 2016c).

Toxicological profile
The BfR estimated the dietary intake of BAC residues in contaminated food. An ADI of 0.1 mg/kg bw/day and an ARfD of 0.1 mg/kg bw was derived, as the residues reported were unlikely to pose a chronic health risk (BfR, 2012a).

In a health risk assessment from BfR, given the available data, residues were unlikely to pose a chronic health risk for European consumers. Most food commodities were unlikely to pose an acute health risk for European consumers except for milk/milk products, as concentrations reported were as high as 6.66 mg/kg. Data on BAC (residues) in poultry were not reported (BfR, 2012a).

The EFSA evaluated the validity of the proposed temporary MRL of 0.1 mg/kg for BAC for all food commodities. For the dietary risk assessment, indicative values for an ADI of 0.1 mg/kg bw per day and ARfD of 0.1 mg/kg bw were used. No consumer health risks were identified given this proposed MRL; however, given the limited data available, there is large uncertainty in the risk assessment (EFSA, 2014c).

According to the available information from the ECHA, BAC is predicted as "likely to meet category 1A or 1B for carcinogenicity, mutagenicity, or reproductive toxicity" as registered under the REACH Regulation Inform (Annex III) (ECHA, 2019i). According to Regulation (EC) 1272/2008, Category 1A is "known to have carcinogenic potential for humans, classification is largely based on human evidence", while Category 1B is "presumed to have carcinogenic potential for humans, classification is largely based on animal evidence" (European Union (EU), 2008). Information on the effects related to endocrine disruption were not described (i.e., data or reference to such data were not noted or summarised) (ECHA, 2019i).

3.8.3.2 Didecyldimethylammonium chloride (DDAC)

Microbial efficacy
The EC_{50} of didecyldimethylammonium chloride for microorganisms was 17.9 mg/L, and the EC_{10} for microorganisms was 5.95 mg/L (ECHA, 2019d).

On the Ctgb website, more than 150 products containing DDAC are listed for use under PT 1, 3, or 4. For instance, EpiCare 5C is made up of DDAC (0.9% w/w) and chlorhexidine digluconate (0.9% w/w) for use in PT 1 (human hygiene). Studies assessed on bacteria and yeast test organisms resulted in log reductions from 3 to > 5 log, depending on the test parameters (Ctgb, 2016a).

Residues and/or by-products
DDAC residues were reported to exceed the default MRL of 0.01 mg/kg in food (BfR, 2012b). Suggested reasons for this exceedance included possible post-harvest treatment of fruits with DDAC, use of a plant strengthener on fresh herbs, as well as possible disinfection of planting pots or equipment, and disinfection of milking equipment, ice cream machines, among other equipment. Data specific to poultry were not mentioned (BfR, 2012b).

EU monitoring data (November 2012 – April 2013) on the residues of DDAC in the category meat (swine, bovine, sheep, goat, and poultry) showed no positive samples (EFSA, 2013).

The Ctgb evaluation of EpicCare 5 indicated that no methods are required to detect residues in food or feed of plant or animal origin, as no exposure is expected (Ctgb, 2016a).

Toxicological profile
The BfR estimated the dietary intake of DDAC residues in contaminated food. An ADI of 0.1 mg/kg bw/day and an ARfD of 0.1 mg/kg bw was derived (BfR, 2012b). The US EPA also derived values of 0.1 mg/kg bw for both a chronic population-adjusted dose (cPAD), based on a 1-year study (dog), and an acute population-adjusted dose (aPAD), based on a developmental toxicity study (rat) (BfR, 2012b).

In the health risk assessment from BfR, residues in food and feed resulting from DDAC use were considered unlikely to occur and consequently were unlikely to pose an acute or chronic health risk for the consumer. However, there is a lack of quantifiable data on DDAC application and exposure. Moreover, among the few available monitoring and surveillance data on DDAC residues, data in poultry were not reported (BfR, 2012b).

The EFSA evaluated the validity of the proposed temporary MRL of 0.1 mg/kg for DDAC for all food commodities. For the dietary risk assessment, indicative values for an ADI of 0.1 mg/kg bw per day and ARfD of 0.1 mg/kg bw were used. No consumer health risks were identified given this MRL; however, given the limited data available, there is large uncertainty in the risk assessment (EFSA, 2014c).

In the general population, the ECHA did not derive thresholds for oral exposure of systemic long-term or acute/short-term effects (ECHA, 2019d). Acute toxicity from oral exposure showed an LD_{50} of 329 mg/kg bw (rat). Dermal acute toxicity showed an LD_{50} of 1,000 mg/kg (rat) (ECHA, 2019d). Repeated dose toxicity for the oral route showed a NOAEL (rat) ranging from 27.3 – 45.5 mg/kg bw/day (ECHA, 2019d). Effects on reproduction via the oral route were reported and developmental toxicity with NOAELs of, respectively, 109 mg/kg bw/day (subacute, rat) and 12 mg/kg bw/day (subacute, rat) (ECHA, 2019d). Data on genetic toxicity and carcinogenicity were not considered, while data on neurotoxicity, immunotoxicity, and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019d).

From EFSA's OpenToxDatabase, the systemic, acute toxicity LD_{50} for rat (oral route) was 65 mg/kg bw/day. No data on genotoxicity were available (Bassan et al., 2018).

The Ctgb concluded that concerning human health, no adverse health effects are expected with the application of Epicare 5C when used in accordance with the label (on the WG/GA) (Ctgb, 2016a). According to the instructions for use, Epicare 5C should be applied using a dispenser, e.g. with a 2 ml dose for both hands and with minimal exposure times of between 30 and 60 seconds. Given possible resistance development and cross-resistance with antibiotics, the instructions recommend using resistance management (Ctgb, 2016a).

3.8.4 Other substances

3.8.4.1 Formaldehyde

Formaldehyde is manufactured on an industrial scale and can be found in (consumer) products (BfR, 2006b). For example, consumer products made of melamine resins such as plates, cups, bowls, or cutlery can release formaldehyde (and melamine) if exposed to temperatures > 70 °C (BfR, 2011). Formaldehyde also forms during metabolism in humans and other living organisms (BfR, 2006b). It can be absorbed after inhalation or from dermal or oral exposure (BfR, 2006a). In the poultry chain, formaldehyde (40%, 15-24 h) and formalin (8%, 10-30 min) have been reported to be used for disinfection procedures (EFSA, 2008a).

Microbial efficacy

Formaldehyde toxicity to microorganisms had a range of values for the EC_{50} (5 d), EC_{50} (3 h), and EC_{10} (5 d), which were, respectively, 34.1, 19 – 20.4, and 14.7 mg/L (ECHA, 2019e).

On the Ctgb website, 14 products containing formaldehyde are listed for use under PT 1, 3, or 4. For instance, the product SYN-Formaline 37% is made up of 37% (w/w) formaldehyde for use in PT 3. In the efficacy evaluation, the available information from 'several' literature studies was 'sufficient' as it can be effective against bacteria (including mycobacteria and excluding bacterial spores), yeasts, fungi, and viruses when used "in animal housing including stables and materials, and on surfaces and equipment in these rooms, when used in accordance with the proposed label (WG/GA)" (Ctgb, 2010b). Efficacy was, however, not demonstrated for hoof disinfection for control of yeast, fungi, and viruses, nor for the animal transport sector. Efficacy on the hooves of cattle and sheep for control of bacteria, including mycobacteria, yet excluding bacterial spores, has been demonstrated (Ctgb, 2010b).

Formation of residues and/or by-products

Background levels of formaldehyde have been measured in several food products such as milk, meat, fish, fruits and vegetables, resulting in variable backgrounds with ranges < 1 mg/kg in milk to > 200 mg/kg in fish. In meat and poultry, background concentrations of formaldehyde, as found in the literature, were 5.7 – 20 mg/kg. The carryover to animal tissues is reported in a few tissue deposition studies, showing maximum increases in formaldehyde concentrations between 0.1 – 0.2 mg/kg milk or meat, representing negligible exposure with about 0.1 – 0.3% of human oral exposure from background levels in a food product (EFSA, 2014a).

In the Ctgb evaluation of SYN-Formaline 37%, there is "adequate residue analytical methodology available to monitor residues of the biocide taking into account all possible exposure scenarios and the toxicity of the active substance(s)" (Ctgb, 2010b). Given livestock exposure to formaldehyde, humans can be indirectly exposed to formaldehyde residues from consuming animal products containing formaldehyde; however, given this product's WG/GA use, it is not expected that humans are indirectly exposure to formaldehyde residues given its use as a PT 3. (Ctgb, 2010b).

Toxicological profile

In the general population, the DNEL for oral exposure of systemic, long-term effects was 4.1 mg/kg bw/day (ECHA, 2019e). Acute toxicity from oral exposure had an LD_{50} ranging from 460 – 832 mg/kg bw (rat) (ECHA, 2019e). Repeated dose toxicity for the oral route had a NOAEL (rat) 10 – 25 mg/kg bw/day and a LOAEL (rat) of 50 – 109 mg/kg bw/day (ECHA, 2019e). Data on genetic toxicity, carcinogenicity, toxicity to reproduction, neurotoxicity, and immunotoxicity was not considered, while data on endocrine disrupter mammalian screening (*in vivo*) was not provided (ECHA, 2019b).

A toxicological assessment by BfR concluded that formaldehyde exposure is carcinogenic in humans, leading to tumours in the upper respiratory tract. An exposure of 0.1 ppm formaldehyde was considered 'safe' for the general population and is about two-fold lower than that derived from animal data (BfR, 2006b). Nonetheless, there is evidence that shows a causal relationship between formaldehyde exposure and induced nasopharyngeal cancer in humans. Moreover, formaldehyde is reactive and has genotoxic properties. In cultured mammalian cells, it induced mutations at the chromosomal level, although there is little to no potential for induction of gene mutations (BfR, 2006a).

From January 2016 onwards, formaldehyde has been reclassified as carcinogen (category 1B) and mutagen (category 2) (EC 1282/2008) (KLB, 2016). This means that formaldehyde may cause cancer and is suspected of causing genetic defects.

According to BRC opinions on the approval for formaldehyde (PT 3), they conclude that a safe use of formaldehyde for human health and environment given the following scenarios: "disinfection of animal housings by fogging, disinfection of egg hatchery by fogging/fumigation, and wet disinfection of small surfaces by wiping" (ECHA, 2015).

However, the reclassification of formaldehyde as carcinogen and mutagen could result in a ban or strong restriction for the use of formaldehyde as a biocide, including disinfection in the poultry sector. Formaldehyde is often used for prevention in the poultry stables, stables can be disinfected with formaldehyde in between two production cycles. Formaldehyde is candidate for substitution, however a substitution for the poultry sector is difficult (KLB, 2016). The review of formaldehyde to be used as a biocide is still ongoing.

3.8.4.2 Glutaraldehyde (syn. glutaral)

In the poultry chain, glutaraldehyde (1-2%, 10-30 min) has been reported to be used for disinfection procedures (EFSA, 2008a).

Microbial efficacy

Glutaraldehyde toxicity to microorganisms had an EC_{50} (30 min) of 80 mg/L (ECHA, 2019f).

On the Ctgb website, 36 products containing glutaraldehyde are listed for use under PT 1, 3, or 4. For instance, the product Virocid F has the following active substances: glutaraldehyde (24%), didecyldimethylammonium chloride (DDAC) (5%), and alkyl (C12-16) dimethylbenzylammonium chloride (ADBAC) (5%) for use as PT 3. Studies assessed test organisms for bacteria (excluding mycobacteria and bacterial spores) and viruses/bacteriophages, which resulted in ≥ 4 log reductions. For yeasts, this was ≥ 3.9 log reductions (Ctgb, 2016b).

Formation of residues and/or by-products

In the Ctgb evaluation of Virocid F, it is indicated that, given its intended use, analytical methods to determine residues of glutaraldehyde in food or feed of plant or animal origin are not needed. The evaluation notes that only trace amounts of glutaraldehyde may accidentally occur on the surface of food or feedstuffs. The methods outlined in the evaluation meets the requirements; details can be found there (Ctgb, 2016b). According to the instructions for use, before application (by spraying), the surfaces and materials to be disinfected need to be thoroughly cleaned. During application, the surfaces should remain moist during the entire exposure time. Further detailed instructions are available, e.g., on the dose and minimal exposure time for the disinfection of animal accommodation places and associated areas for animals, except for means of transport for animals as well as disinfection of means of transport for animals (Ctgb, 2016b).

Toxicological profile

In the general population, the threshold (DNEL) for oral exposure of systemic long-term and acute/short-term effects are unknown, although further information was deemed unnecessary as no exposure is expected (ECHA, 2019f).

Acute toxicity from oral exposure had an LD_{50} ranging from 154 - 246 mg/kg bw (rat) (ECHA, 2019b). Repeated dose toxicity for the oral route showed NOAELs of 14.95 - 46 mg/kg bw/day (rat) in one study, while another study showed NOAELs of 14.6 - 16.6 mg/kg bw/day (dog). In the latter study, the LOAEL (rat) was 116.6 - 153.2 mg/kg bw/day (ECHA, 2019f). Data on genetic toxicity, carcinogenicity, effects on reproduction, and neurotoxicity were not considered, while data on immunotoxicity and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019f).

Studies on genotoxicity showed negative results (Bassan et al., 2018).

BRC opinions on the approval for glutaraldehyde for PT 3 and PT 4 are available. For use as PT 3, human health exposure scenarios for 'mixing and loading,' 'spraying,' 'fogging,' and 'accidental exposure to wet residues' were evaluated. Only the last scenario, based on secondary exposure of children, was considered unacceptable; however, it became 'acceptable' after waiting for 2 hours before re-entering the disinfected barn (i.e. after the 2-hour re-entry period). Details on these scenarios can be found in the BRC opinion (ECHA, 2014).

With respect to human health, for the application of Virocid F in accordance with the WG/GA, no adverse health effects are expected for the general public and animals given indirect exposure to the active substances. Notably, the following sentence should also be included on the WG/GA: "Rinse off the surface using clean drinking water after disinfection" (Ctgb, 2016b).

3.8.4.3 Potassium peroxymonosulphate

Microbial efficacy
Potassium peroxymonosulphate showed toxicity to microorganisms at an EC_{50} (18 h) of 179 mg/L and an EC_{10} (18 h) of 108 mg/L (ECHA, 2019h).

On the Ctgb website, four products containing "pentapotassium bis(peroxymonosulfate) bis(sulfate)" are listed for use under PT 1, 3, or 4. For instance, the product Virkon S is made up of 45.3% (w/w) pentapotassium bis(peroxymonosulphate)bis(sulphate) for use in PT 3. In the efficacy evaluation, the minimum effective dose for bacteria (excluding mycobacteria and bacterial spores) and yeasts is set at 4%. The log reduction for the target organisms tested for use as PT 3 was not provided. Results depend on the test parameters, such as concentration, contact time, test temperature, etc. Since the efficacy tests were performed under clean conditions, surfaces must be cleaned before disinfection (Ctgb, 2010c).

Formation of residues and/or by-products
In the Ctgb evaluation of Virkon S, there is "adequate residue analytical methodology available to monitor residues of the biocide, taking into account all possible exposure scenarios and the toxicity of the active substance(s)" (Ctgb, 2010c). Data on the potential indirect exposure form is not available on residues or secondary exposure, but this is expected to be limited. According to the instructions for use of Virkon S, before the application of Virkon S, the surfaces and materials to be disinfected need to be thoroughly cleaned, and therefore the use of a cleaning agent needs to be rinsed with clean water and excess water should be removed. During application, the surfaces should remain wet during the entire exposure time. Further detailed instructions are available, e.g., for use during a virus outbreak and for the disinfection of rooms, surfaces, tools, and equipment in animal housing places and associated rooms on the farm (Ctgb, 2010c).

Toxicological profile
In the general population, the DNEL for oral exposure of systemic long-term (repeated dose toxicity) and acute/short-term (acute toxicity) effects was 10 mg/kg bw/day (ECHA, 2019h). Acute toxicity from oral exposure showed an LD_{50} of 500 mg/kg bw (rat) (ECHA, 2019h). Repeated dose toxicity for the oral route showed a NOAEL (rat) of 200 mg/kg bw/day and a LOAEL (rat) of 600 mg/kg bw/day (ECHA, 2019h). Data on genetic toxicity, carcinogenicity, effects on reproduction, and neurotoxicity were not considered, while data on immunotoxicity and endocrine disrupter mammalian screening (*in vivo*) were not provided (ECHA, 2019h).

3.8.5 Conclusion

For each of the active ingredients on the intermediate list, the efficacy was described above. However, it is difficult to compare the efficacy of ingredients, since it depends on several factors, like concentration, temperature, contact time, soil type, type of equipment, water properties, pH, and the microbial population and attachment to surfaces.

Some of the chlorine-containing compounds were evaluated by EFSA due to discussions around decontamination of poultry with these substances as performed outside Europe. No safety concerns were identified by EFSA for the use of acidified sodium chlorite and chlorine dioxide for decontamination of poultry. However, by-products that may be of a concern to human health, such as chlorite, chlorate, chlorine dioxide and semicarbazide can be formed with the use of chlorine-containing products. Information on residues of these by-products in food products (including poultry) is limited.

Iodine can be used for disinfection, but it can also enter the food chain via different sources. Iodine is an essential trace element, which can be present in food and of which food is the main source. Iodine deficiency and excessive iodine intake should be prevented. The origin iodine in food is difficult to trace back, therefore monitoring of iodine contamination due to disinfection is challenging.

Monitoring data showed that quaternary ammonium compound residues (BAC and DDAC) are sometimes detected in milk and milk products above the EU MRL. No consumer health risks were identified by EFSA given the MRL of BAC and DDAC. However, EFSA indicated that there is a large uncertainty because of limited available data.

Formaldehyde is a substance which is under discussion for use as a biocide, because of its reclassification as carcinogen and mutagen.

Regarding the other substances, no safety concerns are expected for the general consumer in case of proper use of the products. Exposure through food for many substances is not expected. However, for some substances residues in food can occur, but are likely to be low as stated by Ctgb.

3.9 Issues with cleaning and disinfection in the poultry chain outside Europe

Additional searches were performed to check for possible issues and concerns regarding cleaning and disinfection in the poultry chain outside Europe. First of all, it is important to mention that import of poultry products to the Netherlands is mainly from other EU member states (Germany, Belgium, United Kingdom and Poland). Eurostat data from the last 5 years (2015-2019) showed that this concerns 83% of the poultry products imported to the Netherlands. Import from outside EU to the Netherlands is for 3.9% from Brazil and 3.6% from Ukraine. Imported products can be consumed in the Netherlands or exported to other countries.

A great difference between the approaches of the EU and US, with regards to cleaning and disinfection agents, can be observed in food law. Decontaminating food, in general, is not supported and not allowed in the EU. Biocidal products that are prone to Regulation (EU) No 528/2012, shall not be applied to feed or food as it is described in article 2.5 of this regulation. For that reason, chlorine-based compounds may not be applied directly on feed and food. In the US, no regulation is prohibiting the use of such substances on food. The application of chlorine-based compounds is used to lower the microbiological load on chicken in the US. However, all food that is imported in the EU, should comply to EU food law, according to Regulation (EC) No 178/2002, article 11. Therefore, there is a ban on chicken and products thereof, that had a treatment with chlorine-based compounds from the US. This resulted in a long-lasting conflict at world trade level between US and EU. Arguments for using such treatments on chicken is to prevent outbreaks of food borne illnesses. A trade association for

American chicken farmers, the National Chicken Council, calls the ban on the chickens from US treated with chlorine-based substances an unfair practice of protectionism (Rayner, 2018).

EFSA has investigated the food safety of chicken after treatments with acidified sodium chlorite, chlorine dioxide, trisodium phosphate, or peroxyacid solutions. EFSA describes that residue levels will be lower when the treatments occur through spraying than dipping the chicken in a solution bath. Chicken is able to absorb water, so it is probable that more residues and by-products arise during the latter treatment (EFSA, 2016).Nevertheless, studies suggested that treating chicken with chlorine-based compounds, will not kill all the bacteria present on the chicken. This can result in viable-but-not-culturable bacteria, meaning that test results would suggest that there are no bacteria, while being yet present on the food product. Besides, killing the microbiological load creates a pathway for easy outgrowth of pathogens after cross-contamination, since the natural microflora is not present to compete (Harvey, 2019; Rayner, 2018). Next to food safety, other issues are raised for holding the import ban. The European Commission wants to prevent that decontaminating of food products would hamper the hygiene throughout the food chain. Furthermore, also concerns with regards to animal welfare were raised (Doward, 2019).

The EU ban on the import of chickens treated with chlorine-based compounds from the US applies for more than a decennia. However, given the developments on the withdrawal of the UK as an EU Member State, the discussion is vivid. By leaving the EU, food and imported food in the UK will not be prone to EU food law, meaning the discussion of the use of chlorine-based compounds comes again to the table. Nowadays, American associations and ambassadors in the UK are discussing the potential new trade deals, as well as the import of chicken from the US (Lawrence, 2019). It is important to know if import of chicken from the US will be allowed in the UK and to trace chicken products that will come from the UK.

Import of poultry products to the Netherlands is mainly from EU Member States and all imported products do have to apply to the European legislation. However, there are differences around the world in how poultry products can be treated with cleaning and disinfection agents. Therefore, residues of cleaning and disinfection in poultry products imported from countries outside the EU could be a focus for monitoring. After the Brexit, imports from the UK may be followed more closely. Furthermore, there are cleaning and disinfection products on the worldwide market available of which the intended use is not allowed in Europe, possible sales and use of these products in Europe should also be a focus of monitoring.

4 Conclusions & recommendations

4.1 Conclusions

Cleaning

- Based on questionnaires, interviews and literature study a long list of active ingredients (n=37) of cleaning agents used in the poultry, eggs, leafy greens and sprouts supply chain was established.
- Sodium hydroxide is the most frequently used cleaning agent in the poultry chain.
- The expert study did indicate that incorrect cleaning occurs due to a lack of knowledge or time constraints. Products could be used for the wrong application or unauthorised products could be used.
- Cleaning agents are intended to merely remove dirt and a rinsing-step is generally applied after its application. Therefore, residues are not expected to come into contact with food, and no safety issues are expected.

Disinfection

- A long list of 42 active ingredients in disinfectants used in the poultry, eggs, leafy greens and sprouts supply chain was established based on questionnaires, interviews, literature and the Ctgb database.
- This list was down-sized to a so-called intermediate list (n=18) for possible human health risks. This list contained eight chlorine-containing compounds, two quaternary ammonium compounds, one acid, iodine, ozone and five other compounds.
- The efficacy of these active ingredients is difficult to compare since it depends on many factors, and their interactions, such as concentration, temperature, contact time, soil type, type of equipment, water properties, pH, and the microbial population and attachment to surfaces.
- Further exploration of the active ingredients on the intermediate list for poultry showed that most relevant active ingredients for human health risks are:
  - chloride compounds due to the possible production of by-products, such as chlorite, chlorate, chlorine dioxide and semicarbazide
  - quaternary ammonium compounds, because residues are sometimes found in food products
  - formaldehyde, because this is a substance which is under discussion for use as a disinfectant, due to its reclassification as carcinogen and mutagen
- Disinfectants used have to be authorised by Ctgb and as such are evaluated for their safety for humans and the environment. Proper use of disinfectants will not lead to human health problems.
- The expert study did indicate that incorrect disinfection occurs due to a lack of knowledge or time constraints. Furthermore, unauthorised products could be used or products could be used for the wrong application. These activities may lead to concerning levels of residues in food products.

4.2 Recommendations

Based on this study, the following is recommended:

- Further education of farmers on cleaning and disinfection is needed to increase awareness on safe practices;
- Producers of cleaning agents and disinfectants should improve their labels to promote a proper use of their products;
- Effective authorised alternatives should be developed for formaldehyde used at poultry farms in case use of formaldehyde will be limited;
- Actual use of unauthorised products and possible use of products authorised outside the Netherlands and Europe should be further investigated, because information on this is lacking;
- Monitoring data on residues of cleaning and disinfection agents is limited. Therefore, monitoring should be extended to gain more information on possible presence of residues in end products.

Especially, monitoring of by-products formed by using chlorine-containing products, monitoring of quaternary ammonium compounds and formaldehyde should be performed, because these compounds may be of concern to human health;

- Since this study primarily focused on the poultry chain, it is recommended to further explore cleaning and disinfection in other supply chains and the expected exposure to the public. A start could be the cattle and dairy chain, because residues of quaternary ammonium compounds have been detected in milk.

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Annex 1 List of terms

Term	Definition/explanation	Translation
Adenosine triphosphate (ATP)	Used as indicator for the presence of microorganisms[a]	Adenosine trifosfaat
Arable farming	Land, on which one is able to grow crops.[b]	Akkerbouw
Biocidal product	Any substance or mixture with the intension of destroying, deterring, rendering, harmless, preventing the action of, or otherwise exerting a controlling effect on, any harmful organism by any means other than mere physical or mechanical action[j].	Biociden
Cleaning	The removal of soil, food residue, dirt, grease or other objectionable matter[c].	Reinigen
Cleaning in place (CIP)	The cleaning of complete items of plant or pipeline circuits without dismantling or opening of the equipment and with little or no manual involvement on the part of the operator. The process involves the jetting or spraying of surfaces or circulation of cleaning solutions through the plant under conditions of increased turbulence and flow velocity[d].	CIP
Cleaning out of place (COP)	The cleaning practice employed when plant and equipment are removed from their place or point of use to be cleaned in another location[e].	COP
Corrosion inhibitor	Any substance that prevent the destroying of living tissue[o].	Corrosie inhibitor
Decontamination	The combination of physical and chemical processes that kills or removes pathogenic microorganisms on the food product[g].	Decontaminatie
Degreaser	Solvents to remove grease and oil, which are often use in the preparation of metal parts for further operations, such as welding or painting[r].	Ontvetter
Detergent	Any substance or mixture containing soaps and/or other surfactants intended for washing and cleaning processes. Detergents may be in any form (liquid, powder, paste, bar, cake, moulded piece, shape, etc.) and marketed for or used in household, or institutional or industrial purposes[n].	Detergentia
Disinfectant	A substance which eliminates populations of vegetative bacteria on inanimate surfaces[i].	Desinfectiemiddel
Disinfection	The reduction by means of chemical substances and/or physical methods, of the number of micro-organisms in the environment, to a level that does not comprise food safety or suitability[c].	Desinfectie
European Economic Area (EEA)	European Union and the three EEA EFTA (European Free Trade Association) states being Iceland, Liechtenstein and Norway. Within EEA, the internal market is governed by the same basic rules[k].	Europese Economische Ruimte (EER)
Germicide	Any chemical agent used to control or kill any pathogenic and non-pathogenic micro-organisms[l].	Germicide
Horticulture	High investment crop production using resources intensively for high value product[m].	Tuinbouw
Non-corrosive	Substances which do not destroy living tissues when in contact[o].	Niet corrosief
(to) Peptize protein	Disintegrating particles, so that they form a colloidal solution [f].	Petiseren van eiwitten
Plant protection product (PPP)	Any substance protecting plants or plant products against harmful organisms, or influencing life processes of plants, or preserving plant products, or destroying undesired parts of plant, or preventing undesired growth of plants[p].	Gewasbeschermingsmiddel
Product type (PT)	Product types are specified in the Biocidal Product Regulation (EU) No 528/2012): PT 1 (human hygiene), PT 3 (veterinary hygiene), and PT 4 (food and feed area)	Product type

Term	Definition/explanation	Translation
Sanitation	The act or process of providing adequately hygienic conditions to ensure a safe, sound, wholesome product fit for human consumption and covers hygienic precautions regarding personal hygiene, process hygiene and cleaning and disinfection[i].	Sanering
Sanitizer	A substance that reduces microbial contaminants on inanimate surfaces to levels that are considered safe from a public health stand point[i].	Ontsmettingsmiddel
Sequestrant	Also known as chelants. An additive used in cleaning agents that prevent water hardness by binding to metal ions, e.g., calcium and magnesium[q].	Sequastrant
Sterilant	An agent that eliminates all fungi, bacteria, viruses and spores[g].	Sterilisatiemiddel
Surfactant	Any organic substance and/or mixture used in detergents or cleaning agents, which has surface-active properties and which consists of one or more hydrophilic and one or more hydrophobic groups of such a nature and size that it is capable of reducing the surface tension of water, and of forming spreading or adsorption monolayers at the water-air interface, and of forming emulsions and/or microemulsions and/or micelles, and of adsorption at water-solid interfaces[n].	Oppervlakteactieve stoffen
Ultimate aerobic biodegradability	The level of biodegradation achieved when the surfactant is totally used by micro-organisms in the presence of oxygen resulting in its breakdown to carbon dioxide, water and mineral salts of any other elements present (mineralisation) and new microbial cellular constituents (biomass)[n].	Totale aërobe biologische afbreekbaarheid

a https://www.fimm.nl/microbiologische-methoden-oktober-2011/ (geraadpleegd op 9/7/19)

b European Commission. Eurostat - Agri-environmental indicator - cropping patterns. 2019. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Agri-environmental_indicator_-_cropping_patterns (geraadpleegd op 14/8/19)

c CAC https://www.mhlw.go.jp/english/topics/importedfoods/guideline/dl/04.pdf

d Society of Dairy Technology https://epdf.pub/cleaning-in-place-dairy-food-and-beverage-operations-third-edition.html

e Indian Institute of Public Health http://www.old.fssai.gov.in/Portals/0/Training_Manual/Level%203%20Manufacturing%20-supervisors.pdf

f W. Bancroft. 1916. The theory of peptization.

g FAO http://www.fao.org/ag/againfo/commissions/docs/training/material/AusVet/plan-2009.pdf

h FAO http://www.fao.org/3/x6557e/x6557e00.htm

i EPA https://www.google.com/search?hl=nl&as_q=definition+&as_epq=&as_oq=sanitizer&as_eq=&as_nlo=&as_nhi=&lr=&cr=&as_qdr=all&as_sitesearch=http%3A%2F%2Fwww.fao.org&as_occt=any&safe=images&as_filetype=&as_rights=#

j European Parliament and Council. Regulation (EU) 528/2012. https://eur-lex.europa.eu/legal-content/NL/TXT/PDF/?uri=CELEX:02012R0528-20140425&qid=1562591325230&from=EN

k EFTA https://www.efta.int/

l FAO http://www.fao.org/3/X3910E/X3910E10.htm

m FAO http://www.fao.org/3/x5642e/x5642e05.htm#TopOfPage

n European Parliament and Council. Regulation (EU) 648/2004. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02004R0648-20150601&qid=1563280781190&from=EN

o FAO http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Code/Old_guidelines/label.pdf

p European Parliament and Council. Regulation (EC) No 1107/2009. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02009R1107-20181110&qid=1562591480783&from=EN

q CAC http://www.fao.org/gsfaonline/reference/techfuncs.html & https://www.sciencedirect.com/science/article/pii/B9780128120699000029?via%3Dihub

r EPA https://www.epa.gov/p2/case-studies-safer-alternatives-solvent-degreasing-applications

Annex 2 Description of non-relevant topics in the literature study

Table A2.1 *Examples of non-relevant topics for titles per chain*

Poultry (meat) and eggs	Leafy greens	Sprouts
Alternative laying hen houses (and its influence on nutritional composition and hygienic conditions)	antifouling coatings (shipping)	buckwheat
Avian influenza virus/ bird flu virus and remedy methods (vaccination)	antioxidant capacity/nutrition	chickpeas
Campylobacter contamination (in retail poultry meats and by-products in the world; on poultry carcasses along the slaughter line)	cardiovascular disease	effect of pesticide use
Chicken pox infection	chinchillas	energy use for product production
Control of house fly in layer chicken farms	clove oils (flavoring; as an antioxidant)	heavy metal absorption
Decontamination strategies of antibiotic residues	contaminated soil remediation/soil decontamination/ plant-micro interactions in soil/ root uptake of pathogen	lotus
Effects of clay (antibiotic growth promoter alternative)	contracting employees in horticulture/employee hand washing or hygiene	nutrition for animals
Egg and egg products production and consumption	dental hygiene	rapeseed
Feed quality	ecological sanitation	wheat
Fermented poultry sausages	economic aspects	
Fish and fish eggs	effluent use cultivation	
Fusarium wilt in chickpea	employees in schools	
Heavy metal concentration in egg white	farmers markets	
Keratin fibers from chicken feathers	fresh fruits (e.g., berries)	
Methods to calculate helminths' eggs	general information on parasites or viruses	
Mycotoxins in feed and broilers	grower trends	
Nest sanitation	hospital setting	
Nutrition	hygienic design of machinery	
On-farm sources of campylobacter for broiler chickens	oil spills	
Protection of poultry workers	preservation (packaging)	
Salmonella contamination in chicken layer farms	silver particles	
Spread of pathogens through trade	soilless growing	
Welfare of laying hens	vaccines	

Table A2.2 *Examples of non-relevant topics for articles per chain*

Poultry (meat) and eggs	Leafy greens	Sprouts
experimental and laboratory studies	best practices including tools thereof/ preventative measures/ food safety culture	(best) management practices
bacterial treatments	biofilm formation	bacterial treatment (phages, bacteriocins, etc.)
physical treatments	ecology of microorganisms	ecology of microorganisms, including survival
references not outlining disinfectants or cleaning agents	non-thermal technologies (cold plasma)	hygiene requirements/validation thereof
	physical treatments (UV-C, ultrasound, etc.)	non-thermal treatments (e.g., cold plasma)
	prevalence or modelling studies	outbreaks
	shelf life or storage	physical treatments (irradiation, infrared, ultraviolet, high hydrostatic pressure, etc.)
	spoilage	prevalence studies
	thermal treatments	thermal treatments (dry heat, hot air, etc.)

Annex 3 Questionnaires (Phase I)

A3.1 General questionnaire (in Dutch)

Vragenlijst
Zou u svp onderstaande vragen zo gedetailleerd mogelijk willen beantwoorden?

Reiniging
1. Welke actieve stoffen worden gebruikt voor het reinigen van **de stallen in de pluimveesector** (niet alleen de stallen zelf, maar ook de materialen, transportwagens en de mensen (handen)?
2. Welke actieve stoffen worden gebruikt voor het reinigen van **in de groenteteelt** (Bladgroente en kiemgroente: opslagruimte, materialen en de mensen (handen)?
3. Welke actieve stoffen worden gebruikt voor het reinigen **bij de slacht en de verdere verwerking** van pluimveevlees en/of de verwerking van eieren (reiniging van vloeren, apparatuur, handen etc.)?
4. Welke actieve stoffen worden gebruikt voor de reiniging tijdens **de verwerking van bladgroenten en kiemgroenten** (reiniging van vloeren, apparatuur, handen etc.)?
5. Welke actieve stoffen worden gebruikt voor de reiniging **in de retail** (vloeren, snijmachines, mensen (handen))?

Desinfectie
1. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de desinfectie van **de stallen in de puimveesector** (niet alleen de stallen zelf, maar ook de materialen en de mensen (handen)?
2. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de desinfectie **tijdens de teelt van bladgroenten en kiemgroenten** (opslagruimte, materiaal, mensen (handen))?
3. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de desinfectie **bij de slacht en de verdere verwerking** van pluimveevlees en/of bij de verwerking van eieren (reiniging van vloeren, apparatuur, handen etc.)?
4. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de desinfectie **tijdens de verwerking van bladgroenten en kiemgroenten** (reiniging van vloeren, apparatuur, handen etc.)?
5. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de desinfectie **in de retail** (vloeren, snijmachines, mensen (handen))?

Mogelijke knelpunten
1. Welke hardnekkige problemen, indien aanwezig, maken reiniging en desinfectie op de boerderij lastig (bv. aanwezigheid van pathogenen (*Campylobacter, Listeria*) of bloedluis)?
2. Welke actieve ingrediënten voor reiniging en desinfectie kunnen een potentieel gevaar opleveren voor de volksgezondheid indien residuen in het product terechtkomen (bv. de productie van bijproducten)?
3. Hoe wordt voorkomen dat niet-toegelaten stoffen gebruikt worden (ter voorkoming van gebruik van illegale producten zoals Dega-16/ fipronil case)
4. Hoe wordt ervoor gezorgd dat de gebruikte middelen op de juiste manier toegepast worden?
   a. Wordt er altijd gereinigd voordat er gedesinfecteerd wordt? Zo nee, wanneer niet?
   b. Wordt er altijd gespoeld na reiniging of desinfectie? Zo nee, wanneer niet?
   c. Hoe wordt ervoor gezorgd dat de minimale inwerkingsduur aangehouden wordt?
   d. Hoe wordt ervoor gezorgd dat de juiste concentratie toegepast wordt?
   e. Hoe wordt ervoor gezorgd dat de juiste middelen voor de juiste toepassing gebruikt worden?
   f. Hoe wordt de minimale temperatuur geborgd onder winterse omstandigheden?

A3.2 Questionnaire for horticulture – primary production

Vragenlijst
Zou u svp onderstaande vragen zo gedetailleerd mogelijk willen beantwoorden?

1. Welke actieve stoffen worden gebruikt voor de **reiniging** tijdens de teelt van bladgroenten en kiemgroenten (opslagruimte, materiaal, mensen (handen))?
2. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de **desinfectie** tijdens de teelt van bladgroenten en kiemgroenten (opslagruimte, materiaal, mensen (handen))?
3. Welke hardnekkige problemen, indien aanwezig, maken reiniging en desinfectie bij de teelt lastig (bv. aanwezigheid van bepaalde plantziekten)?
4. Welke actieve ingrediënten voor reiniging en desinfectie kunnen een potentieel gevaar opleveren voor de volksgezondheid indien residuen in het product terechtkomen (bv. de productie van bijproducten)?
5. Hoe wordt voorkomen dat niet-toegelaten stoffen gebruikt worden (ter voorkoming van gebruik van illegale producten)
6. Hoe wordt ervoor gezorgd dat de gebruikte middelen op de juiste manier toegepast worden?
   a. Wordt er altijd gereinigd voordat er gedesinfecteerd wordt? Zo nee, wanneer niet?
   b. Wordt er altijd gespoeld na reiniging of desinfectie? Zo nee, wanneer niet?
   c. Hoe wordt ervoor gezorgd dat de minimale inwerkingsduur aangehouden wordt?
   d. Hoe wordt ervoor gezorgd dat de juiste concentratie toegepast wordt?
   e. Hoe wordt ervoor gezorgd dat de juiste middelen voor de juiste toepassing gebruikt worden?

A3.3 Questionnaire for horticulture – processing

Vragenlijst
Zou u svp onderstaande vragen zo gedetailleerd mogelijk willen beantwoorden?

1. Welke actieve stoffen worden gebruikt voor de **reiniging** tijdens de verwerking van bladgroenten en kiemgroenten (reiniging van vloeren, apparatuur, handen etc.)?
2. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de **desinfectie** tijdens de verwerking van bladgroenten en kiemgroenten (reiniging van vloeren, apparatuur, handen etc.)?
3. Welke hardnekkige problemen, indien aanwezig, maken reiniging en desinfectie tijdens verwerking van bladgroenten en kiemgroenten lastig (bijvoorbeeld aanwezigheid van *Listeria*)?
4. Welke actieve ingrediënten voor reiniging en desinfectie kunnen een potentieel gevaar opleveren voor de volksgezondheid indien residuen in het product terechtkomen (bv. de productie van bijproducten)?
5. Hoe wordt voorkomen dat niet-toegelaten stoffen gebruikt worden (ter voorkoming van gebruik van illegale producten)
6. Hoe wordt ervoor gezorgd dat de gebruikte middelen op de juiste manier toegepast worden?
   a. Wordt er altijd gereinigd voordat er gedesinfecteerd wordt? Zo nee, wanneer niet?
   b. Wordt er altijd gespoeld na reiniging of desinfectie? Zo nee, wanneer niet?
   c. Hoe wordt ervoor gezorgd dat de minimale inwerkingsduur aangehouden wordt?
   d. Hoe wordt ervoor gezorgd dat de juiste concentratie toegepast wordt?
   e. Hoe wordt ervoor gezorgd dat de juiste middelen voor de juiste toepassing gebruikt worden?
   f. Hoe wordt de minimale temperatuur geborgd onder winterse omstandigheden?

A3.4 Questionnaire for poultry – primary production

Vragenlijst
Zou u svp onderstaande vragen zo gedetailleerd mogelijk willen beantwoorden?

1. Welke actieve stoffen worden gebruikt voor **reiniging** op de boerderij (de stallen, materialen, transportwagens en de mensen (handen))?
2. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de **desinfectie** op de boerderij (de stallen, materialen, transportwagens en de mensen (handen)?
3. Welke hardnekkige problemen, indien aanwezig, maken reiniging en desinfectie op de boerderij lastig (bv. aanwezigheid van *Campylobacter* of bloedluis)?
4. Welke actieve ingrediënten voor reiniging en desinfectie kunnen een potentieel gevaar opleveren voor de volksgezondheid indien residuen in het product terechtkomen (bv. de productie van bijproducten)?
5. Hoe wordt voorkomen dat niet-toegelaten stoffen gebruikt worden (ter voorkoming van gebruik van illegale producten zoals Dega-16/ fipronil case)
6. Hoe wordt ervoor gezorgd dat de gebruikte middelen op de juiste manier toegepast worden?
   a. Wordt er altijd gereinigd voordat er gedesinfecteerd wordt? Zo nee, wanneer niet?
   b. Wordt er altijd gespoeld na reiniging of desinfectie? Zo nee, wanneer niet?
   c. Hoe wordt ervoor gezorgd dat de minimale inwerkingsduur aangehouden wordt?
   d. Hoe wordt ervoor gezorgd dat de juiste concentratie toegepast wordt?
   e. Hoe wordt ervoor gezorgd dat de juiste middelen voor de juiste toepassing gebruikt worden?
   f. Hoe wordt de minimale temperatuur geborgd onder winterse omstandigheden?

A3.5 Questionnaire for poultry – processing

Vragenlijst
Zou u svp onderstaande vragen zo gedetailleerd mogelijk willen beantwoorden?

1. Welke actieve stoffen worden gebruikt voor het **reinigen** bij de slacht en de verdere verwerking van pluimveevlees en/of de verwerking van eieren (reiniging van vloeren, apparatuur, handen etc.)?
2. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de **desinfectie** bij de slacht en de verdere verwerking van pluimveevlees en/of bij de verwerking van eieren (reiniging van vloeren, apparatuur, handen etc.)?
3. Welke hardnekkige problemen, indien aanwezig, maken reiniging en desinfectie tijdens verwerking van pluimveevlees of eieren lastig (bijvoorbeeld aanwezigheid van *Listeria*, *Salmonella*)?
4. Welke actieve ingrediënten voor reiniging en desinfectie kunnen een potentieel gevaar opleveren voor de volksgezondheid indien residuen in het product terechtkomen (bv. de productie van bijproducten)?
5. Hoe wordt voorkomen dat niet-toegelaten stoffen gebruikt worden (ter voorkoming van gebruik van illegale producten)
6. Hoe wordt ervoor gezorgd dat de gebruikte middelen op de juiste manier toegepast worden?
   a. Wordt er altijd gereinigd voordat er gedesinfecteerd wordt? Zo nee, wanneer niet?
   b. Wordt er altijd gespoeld na reiniging of desinfectie? Zo nee, wanneer niet?
   c. Hoe wordt ervoor gezorgd dat de minimale inwerkingsduur aangehouden wordt?
   d. Hoe wordt ervoor gezorgd dat de juiste concentratie toegepast wordt?
   e. Hoe wordt ervoor gezorgd dat de juiste middelen voor de juiste toepassing gebruikt worden?
   f. Hoe wordt de minimale temperatuur geborgd onder winterse omstandigheden?

A3.6 Questionnaire for retail

Vragenlijst

Zou u svp onderstaande vragen zo gedetailleerd mogelijk willen beantwoorden?

1. Welke actieve stoffen worden gebruikt voor de **reiniging** in de retail (vloeren, snijmachines, mensen (handen))?
2. Na het schoonmaken, welke actieve stoffen worden gebruikt voor de **desinfectie** in de retail (vloeren, snijmachines, mensen (handen))?
3. Welke hardnekkige problemen, indien aanwezig, maken reiniging en desinfectie in de retail lastig (bijvoorbeeld aanwezigheid van *Listeria*)?
4. Welke actieve ingrediënten voor reiniging en desinfectie kunnen een potentieel gevaar opleveren voor de volksgezondheid indien residuen in het product terechtkomen (bv. de productie van bijproducten)?
5. Hoe wordt voorkomen dat niet-toegelaten stoffen gebruikt worden (ter voorkoming van gebruik van illegale producten)?
6. Hoe wordt ervoor gezorgd dat de gebruikte middelen op de juiste manier toegepast worden?
   a. Wordt er altijd gereinigd voordat er gedesinfecteerd wordt? Zo nee, wanneer niet?
   b. Wordt er altijd gespoeld na reiniging of desinfectie? Zo nee, wanneer niet?
   c. Hoe wordt ervoor gezorgd dat de minimale inwerkingsduur aangehouden wordt?
   d. Hoe wordt ervoor gezorgd dat de juiste concentratie toegepast wordt?
   e. Hoe wordt ervoor gezorgd dat de juiste middelen voor de juiste toepassing gebruikt worden?
   f. Hoe wordt de minimale temperatuur geborgd onder winterse omstandigheden?

Annex 4 Questionnaires (Phase II)

A4.1 Questionnaire for cleaning agents in stables

Introductie Voor een onderzoek naar reinigings- en desinfectiemiddelen voor de Nederlandse Voedsel- en Warenautoriteit wordt er bekeken welke reinigingsmiddelen in de praktijk gebruikt worden in de pluimveeketen. Hierbij kan uw input zeer waardevol zijn. Derhalve willen wij u vriendelijk enkele minuten van uw tijd vragen om de onderstaande vragen te beantwoorden.

Voor het doel van deze vragenlijst wordt de volgende definitie gebruikt;
Reinigingsmiddel: een middel voor het verwijderen van aarde, voedselresidu, vuil, vet, etcetera.

Vraag 1
Welke van de onderstaande reinigingsmiddelen worden gebruikt voor het reinigen van de stallen, handen en overige materialen, die worden gebruikt in de stallen?

	Stallen (vloeren, wanden) (1)	Handen (2)	Overige materialen* (3)
1-dodecanaminium, n-(2-hydroxy-3-sulfopropyl)-n,n-dimethyl-, inner salt (1)	☐	☐	☐
2-(2-butoxyethoxy)ethanol (2)	☐	☐	☐
3-butoxy-2-propanol (3)	☐	☐	☐
alcohol, C12-14 geëthoxyleerde sulfaten (4)	☐	☐	☐
alkaline fosfaten (5)	☐	☐	☐
alkyl amidopropyl betaines/ C12-C14 pareth-4, cocamidopropylbetaïne (6)	☐	☐	☐
alkylamine oxides (Amines, C12-14 alkyldimethyl, N-oxides) (7)	☐	☐	☐
amines, C8-C18 (even genummerd) en C18 onverzadigd, N, N-bishydroxyethyl (8)	☐	☐	☐
arylsulfonaten (bv cumeensulfonaat) (9)	☐	☐	☐
C14-16 (even genummerd)-alkane hydroxy en C14-16 (even genummerd)-alkene natrium zouten (10)	☐	☐	☐
D-glucopyranose, oligomeric, decyl octyl glycoside (11)	☐	☐	☐
ethanolamines (12)	☐	☐	☐
ethyleendiaminetetraacetaat (EDTA) (13)	☐	☐	☐
vetalcoholethoxylaat (getoxyleerd) (14)	☐	☐	☐
N-C8-22-alkyltrimethyleendi- acrylated natrium zouten (15)	☐	☐	☐

	Stallen (vloeren, wanden) (1)	Handen (2)	Overige materialen* (3)
salpeterzuur (16)	☐	☐	☐
fosfaatesters (17)	☐	☐	☐
fosforzuur (18)	☐	☐	☐
kaliumhydroxide (19)	☐	☐	☐
natriumhydroxide (20)	☐	☐	☐
sulfoniczuur (natrium C12-C14, olefin sulfonaat) (21)	☐	☐	☐
sulfamidezuur (22)	☐	☐	☐
Anders, namelijk (23)	☐	☐	☐
Anders, namelijk (24)	☐	☐	☐
Anders, namelijk (25)	☐	☐	☐

* Kunt u aangeven voor welke overige materialen u de vraag hierboven heeft beantwoord?

____

Vraag 2
Wordt er na het reinigen altijd gespoeld met water?

- ☐ Ja (1)
- ☐ Nee, omdat (2) ____

Vraag 3
Wordt er na het reinigen altijd gedesinfecteerd?

- ☐ Ja (1)
- ☐ Nee, omdat (2) ____

Bedankt voor uw medewerking!

A4.2 Questionnaire for cleaning agents in processing facilities

Voor een onderzoek naar reinigings- en desinfectiemiddelen voor de Nederlandse Voedsel- en Warenautoriteit wordt er bekeken welke reinigingsmiddelen in de praktijk gebruikt worden in de pluimveeketen. Hierbij kan uw input zeer waardevol zijn. Derhalve willen wij u vriendelijk enkele minuten van uw tijd vragen om de onderstaande vragen te beantwoorden.

Definitie Voor het doel van deze vragenlijst wordt de volgende definitie gebruikt;
Reinigingsmiddel: een middel voor het verwijderen van aarde, voedselresidu, vuil, vet, etcetera.

Vraag 1
Welke van de onderstaande reinigingsmiddelen worden gebruikt voor het reinigen van de vloeren in de verwerking, bij het wassen van handen van medewerkers en voor het reinigen van apparatuur (bv. snijmachines, transportbanden)?

	Vloeren, wanden (1)	Handen (2)	Apparatuur (bv. snijmachines, transportbanden) (3)
1-dodecanaminium, n-(2-hydroxy-3-sulfopropyl)-n,n-dimethyl-, inner salt (1)	☐	☐	☐
2-(2-butoxyethoxy)ethanol (2)	☐	☐	☐
3-butoxy-2-propanol (3)	☐	☐	☐
alcohol, C12-14 geëthoxyleerde sulfaten (4)	☐	☐	☐
alkaline fosfaten (5)	☐	☐	☐
alkyl amidopropyl betaines/ C12-C14 pareth-4, cocamidopropylbetaïne (6)	☐	☐	☐
alkylamine oxides (Amines, C12-14 alkyldimethyl, N-oxides) (7)	☐	☐	☐
amines, C8-C18 (even genummerd) and C18 onverzadigd, N, N-bishydroxyethyl (8)	☐	☐	☐
arylsulfonaten (bv cumeensulfonaat) (9)	☐	☐	☐
C14-16 (even genummerd)-alkane hydroxy en C14-16 (even genummerd)-alkene natrium zouten (10)	☐	☐	☐
D-glucopyranose, oligomeric, decyl octyl glycoside (11)	☐	☐	☐
ethanolamines (12)	☐	☐	☐
ethyleendiaminetetraacetaat (EDTA) (13)	☐	☐	☐
vetalcoholethoxylaat (getoxyleerd) (14)	☐	☐	☐
N-C8-22-alkyltrimethyleendi- acrylated natrium zouten (15)	☐	☐	☐
salpeterzuur (16)	☐	☐	☐
fosfaatesters (17)	☐	☐	☐
fosforzuur (18)	☐	☐	☐
kaliumhydroxide (19)	☐	☐	☐
natriumhydroxide (20)	☐	☐	☐
sulfoniczuur (natrium C12-C14, olefin sulfonaat) (21)	☐	☐	☐

	Vloeren, wanden (1)	Handen (2)	Apparatuur (bv. snijmachines, transportbanden) (3)
sulfamidezuur (22)	☐	☐	☐
Anders, namelijk (23)	☐	☐	☐
Anders, namelijk (24)	☐	☐	☐
Anders, namelijk (25)	☐	☐	☐

* Kunt u aangeven voor welke overige materialen u de vraag hierboven heeft beantwoord?

____

Vraag 2
Wordt er na het reinigen altijd gespoeld met water?

- ☐ Ja (1)
- ☐ Nee, omdat (2) ____

Vraag 3
Wordt er na het reinigen altijd gedesinfecteerd?

- ☐ Ja (1)
- ☐ Nee, omdat (2) ____

Bedankt voor uw medewerking!

A4.3 Questionnaire for cleaning agents in stables and processing facilities

Voor een onderzoek naar reinigings- en desinfectiemiddelen voor de Nederlandse Voedsel- en Warenautoriteit wordt er bekeken welke reinigingsmiddelen in de praktijk gebruikt worden in de pluimveeketen. Hierbij kan uw input zeer waardevol zijn. Derhalve willen wij u vriendelijk enkele minuten van uw tijd vragen om de onderstaande vragen te beantwoorden.

Definitie Voor het doel van deze vragenlijst wordt de volgende definitie gebruikt;
Reinigingsmiddel: een middel voor het verwijderen van aarde, voedselresidu, vuil, vet, etcetera.

Vraag 1
Welke van de onderstaande reinigingsmiddelen worden gebruikt voor het reinigen van de stallen en bij de verwerking?

	Stallen (vloeren, wanden) (1)	Handen (mede-werkers stal) (2)	Overige materialen, die gebruikt worden in de stallen* (3)	Vloeren, wanden in de verwerking (4)	Handen (mede-werkers verwerking) (5)	Apparatuur, materiaal in de verwerking (bv. snijmachines, transport-banden) (6)
1-dodecanaminium, n-(2-hydroxy-3-sulfopropyl)-n,n-dimethyl-, inner salt (1)						
2-(2-butoxyethoxy)ethanol (2)						
3-butoxy-2-propanol (3)						
alcohol, C12-14 geëthoxyleerde sulfaten (4)						
alkaline fosfaten (5)						
alkyl amidopropyl betaines/ C12-C14 pareth-4, cocamidopropylbetaïne (6)						
alkylamine oxides (Amines, C12-14 alkyldimethyl, N-oxides) (7)						
amines, C8-C18 (even genummerd) en C18 onverzadigd, N, N-bishydroxyethyl (8)						
arylsulfonaten (bv cumeensulfonaat) (9)						
C14-16 (even genummerd)-alkane hydroxy en C14-16 (even genummerd)-alkene natrium zouten (10)						
D-glucopyranose, oligomeric, decyl octyl glycoside (11)						
ethanolamines (12)						
ethyleendiaminetetraacetaat (EDTA) (13)						
vetalcoholethoxylaat (getoxyleerd) (14)						
N-C8-22-alkyltrimethyleendi-acrylated natrium zouten (15)						
salpeterzuur (16)						
fosfaatesters (17)						
fosforzuur (18)						
kaliumhydroxide (19)						

	Stallen (vloeren, wanden) (1)	Handen (mede-werkers stal) (2)	Overige materialen, die gebruikt worden in de stallen* (3)	Vloeren, wanden in de verwerking (4)	Handen (mede-werkers verwerking) (5)	Apparatuur, materiaal in de verwerking (bv. snijmachines, transport-banden) (6)
natriumhydroxide (20)	☐	☐	☐	☐	☐	☐
sulfoniczuur (natrium C12-C14, olefin sulfonaat) (21)	☐	☐	☐	☐	☐	☐
sulfamidezuur (22)	☐	☐	☐	☐	☐	☐
Anders, namelijk (23)	☐	☐	☐	☐	☐	☐
Anders, namelijk (24)	☐	☐	☐	☐	☐	☐
Anders, namelijk (25)	☐	☐	☐	☐	☐	☐

* Kunt u aangeven voor welke overige materialen u de vraag hierboven heeft beantwoord?

____

Vraag 2
Wordt er na het reinigen altijd gespoeld met water?
- ☐ Ja (1)
- ☐ Nee, omdat (2) ____

Vraag 3
Wordt er na het reinigen altijd gedesinfecteerd?
- ☐ Ja (1)
- ☐ Nee, omdat (2) ____

Bedankt voor uw medewerking!

Annex 5 Interviews poultry (Phase II)

A5.1 Interview met pluimveehouders of transporteurs

1. Hoe gaat het proces van reiniging in zijn werk? Hoe wordt er gekozen welke reinigingsmiddelen gebruikt worden?
2. Welke reinigingsmiddelen worden het meest toegepast:
   a. Voor het reinigen van stallen en materialen
   b. Voor de transportkratten en -wagens
   c. Voor het wassen van de handen
3. Welke concentraties worden meestal gebruikt bij aangegeven middelen?
4. Hoe vaak wordt er met deze middelen schoongemaakt? (bv: dagelijks of iedere keer na het uitladen,.....)
5. Zijn er procedures om het reinigen te controleren? Hoe gaat dit in zijn werk?
6. Welke van de onderstaande fouten kunnen plaatsvinden bij de reiniging:
   a. Verwisselen van reinigings- en/ of desinfectiemiddelen. Dit gebeurt:
      i. dagelijks
      ii. 1x/week
      iii. 1x/maand
      iv. 1x/jaar
      v. <1x/jaar
   b. Gebruik van verkeerde concentraties. Dit gebeurt:
      i. dagelijks
      ii. 1x/week
      iii. 1x/maand
      iv. 1x/jaar
      v. <1x/jaar
   c. Te kort of te lang reinigen. Dit gebeurt:
      i. dagelijks
      ii. 1x/week
      iii. 1x/maand
      iv. 1x/jaar
      v. <1x/jaar
   d. Niet spoelen na de reiniging. Dit gebeurt:
      i. dagelijks
      ii. 1x/week
      iii. 1x/maand
      iv. 1x/jaar
      v. <1x/jaar
7. Hoe komt het dat a, b, c of d wel eens misgaat?
8. Waar en hoe kunnen residuen van reinigingsmiddelen in contact komen met de kip? Wat wordt er gedaan om dit te voorkomen?

A5.2 Interview met pluimveeverwerkers

1. Hoe gaat het proces van reiniging in zijn werk? Hoe wordt er gekozen welke reinigingsmiddelen gebruikt worden?
2. Welke reinigingsmiddelen worden het meest toegepast:
   a. Voor reinigen van apparatuur (snijmachines, transportbanden)
   b. Voor het reinigen van vloeren en wanden
   c. Voor het wassen van de handen

3. Welke concentraties worden meestal gebruikt bij aangegeven middelen?
4. Hoe vaak wordt er met deze middelen schoongemaakt? (1x/dag, 1x/week?)
5. Zijn er procedures om het reinigen te controleren? Hoe gaat dit in zijn werk?
6. Welke van de onderstaande fouten kunnen plaatsvinden bij de reiniging:
    a. Verwisselen van reinigings- en desinfectiemiddelen. Dit gebeurt:
        i. dagelijks
        ii. 1x/week
        iii. 1x/maand
        iv. 1x/jaar
        v. <1x/jaar
    b. Gebruik van verkeerde concentraties. Dit gebeurt:
        i. dagelijks
        ii. 1x/week
        iii. 1x/maand
        iv. 1x/jaar
        v. <1x/jaar
    c. Te kort of te lang reinigen. Dit gebeurt:
        i. dagelijks
        ii. 1x/week
        iii. 1x/maand
        iv. 1x/jaar
        v. <1x/jaar
    d. Niet spoelen na de reiniging. Dit gebeurt:
        i. dagelijks
        ii. 1x/week
        iii. 1x/maand
        iv. 1x/jaar
        v. <1x/jaar
7. Hoe komt het dat a, b, c of d wel eens misgaat?
8. Waar en hoe kunnen residuen van reinigingsmiddelen in contact komen met de kipproducten? Wat wordt er gedaan om dit te voorkomen?

Annex 6 Decontamination and surfactants

Table A6.1 *Types of decontamination agents reported during the literature study for poultry and eggs*

Groups	Type of decontaminant agent	References
Chlorine-containing compounds	Chlorine dioxide (poultry)	(Johnson, 2014; Umaraw et al., 2017)
	Acidified sodium chlorite (poultry)	(Johnson, 2014; Umaraw et al., 2017)
	Chlorine (poultry)	(Barbut & Pronk, 2014; Umaraw et al., 2017)
	Chlorhexidine (poultry)	(GonÇalo, 2012)
Quaternary ammonium compounds	Quaternary ammonium compounds (eggs)	(Turtoi & Borda, 2014)
Acids	Lactic acid (poultry)	(Barbut & Pronk, 2014; Umaraw et al., 2017)
	Acetic acid (poultry)	(Umaraw et al., 2017)
	Peroxyacids (poultry)	(Johnson, 2014; Umaraw et al., 2017)
Others	Formaldehyde (poultry and eggs)	(GonÇalo, 2012; Turtoi & Borda, 2014)
	Glutardehyde (poultry)	(GonÇalo, 2012)
	Hydrogen peroxide (eggs)	(Galis et al., 2013; Turtoi & Borda, 2014)
	Phenol (eggs)	(Turtoi & Borda, 2014)
	Sodium hydroxide (eggs)	(Turtoi & Borda, 2014)
	Triphenylphosphate (TPP) (poultry)	(Barbut & Pronk, 2014)
	Trisodium phosphate (TSP) (poultry)	(Barbut & Pronk, 2014; Johnson, 2014; Umaraw et al., 2017)

Table A6.2 *Types of decontamination agents during processing of leafy greens*

Group	Type of disinfectant	References
Chlorine containing compounds	Acidified sodium chlorite (ASC)	(Foong-Cunningham, Verkaar, & Swanson, 2012; Niemira & Fan, 2014; Olaimat & Holley, 2012)
	Calcium hypochlorite	(Erickson, 2012)
	Chlorinated trisodium phosphate	(Koseki, 2014)
	Chlorine (free or gas)	(Baert, Debevere, & Uyttendaele, 2009; Erickson, 2012; Foong-Cunningham et al., 2012; Goodburn & Wallace, 2013; Joshi, Mahendran, Alagusundaram, Norton, & Tiwari, 2013; Keskinen & Annous, 2011; Koseki, 2014; Niemira & Fan, 2014; Olmez & Kretzschmar, 2009)
	Chlorine dioxide (aq. or gas)	(Baert et al., 2009; Foong-Cunningham et al., 2012; Garg, Abela, Tiwari, & Valdramidis, 2016; Gomez-Lopez, Rajkovic, Ragaert, Smigic, & Devlieghere, 2009; Goodburn & Wallace, 2013; Joshi et al., 2013; Keskinen & Annous, 2011; Koseki, 2014; Murray et al., 2017; Niemira, 2010; Niemira & Fan, 2014; Olaimat & Holley, 2012; Olmez & Kretzschmar, 2009)
	Mercury chloride	(Erickson, 2012)
	Sodium hypochlorite	(Afari & Hung, 2018; Erickson, 2012; Koseki, 2014; Niemira, 2010)
Alcohols	Ethanol	(Erickson, 2012)

Group	Type of disinfectant	References
Acids	Organic acids (acetic acid, citric acid, fumaric acid, lactic acid, levulinic acid, malic acid)	(Foong-Cunningham et al., 2012; Garg et al., 2016; Koseki, 2014; Koutsoumanis & Skandamis, 2013; Niemira & Fan, 2014; Olaimat & Holley, 2012; Olmez & Kretzschmar, 2009)
	Peracetic acid or peroxyacetic acid	(Baert et al., 2009; Joshi et al., 2013; Koseki, 2014; Koutsoumanis & Skandamis, 2013; Niemira & Fan, 2014; Olaimat & Holley, 2012; Olmez & Kretzschmar, 2009)
	Tartatric acid	(Koutsoumanis & Skandamis, 2013)
Ozone	Ozone (aq. or gas)	(Baert et al., 2009; Foong-Cunningham et al., 2012; Garg et al., 2016; Joshi et al., 2013; Koseki, 2014; Murray et al., 2017; Niemira, 2010; Niemira & Fan, 2014; Olmez & Kretzschmar, 2009; Perry & Yousef, 2011)
Hydrogen peroxide	Hydrogen peroxide	(Baert et al., 2009; Foong-Cunningham et al., 2012; Joshi et al., 2013; Koseki, 2014; Olaimat & Holley, 2012; Olmez & Kretzschmar, 2009)
Electrolyzed water	Electrolyzed oxidizing water (EOW) - acidic, slightly acidic, neutral, alkaline, e.g., from the use of sodium chloride	(Afari & Hung, 2018; Foong-Cunningham et al., 2012; Garg et al., 2016; Goodburn & Wallace, 2013; Joshi et al., 2013; Koseki, 2014; Niemira, 2010; Niemira & Fan, 2014; Olaimat & Holley, 2012; Olmez & Kretzschmar, 2009)
Others	Chitosan film enriched with oleoresins	(Moreira, Ponce, & Roura, 2008)
	Essential oils	(Garg et al., 2016; Goodburn & Wallace, 2013; Joshi et al., 2013; Koseki, 2014; Moreira, Alvarez, & Ponce, 2016; Moreira et al., 2008)
	Lactic acid bacteria	(Moreira et al., 2008)
	Potassium sorbate	(Garg et al., 2016)
	Silver nitrate	(Erickson, 2012)
	Silver nitrate and hydrogen peroxide	(Goodburn & Wallace, 2013)
	Sodium lactate	(Garg et al., 2016)

Table A6.3 *Types of surfactants reported during the literature study for leafy greens*

Group	Type of surfactant	References
Surfactants	Anionic (dodecyle sulphate; SDS)	(Warriner & Namvar, 2013)
	Catonic (quaternary ammonium compounds)	(Warriner & Namvar, 2013)
	Caprylic acid	(Warriner & Namvar, 2013)
	Non-ionic (Tween, Triton X-100)	(Warriner & Namvar, 2013)
	Sodium 2-ethylhexyl sulphate	(Sapers, 2009)
	Sodium dodecylbenzene sulfonate	(Sapers, 2009)
	Sodium mono- and dimethyl naphthalene sulfonates	(Sapers, 2009)
	Sodium n-alkylbenzene sulfonate	(Sapers, 2009)

Table A6.4 *Types of disinfectants reported to be used to decontaminate seeds and/or sprouts*

Group	Type of disinfectant (purpose: decontamination) *
Chlorine containing compounds	Acidified sodium chlorite (ASC)
	Calcium hypochlorite
	Chlorine
	Chlorine dioxide
	Sodium hypochlorite
	Sodium chloride
	Stabilised oxychloro complex (SOC)
Quaternary ammonium compounds	Cetylpyridinium chloride (CPC)
Alcohols	Ethanol
Acids	Acetic acid (incl. gaseous acetic acid)
	Caprylic acid and monocaprylin
	Ethylenediaminetetraacetic acid (EDTA)
	Fatty acids
	Fumaric acid
	Hydrocinnamic acid
	Lactic acid
	Malic acid
	Oxalic acid
	Peracetic acid or peroxyacetic acid
	Phytic acid
	Polyphosphoric acid
Ozone	Ozone (incl. ozonated water)
Hydrogen peroxide	Hydrogen peroxide
Electrolyzed water	Electrolyzed oxidizing water (EOW) - acidic, slightly acidic, alkaline
	Ozone (incl. ozonated water)
Others	1% grapefruit seeds extract
	Bayleaf
	Calcium oxide (cao)
	Carvacrol
	Propyl-p-hydroxybenzoate
	Summer savoury
	Silver nitrate
	Thiamine dilaurylsulphate (TDS)
	Thiram
	Thyme hydrosols
	Trisodium phosphate (TSP)
	Vinegar

* References: (Annous & Burke, 2015; L. Bari, K. Enomoto, D. Nei, & S. Kawamoto, 2010; M. L. Bari, K. Enomoto, D. Nei, & S. Kawamoto, 2010; Bari, Enomoto, Nei, & Kawamoto, 2011; Bari, Nei K, Enomoto, Todoriki, & Kawamoto, 2009; Bari, Sugiyama, & Kawamoto, 2009; Buchholz & Matthews, 2010; Chiu, 2015; Choi, Beuchat, Kim, & Ryu, 2016; Cobo Molinos et al., 2008; Cui, Walcott, & Chen, 2017; Dikici, Koluman, & Calicioglu, 2015; Ding, Fu, & Smith, 2013; Fransisca & Feng, 2012; Fransisca, Park, & Feng, 2012; Ge, Rymut, Lee, & Lee, 2014; Inatsu et al., 2017; Issa-Zacharia, Kamitani, Miwa, Muhimbula, & Iwasaki, 2011; Kordusiene, Danilcenko, Taraseviciene, Jariene, & Jeznach, 2010; Kwack, Kim, Hwang, & Chun, 2014; Landry et al., 2016; Liao, 2009; Liu, Shi, et al., 2014; Liu & Yu, 2017; Liu, Zhang, et al., 2014; Millan-Sango, Sammut, Van Impe, & Valdramidis, 2017; Nei, Bari, & Enomoto, 2013; Nei, Enomoto, & Nakamura, 2015; Nei, Enomoto, & Yamamoto, 2014; Nei, Latiful, Enomoto, Inatsu, & Kawamoto, 2011; Neo et al., 2013; Ngnitcho, Khan, Tango, Hussain, & Oh, 2017; Ngnitcho et al., 2018; Peñas, Gómez, Frías, & Vidal-Valverde, 2009; Phua, Neo, Khoo, & Yuk, 2014; Prodduk, Annous, Liu, & Yam, 2014; Sahan & Tornuk, 2016; Sikin, Zoellner, & Rizvi, 2013; Singla, Ganguli, & Ghosh, 2011; Smith & Herges, 2018; Trząskowska, Dai, Delaquis, & Wang, 2018; C. J. Wang et al., 2013; Q. Wang & Kniel, 2014; Q. Wang, Markland, & Kniel, 2015; Xu & Ma, 2016; Yang et al., 2013)

Annex 7 Active ingredients authorised for use in Dutch biocide products according to the Ctgb database

Table A7.1 *Number of products approved under PT 1, PT 3, and/or PT 4 per active ingredient (www.ctgb.nl, June 2018)*

Active ingredient	PT 1	PT 3	PT 4	Total
1-propanol	2	0	0	2
1-propanol,2-propanol	2	0	1	3
1-propanol,2-propanol,ethanol	0	0	2	2
1-propanol,ethanol	1	0	4	5
2-fenoxyethanol,chloorhexidinedigluconaat	1	0	0	1
2-propanol	6	0	1	7
2-propanol,1-propanol	1	0	0	1
2-propanol,chloorhexidinedigluconaat	4	0	0	4
2-propanol,ethanol	1	0	0	1
2-propanol,ethanol,chloorhexidinedigluconaat	1	0	0	1
alkyl (C12-14) dimethyl (ethylbenzyl) ammoniumchloride,Alkyl (C12-18) dimethylbenzylammoniumchloride	0	0	1	1
Alkyl (C12-16) dimethylbenzylammoniumchloride	1	1	5	7
Alkyl (C12-16) dimethylbenzylammoniumchloride,didecyldimethylammoniumchloride	0	0	4	4
Alkyl (C12-16) dimethylbenzylammoniumchloride,didecyldimethylammoniumchloride,glutaaraldehyde	0	1	0	1
Alkyl (C12-16) dimethylbenzylammoniumchloride,glutaaraldehyde	0	4	0	4
Alkyl (C12-16) dimethylbenzylammoniumchloride,glutaaraldehyde,didecyldimethylammoniumchloride	0	1	0	1
Alkyl (C12-16) dimethylbenzylammoniumchloride,glutaaraldehyde,didecyldimethylammoniumchloride, formaldehyde	0	1	0	1
Alkyl (C12-16) dimethylbenzylammoniumchloride,N-(3-aminopropyl)-N-dodecylpropaan-1,3-diamine	0	0	1	1
Alkyl (C12-18) dimethylbenzylammoniumchloride,alkyl (C12-14) dimethyl (ethylbenzyl) ammoniumchloride	0	0	1	1
Alkyl (C12-18) dimethylbenzylammoniumchloride,glutaaraldehyde	0	1	0	1
Alkyl (C12-18) dimethylbenzylammoniumchloride,N-(3-aminopropyl)-N-dodecylpropaan-1,3-diamine	0	0	1	1
alkyl (C8-18) dimethylbenzylammoniumchloride	0	1	8	9
bifenyl-2-ol	0	0	1	1
broomazijnzuur	0	0	2	2
chloorhexidinedigluconaat	2	7	0	9
chloorhexidinedigluconaat,2-propanol	3	0	0	3
chloorhexidinedigluconaat,alkyl (C8-18) dimethylbenzylammoniumchloride	0	1	0	1
chloorhexidinedigluconaat,ethanol	1	0	0	1
chloorhexidinedigluconaat,polyhexamethyleenbiguanide hydrochloride	0	1	0	1
chloorkresol	0	5	0	5
decaanzuur,L-(+)-melkzuur	0	2	0	2
didecyldimethylammoniumchloride	0	5	127	132
didecyldimethylammoniumchloride,Alkyl (C12-16) dimethylbenzylammoniumchloride	0	1	0	1
didecyldimethylammoniumchloride,Alkyl (C12-16) dimethylbenzylammoniumchloride,glutaaraldehyde	0	2	0	2
didecyldimethylammoniumchloride,formaldehyde,Alkyl (C12-16) dimethylbenzylammoniumchloride,glutaaraldehyde	0	1	0	1
didecyldimethylammoniumchloride,formaldehyde,glutaaraldehyde	0	2	0	2
didecyldimethylammoniumchloride,glutaaraldehyde,Alkyl (C12-16) dimethylbenzylammoniumchloride	0	2	1	3

Active ingredient	PT 1	PT 3	PT 4	Total
didecyldimethylammoniumchloride,glutaaraldehyde,formaldehyde	0	3	0	3
ethanol	38	0	33	71
ethanol,1-propanol	5	0	0	5
ethanol,2-propanol	1	0	0	1
ethanol,amines, n-C10-16-alkyltrimethyleendi-, reactieproducten met chloorazijnzuur, 1-propanol,2-propanol	0	0	1	1
ethanol,bifenyl-2-ol	2	0	0	2
ethanol,chloorhexidinedigluconaat	2	0	0	2
ethanol,glutaaraldehyde	0	0	1	1
ethanol,waterstofperoxide	1	0	0	1
formaldehyde	0	3	0	3
formaldehyde,glutaaraldehyde,didecyldimethylammoniumchloride	0	3	0	3
glutaaraldehyde,Alkyl (C12-16) dimethylbenzylammoniumchloride	0	4	1	5
glutaaraldehyde,Alkyl (C12-16) dimethylbenzylammoniumchloride,didecyldimethylammoniumchloride	0	2	1	3
glutaaraldehyde,Alkyl (C12-18) dimethylbenzylammoniumchloride	0	1	0	1
glutaaraldehyde,didecyldimethylammoniumchloride,Alkyl (C12-16) dimethylbenzylammoniumchloride	0	3	1	4
glutaaraldehyde,ethanol	0	0	3	3
jood	0	31	0	31
L-(+)-melkzuur	0	7	1	8
L-(+)-melkzuur,decaanzuur	0	2	0	2
L-(+)-melkzuur,glycolzuur	0	0	2	2
L-(+)-melkzuur,natriumchloriet	0	3	0	3
L-(+)-melkzuur,salicylzuur	0	3	0	3
N-(3-aminopropyl)-N-dodecylpropaan-1,3-diamine	0	2	4	6
N-(3-aminopropyl)-N-dodecylpropaan-1,3-diamine,Alkyl (C12-16) dimethylbenzylammoniumchloride	0	1	2	3
natriumchloriet	0	0	1	1
natriumchloriet,L-(+)-melkzuur	0	4	0	4
natriumchloriet,natriumbisulfaat	0	0	3	3
natriumchloriet,zoutzuur	0	0	2	2
natriumdichloorisocyanuraat	0	9	15	24
natriumdichloorisocyanuraat,pentakalium bis(peroxymonosulfaat)bis(sulfaat)	0	3	3	6
natriumdichloorisocyanuraatdihydraat	0	2	3	5
natriumhypochloriet	9	37	102	148
natriumpercarbonaat,tetra-acetylethyleendiamine	0	2	1	3
natriumpersulfaat,natriumchloriet	0	0	1	1
natrium-p-tolueensulfonchloramide	0	2	2	4
octaanzuur,decaanzuur	0	0	2	2
p-chloor-m-cresol	0	1	0	1
pentakalium bis(peroxymonosulfaat)bis(sulfaat)	0	1	0	1
pentakalium bis(peroxymonosulfaat)bis(sulfaat),natriumdichloorisocyanuraat	0	1	1	2
perazijnzuur,waterstofperoxide	0	12	31	43
peroctaanzuur,perazijnzuur,waterstofperoxide	0	0	1	1
peroctaanzuur,waterstofperoxide,perazijnzuur	0	0	2	2
salicylzuur	0	5	3	8
salicylzuur,L-(+)-melkzuur	0	2	0	2
waterstofperoxide	1	4	46	51
waterstofperoxide,ethanol	1	0	0	1
waterstofperoxide,L-(+)-melkzuur	0	4	11	15
waterstofperoxide,perazijnzuur	0	29	34	63
Total	**86**	**225**	**474**	**785**

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