Disinfectants in consumer products

Gezondheidsraad **President**
Health Council of the Netherlands

To the Minister of Health, Welfare and Sport

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Madam Minister,

I hereby present you with an advisory report of the Health Council of the Netherlands on the benefits and risks of the increasing use made by consumers of products containing disinfectants. The advisory report was prepared at my request by the Health Council's Secretariat and was assessed by the Standing Committee on Health and the Environment and the Standing Committee on Infection and Immunity. I endorse the considerations, conclusions and recommendations it contains, including the call for restraint in the addition of disinfectants to consumer products and in the use of products containing such substances. This applies in particular to products for which there is no evidence that they actually help to reduce the burden of disease by infections.

Today, I have also presented this advisory report to the Minister of Housing, Spatial Planning and the Environment.

Yours sincerely,

(signed)

prof. dr JJ Sixma

P.O Box 16052
NL-2500 BB Den Haag
Telephone +31 (70) 340 75 20
Telefax +31 (70) 340 75 23

Visiting Address
Parnassusplein 5
NL - 2511 VX Den Haag
email: GR@gr.nl

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to:

the Minister of Health, Welfare and Sport

the Minister of Housing, Spatial Planning and the Environment

No. 2001/05E, The Hague, 16 February 2001

The Health Council of the Netherlands, which was established in 1902, is an advisory body with the task "to advise the government and Parliament on the current level of knowledge with respect to public health issues" (art. 21 Health Act).

The Health Council receives most of its requests for advisory reports from the ministers of Health, Welfare & Sport; Housing, Spatial Planning and the Environment; Social Affairs and Employment; and Agriculture, Nature Management and Fisheries. The Council may also produce advisory reports on its own initiative. As a rule, this then concerns calling attention to developments or trends that may be relevant to government policy.

The Health Council's advisory reports are made public and are almost always compiled by multidisciplinary committees of Dutch and, occasionally, foreign experts who are appointed in a personal capacity.

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Contents

Executive summary

Over the last few years an increasing number of consumer products containing disinfectant substances, such as triclosan, chlorhexidine or quaternary ammonium compounds, have come onto the market. In particular, their inclusion in cleaning agents and in personal hygiene products, such as hand soap, shower gel, deodorant and toothpaste, has been on the increase. Producers claim that these supplemented products offer consumers increased protection against harmful micro-organisms. Because infections represent a considerable proportion of the burden of disease in our country, a greater use of disinfectant substances might yield benefits to health. At the same time, however, the disinfectant effect of the substances is due to the fact that they are toxic to certain organisms, with the corollary that they may be not entirely harmless. In the present report, the pros and cons are weighed against each other. Both the importance of disinfectants for public health and their effect on the environment are considered. Greater emphasis is placed on the former.

There is no scientific evidence that the routine use of disinfectants in the home is beneficial. This applies in particular to disinfectant and so-called 'hygienic' cleaning agents and to antibacterial (hand) soap and other skin care products. If the instructions on good hygiene are followed, such as regularly washing one's hands, cleaning and drying the worktop and keeping raw and cooked food separate, the risk of contracting an infection at home is small. Disinfection in most cases will help little in reducing the risk. Antibacterial substances in toothpaste and deodorant, however, do contribute to the efficacy of the product.

It is not possible to answer the question of whether (large-scale) domestic use of disinfectant substances is associated with risks to public health and the quality of the environment. On theoretical grounds and on the basis of results from laboratory investigations, it cannot be ruled out that there will be problems as a result of toxicity to humans (for example skin irritation), changes in the normal microbial flora of the skin and mucous membranes (with the associated increase in the risk of infections from pathogens), resistance development and contamination of the environment. In particular, the possibility of micro-organisms becoming increasingly resistant to disinfectants, and perhaps also to antibiotics, is a cause for concern. There is indeed no firm evidence that serious problems occur in practice, but few practical studies have been undertaken to date. Moreover, the use of disinfectants can instil a(n) (unjustified) sense of security, which may encourage the neglect of normal hygiene.

In view of the unproven benefit to health and the possible risks of large-scale domestic use of disinfectants, restraint in adding these substances to consumer products and in using these supplemented products is advisable. In particular, cleaning agents and skin care products with an antibacterial or 'hygienic' effect should only be used on a doctor's advice on the basis of medical indications. It is recommended that these indications should be specified further. Proper instruction of the user by an expert is necessary.

There is a need to gain insight into the extent to which, under practical conditions, micro-organisms become resistant to disinfectants and into the effects of large-scale and long-term use of these substances by consumers on antibiotic resistance. More knowledge is also required about the effect of the use of disinfectants on the normal microflora and the possible consequences for human health. There is also a need to gain insight into the extent to which disinfectants enter the environment, into their fate there and into the ecological consequences.

The legal options for restricting the marketing of consumer products containing disinfectants are limited. Under the Pesticides Act and the Drug Supply Act it is not possible to keep products off the market just because there are good alternatives available, in this case 'ordinary' cleaning. Under the Commodities Act registration is not required, which makes it not feasible as a management tool. Even so, there are plans and initiatives, both on a national and an international level, to get a firmer grip on the addition of disinfectants to consumer products by changing legislation or changing the interpretation of the law. Voluntary agreements with the industry and public information represent other policy instruments. The message to the consumer should be that good household and personal hygiene is the best way of limiting the risk of infection and that for many antibacterial and hygienic products there is no evidence that they actually help to reduce the burden of disease. Furthermore, it is important to

stress that most micro-organisms are harmless or even beneficial and that only a few are pathogenic.

Chapter 1

Introduction

Nowadays, man disposes of an impressive array of substances for combating micro-organisms. These so-called antimicrobial agents include preservatives, antibiotics and disinfectants. Preservatives are intended to protect water-based products from decay caused by bacterial or fungal growth. Antibiotics are used to combat bacterial infections with humans and animals. Disinfectants are meant to prevent humans and animals or products from becoming contaminated with micro-organisms. Disinfectants have long been used in hospitals and other health care institutions to disinfect rooms, medical equipment and the skin of patients and health care workers. They have also long been used on a large scale in industry and agriculture. A more recent development is the practice of adding disinfectants to consumer products, especially products for personal hygiene and cleaning agents, to protect the user from micro-organisms. There has been a similar trend in other countries, including the United States and Great Britain.

Infections form a substantial part of the total burden of disease in the Netherlands. It is therefore conceivable that more widespread use of disinfectant substances could be beneficial to health. At the same time, the disinfectant effect of these substances is based on the fact that they are toxic to certain organisms; therefore, they may not be completely harmless.

This advisory report examines the increasing use of disinfectant substances by consumers in the West and the resulting impact on health and the environment. The

following chapters consider the term disinfection and the use of disinfectant substances in consumer products, along with the benefits of using disinfectants in households and with personal hygiene, as well as the possible hazards of such use. The final chapter considers the legislation and regulations relating to these agents and the use of consumer information as a means of control.

Chapter **2**

Disinfection using chemicals

2.1 Definition of concepts

Bacteria, viruses, fungi and other micro-organisms are almost ubiquitous; they are found in soil, on objects, plants and animals, and also on the human skin and mucous membranes. They are generally not very harmful, in fact quite the contrary (see chapter 4). However, if they enter parts of the body where they do not belong, they can cause infections. Therefore, potential pathogens have to be removed from objects or skin that may facilitate their transfer. Typical examples would be medical instruments, for example, which are used in examinations or that are brought into a patient's body during an operation, a surgeon's hands and kitchen utensils that have been in contact with raw food, such as chicken meat. Disinfection involves treating objects, skin or mucous membranes[a] to reduce the number of micro-organisms on them to an acceptable level (WIP00). Not all the pathogens are always killed; bacterial spores are particularly likely to survive a disinfection process. Disinfection can be performed using hot water, steam or chemical substances. Such substances are known as disinfectants. A disinfectant must at least be capable of killing bacterial cells, with the exception of spores, at a certain concentration, within a specific contact time. Many chemical compounds have this property (table 1). Some of them are used in consumer products.

[a] Skin or mucous membrane disinfection is also known as antisepsis. This term is deprecated (GR90).

2.2 Modes of action

There are various ways in which disinfectants achieve their disinfectant effect (Sev92). Some frequently occurring modes of action are:

- damage to the cell wall that results in the cell bursting open (lysis)
- damage to the cytoplasmic membrane, which causes the cell to leak
- interaction with the cytoplasm, which causes proteins or nucleic acids, for example, to coagulate or to lose their spatial structure, or other disruptions of cell structures or metabolism.

In contrast to antibiotics, which generally work very specifically, disinfectants often affect several structures or processes simultaneously (Rus99). Therefore, they are usually effective against a wide variety of micro-organisms, although some agents are more effective against one group of organisms and other agents are more effective against other groups (Sev92, WIP00).

The degree to which micro-organisms are resistant to disinfectant substances varies considerably (McD99 Rus98b, Sev92). In particular, bacterial spores are relatively insusceptible. Some organisms are naturally resistant; in which case the term intrinsic resistance is used. Cells may often have outside layers that are difficult to penetrate (spore wall, cell wall, mucus layer) and which prevent or inhibit a disinfectant's ability to reach its target. Micro-organisms that are naturally susceptible may become resistant as a result of genetic changes. This is known as acquired resistance. This may involve a mutation in the original genetic material or the acquisition of new strands of DNA (plasmids). The genetic change may result in a reduced penetrability of the outside layers of the cell, in the formation of pump systems that quickly expel the disinfectant from the cell, before it can do any harm, or the result may be that formerly susceptible enzymes become insusceptible.

The effectiveness of disinfectants also depends on other factors, including the quantity of micro-organisms, the concentration of the agent used, the contact time, external conditions such as temperature, the pH and hardness of the water, the presence of absorbent organic material and the presence of additives in the commercial product, i.e. the formulation (Lev99b, Rus00b, Sev92, Sul00).

Table 1 Disinfectant substances and their uses (adapted from McD99).

substance	*substance group*	*application*
ethanol	alcohols	disinfection
isopropanol		skin/mucous membrane disinfection
glutaraldehyde	aldehydes	disinfection
formaldehyde		
triclocarban	anilides	skin/mucous membrane disinfection
chlorhexidine	biguanides	skin/mucous membrane
alexidine		disinfection
polymeric biguanides		anti-dental-plaque agent disinfection
triclosan	bisphenols	skin/mucous membrane
hexachlorophene		disinfection
		anti-dental-plaque agent deodorant
propamidine	diamidines	skin/mucous membrane
dibromopropamidine		disinfection
chlorine compounds	halogen-releasing compounds	disinfection
iodine compounds		skin/mucous membrane disinfection
PCMX (*p*-chloro-*m*-xylenol)	halophenols	skin/mucous membrane disinfection
silver compounds	heavy metals	skin/mucous membrane
mercury compounds		disinfection
		disinfection
hydrogen peroxide	peroxides	disinfection
ozone		
per-acetic acid		
phenol	phenols and cresols	disinfection
cresol		
cetrimide	quaternary ammonium	disinfection
benzalkoniumchloride	compounds	skin/mucous membrane
cetylpyridiniumchloride		disinfection
		anti-dental-plaque agent
ethylene oxide	gaseous substances	disinfection
formaldehyde		

2.3 Consumer products that contain disinfectant substances

In itself, the addition of antimicrobial substances to consumer products is nothing new. Foods and many (liquid) industrial products have long contained preservatives that increase their shelf life. Fungicides have been in use for many years in bathroom paint and sealants, for example. A new development is that these substances are now

increasingly being added to consumer products to protect man himself from harmful micro-organisms. Until recently, only a limited range of products was available, often for specific purposes. It has long been common practice to use iodine-containing preparations against wound infections and alcohol to remove micro-organisms from medical thermometers. A stream of new products has recently come onto the market to enable consumers to protect themselves – so they are told – from bacteria. Headlines and advertising campaigns underscore the fact that consumers need to protect themselves from the many bacteria with which they come into contact every day. Examples include antibacterial hand soaps, hand cleansers and hygienic tissues containing alcohol or triclosan. The products can be obtained in convenient packages, so they can be used anywhere. Triclosan is also now used in other products for personal hygiene, such as shower gel, deodorant, aftershave and toothpaste. Chlorhexidine, amongst other substances, is added to mouthwashes, mouth sprays and lozenges. These products for personal hygiene are widely available in supermarkets and chemist shops.

Furthermore, an increasing number of cleaning agents contain antibacterial substances. In addition to the familiar chlorine-containing agents, consumers can now choose household disinfectants based on a quaternary ammonium compound. An increasing number of washing-up liquids, all-purpose cleaning agents, washing-powders and cleaning cloths are being marketed for so-called 'hygienic' cleaning. This suggests that the products not only remove dirt but also fight (pathogenic) micro-organisms. The packaging does not always state which ingredients are supposed to be responsible for the 'hygienic effect'.

Recently, sanitary fittings became available in the Netherlands 'with natural protection against' bacteria. The glazing contains small amounts of silver ions, which the manufacturer claims provide long-term inhibition of bacterial growth.

Antimicrobial products for consumers are more popular in the south of Europe, the United Kingdom and the United States than they are in the Netherlands. In the US, cutting boards, clothing, bedding, children's toys and wall paint for children's rooms are available to which antibacterial substances have been added to reduce the risk of contagion with pathogens (Ros97).

Chapter 3

Benefits of using disinfectant substances in households and with personal hygiene

When considering benefits of using disinfectant substances in the home, it is useful to distinguish between, on the one hand, products for removing micro-organisms in general, such as disinfectant cleaning agents and antibacterial hand soaps and, on the other hand, products for specific purposes, such as toothpastes and deodorants.

3.1 Disinfectant cleaning agents and antibacterial soap

Opinions differ about the benefits of using disinfectant cleaning agents in the home. The National Center for Infectious Diseases (NCID) in the United States recommends routine cleaning and disinfection of surfaces in the home. In an information poster, the institute points out that disinfection provides an extra margin of safety (NCID00). Especially places in the home where there are high concentrations of 'germs' and where there is a high likelihood of them spreading should be disinfected regularly. The NCID says the kitchen presents a particular risk, but also recommends disinfecting bathrooms, children's potties and nappy bins. In a brochure, the British Ministry of Agriculture, Fisheries and Food (MAFF) also recommends to regularly disinfect worktops, especially after preparing chicken or other raw meat (MAFF98).

The International Scientific Forum on Home Hygiene (IFH)[a] believes that for proper hygiene it is usually sufficient to thoroughly clean surfaces in the home with ample flowing, preferably hot water and soap, followed by careful drying (IFH98, IFH00b). Cleaning articles, such as kitchen cloths and floor cloths, should be regularly washed at a temperature of at least 60°C. Disposable cloths provide a useful alternative, provided they are only used once. There are surfaces that frequently come into contact with hands or food but that cannot be readily rinsed using copious water, such as worktops, taps, door handles, toilet seats and changing mats for babies. The IFH believes that using a disinfectant in addition to thorough cleaning can provide an extra margin of safety for such items. It is important to use the right agent and amount and to allow a sufficiently long contact time. With regard to hand hygiene, the IFH considers thorough hand washing with soap and flowing water to be generally sufficient to prevent the spread of pathogens. After preparing raw and possibly contaminated food, using antimicrobial soap can provide an extra margin of safety. If no water is available, it is advisable to use tissues or a gel with alcohol, certainly after going to the toilet or after contact with raw and possibly contaminated food. The IFH also considers it advisable to use disinfectant substances to remove micro-organisms from the hands as well as surfaces in the home when a member of the household suffers from an infectious disease or weakened immunity. The IFH considers it to be not scientifically proven that incorporating antimicrobial substances in plastic utensils and food packaging materials helps reduce the burden of disease attributable to infections. Finally, the organisation points out that proper hygiene, including the well-considered (preventive) use of disinfectant substances, can help reduce the (curative) use of antibiotics and thereby help reduce resistance to antibiotics (IFH98, IFH00a, see also Jon99, Och99).

The Association for Professionals in Infection Control and Epidemiology (APIC) in the US does not support the use of antimicrobial household products that are marketed to prevent infections, because it was unable to find any evidence in scientific literature or in the information provided by manufacturers that this could prevent infections (APIC97, Sla99). Recently, also the American Medical Association (AMA) concluded on the basis of literature research that no research data is available to demonstrate the effectiveness of antimicrobial substances in consumer products, such as hand soaps and lotions (AMA00). Other researchers and organisations share this

[a] The IFH is a group of health care workers and scientists who play an active role in the policy and research concerned with hygiene. Through international activities and initiatives, the IFH seeks to emphasise the fundamental role that hygiene plays in the prevention of infections and disease. It would like to increase the available information on the principles of proper hygiene and promote the use of suitable hygiene procedures in situations where there is a risk of infection. It places particular emphasis on the situation in the home (see http://www.ifh-homehygiene.org).

viewpoint (Fav00, Lev98a, Lev99b, MST00). The Netherlands Nutrition Centre believes that proper, regular cleaning is generally sufficient to limit the likelihood of infection in the normal home situation (Voe99).

Most disinfectant substances are not equally effective against all groups of micro-organisms. For example, alcohols, triclosan and chlorhexidine are not very effective against certain viruses (IFH00b). The effect spectrum of quaternary ammonium compounds is likewise limited (WIP00). Moreover, improper use may reduce the effectiveness against organisms that are susceptible. In the case of application by a non-professional, such improper use is not unlikely, all the more so because the instructions for use on the packaging are often not read (Wee97). For example, when disinfecting a kitchen cutting board, the effectiveness can be reduced by adsorption of the disinfectant by organic material, if food residues are not removed by 'ordinary' cleaning first. Excessive dilution may also reduce the effectiveness; in particular, this applies to alcohols, phenolic compounds and triclosan (Rus00b). Too brief a period of contact may likewise be detrimental to the result of the attempted disinfection. Levy illustrates this using triclosan-containing hand soap. Undiluted, contact with the soap for 1 minute is required to kill 80 percent of the *E. coli* bacteria that are present. However, the time people spend washing their hands is generally 4 to 6 times shorter (Lev99b). This is the reason why the Board for the Authorisation of Pesticides has decided that from now on manufacturers who market disinfectants for consumers will be required to provide additional information, to show that their product is sufficiently effective not only under controlled laboratory conditions, but also in daily household practice (CTB00, see also Fav00). Finally, the result of disinfection in the home is not long lasting and after a short time there is hardly any difference in bacterium counts between disinfection and ordinary cleaning (Con98ab).

The above leads to the conclusion that there is no scientific evidence that routine use of disinfectant cleaning agents and antibacterial soaps by consumers is beneficial. Proper cleaning with soap and water followed by proper drying is probably almost always sufficient. Provided the principles of good hygiene (see Voe99) are followed, especially in the storage and preparation of food, the risk of infection in the home is generally small. It is therefore unlikely that chemical disinfection leads to health benefits in general. The use of disinfectants in the home is only worthwhile in the case of medical indications, which require further specification. Indications could, for example, include home nursing of sick people with particular infections or with compromised immunity (cancer patients who undergo irradiation treatment or treatment with cytostatics, aids-patients, people who have undergone an organ transplant). The disinfection should then preferably be performed on the advice of a

physician and after instruction by people who are suitably qualified. The guidelines for nursing homes of the Dutch Working party for Infection Prevention (WIP92) could serve as a guide for this.

Such a policy fits in well with developments in hospitals, where the likelihood of contracting an infectious disease is relatively great, owing to the simultaneous presence of pathogenic micro-organisms and people with compromised immunity. In institutions of this kind, the previous indiscriminate use of disinfectants has been replaced by selective use according to strict protocols (Sev92). The starting point adopted is that there must be a clear risk of infection and that other measures, such as 'ordinary' cleaning, high-temperature disinfection or the use of disposable equipment, are not possible or not adequate.

3.2 Toothpastes and deodorants

Disinfectant substances in toothpastes, mouthwashes and deodorants are targeted at specific groups of micro-organisms. Added to toothpastes and mouthwashes, by virtue of their antibacterial action, they reduce dental plaque formation and the development of gingivitis (Ele99, Pit00, Vol93). In deodorants, they prevent the propagation of bacteria that convert perspiration, that in its own right is odourless, into malodorous compounds (Cox87). Used in this way, the disinfectants contribute to the product's efficacy and their use can be considered to be functional and useful.

Chapter **4**

Risks of using disinfectant substances in households and with personal hygiene

As was shown in the previous chapter, the benefits of using disinfectant substances in the home and with personal hygiene often are questionable. This chapter examines whether the attitude that 'it doesn't hurt to try' is justified. In other words: what are the risks? The chapter discusses the direct consequences for the user's health, the danger of ordinary cleaning and hygiene being neglected, the risk of disrupting the normal human microflora, the risk of resistance development and the possible impact on the environment.

4.1 Direct consequences for the user's health

Triclosan has been subjected to extensive toxicological research and appears to have a favourable safety profile (Bha96, DeS89). The substance almost never causes allergies. Triclosan that enters the body through the skin or mouth is mainly excreted with the urine (DeS89). However, triclosan has recently been detected in human milk (Ado00). The significance of this is unclear.

Likewise, chlorhexidine has low toxicity (Ele99, Fou73). The main side effect of oral use is the production of staining on the teeth, especially when used in combination with drinking coffee, tea and red wine or with smoking. This staining is difficult to remove. Another disadvantage is that it encourages calculus formation (Ele99). These side-effects make long-term use of chlorhexidine-containing products inadvisable,

unless normal oral hygiene (brushing, flossing) is not possible for a longer period of time (Ele99, Pit00). Moreover, contact with the middle ear and eyes must be avoided because chlorhexidine is harmful to these organs (Hac00). It rarely causes skin irritation or allergic reactions when used on the skin (WIP00).

In general, quaternary ammonium compounds are not very toxic (Hac00), although they can irritate the skin and the eyes (Wee99, WIP00). Iodine-containing preparations may irritate the skin. Hydrogen peroxide and chlorine compounds are corrosive. The latter can also react with organic material, thereby giving rise to harmful substances. Toxic chlorine gas forms when chlorine compounds come into contact with acids (WIP00). Internal use of all these substances, for example by children, may result in poisoning.

Clearly, disinfectant substances have a potential for doing harm and precautions have to be taken for their safe use and storage, which non-professionals may not always be aware of. However, the National Institute of Public Health and the Environment expects on the basis of model calculations that the normal use of disinfectant or 'hygienic' cleaning agents in the kitchen does not present any major health risk (Wee99). A cautionary note is called for here: risk evaluations of this kind are based on exposure to a single product. In reality, consumers may be exposed to the same substance through many of these products. An example of this is triclosan, which may be present in toothpaste, deodorant, hand soap, shower gel and aftershave. However, there is little evidence of health complaints caused by disinfectant substances in cosmetic products, or at least hardly any patients report to dermatologists about skin irritations caused by these substances. In short, there are currently no specific indications that direct consequences for the user present a serious problem.

4.2 Neglect of 'ordinary' cleaning

Use of disinfectant cleaning agents and antibacterial soap could give consumers a false sense of security. Although disinfectants generally work against a large variety of micro-organisms, they are not effective against all pathogens; some viruses in particular are unsusceptible to a number of agents. Moreover, a good result is only ensured if the concentration used is high enough and the contact time is sufficiently long. Thorough ordinary cleaning must also always precede disinfection, to prevent the disinfectant from insufficiently coming into contact with the micro-organisms as a result of adsorption to food remains, for example. It is very likely that these preconditions are not met in the home, owing to a lack of knowledge among users. Finally, the result of using disinfectants in the home is only short-lived (Con98ab). Disinfection can therefore never replace ordinary hygiene measures. However, it is

feared that the use of disinfectants will lead to ordinary cleaning being neglected (APIC97, Fav00, IFH00b, Voe99).

4.3 Disruption of the normal bacterial flora

In a healthy human body, the body cells are outnumbered by bacteria. They normally inhabit the skin and mucous membranes in the airways, digestive tract, urinary passages and reproductive tract. Each place has its own characteristic, relatively constant flora, which is not harmful to the host but in fact fulfils a number of useful functions (Hoo92). One of these is to protect against intruders from outside the body, the so-called colonisation resistance (EU99, GAO99, Led00, Lev98a, Ram92, Ver92). Disinfectants could harm this function because they disturb the normal flora and thereby create space for colonisation by potentially hazardous micro-organisms. A similar process sometimes occurs when antibiotics are used (EU99, Ram92, Ver92, Wil96). The use of disinfectants such as triclosan and chlorhexidine is known to result in a considerable reduction in the normal flora of the skin and mouth (Cox87, Vos75, Wil76). However, once these disinfectants are no longer used, the bacterium counts quickly return to their original level. In a few older publications mention is made of an increased incidence of colonisation and in the number of infections by Gram-negative bacteria in newborns in hospitals, after disinfecting the skin with hexachlorophene (For68, Hac00, Lig68). Nowadays, chlorhexidine is used for this. There are no indications that this substance promotes colonisation by Gram-negative bacteria (Hac00). Likewise, trial subjects who used disinfectant-containing soap or deodorant at home for some time did not display any increase in Gram-negative bacteria in the skin flora (Cox87, Vos75, Wil76). Likewise, long-term use of triclosan-containing toothpaste does not appear to promote the development of pathogenic micro-organisms in the mouth (Fin98, Vol93). Various authors conclude that attempts to demonstrate shifts in bacterial flora resulting from the use of antimicrobial skin and mouth care products have yielded little result (Jon99, Jon00, Sut97).

Micro-organisms also seem to be important for a proper and balanced development of the immune system. In particular the intestinal flora plays a prominent role in this (Bjö99ab, Hoo92, Mat99, Mat00, Pre99, Sau98, Wol98). Through changes in life style and habits, people in the West nowadays from an early age come into contact with micro-organisms less than used to be the case. The greater attention paid to both personal hygiene and hygiene in and around the home, including the use of disinfectant substances, contributes to this. Consequently, colonisation of the intestinal tract after birth will be slower and the composition of the intestinal flora will be different. For some time now, the so-called ‘hygiene hypothesis’ has been gaining

acceptance. It states that the rapidly rising rates of atopic disorders - such as asthma, hay fever, eczema and food allergies - in recent decades in the West is the result of the reduced contact with micro-organisms (Ham98, Kay01, Roo98, Wol98). Epidemiological research is increasingly producing data that fit this hypothesis (Coo97, Ham98, Mar99, Mat99, Mat00, Pre99, Roo98, Str89, Str99). However, some research data are not easy to reconcile with this theory (Kay01). Hence, some say that the scientific basis for this hypothesis is weak (Zeij00).

In summary: there are no clear indications that disinfectant substances in consumer products drastically change the composition of the flora of the skin and mouth and promote infections. Excessive hygiene may play a role in the observed increase in asthma, eczema and hay fever in Western countries during recent decades. However, there is a lot of scientific uncertainty about this.

4.4 Resistance development

The increasing resistance of bacteria to antibiotics is widely seen as a serious health problem because pathogens are becoming increasingly difficult to fight (EU99, GAO99, GR98, Lev98a, Wis98). Micro-organisms can also become resistant to disinfectants (IFH00a, McD99, Rus98ab), although this is less likely to occur because of the many target sites these substances have on and in the cell (IFH00a, Och99, Rus98a, Rus00c, Sul00). Much of the current knowledge about resistance to disinfectant substances is based on laboratory research (IFH00a). This applies to triclosan, for example. Until recently, it was assumed that this compound caused cell membranes to become leaky in a non-specific manner. However, it has emerged that in the bacterium *E. coli*, triclosan inhibits a specific enzyme in fatty-acid synthesis. This increases the likelihood of resistance, because a single mutation in the gene that codes for that enzyme can make the bacterium less susceptible to the disinfectant (Hea99, Lev99a, McM98a, Ste99). Recently, it was demonstrated that the aforementioned enzyme is the only target site for triclosan in *E. coli* (Hea00ab). In other bacteria, presumably (also) other target sites play a role (McD98, Hea00ab, Sul00). McMurry and her colleagues speculate that other disinfectants may also have a more specific mechanism of action than was assumed up to now (McM98a). In addition to changes in the target site, resistance to triclosan may also be based on the formation or activation of pump systems that pump the substance out of the cell before any damage occurs (Chu01, McM98b). Another mechanism that has been suggested is the excretion of enzymes that break down triclosan outside the bacterial cell (Mea00). A combination of various resistance mechanisms could lead to an extra high level of resistance (McM98b). Research on other disinfectants has resulted in similar findings.

Some authors question the practical relevance of laboratory data about resistance to disinfectants. They point out that no evidence can be found in scientific literature of a reduced efficacy of these substances in practice as a result of resistance development, in spite of their use in health care and in consumer products over many years (Jon99, Jon00, Och99, Tie99). Nevertheless, resistance to disinfectant substances appears to be increasing. Resistant strains of bacteria have been found in places where disinfectants are used continuously, such as hospitals and in the food industry (see for example Dan87, Sun98). Bamber and Neal discovered that some hospital strains of the MRSA bacterium[a] are so insusceptible to triclosan that the effectiveness of triclosan baths to counteract MRSA bacteria in infected patients may be jeopardised (Bam99). According to the IFH, insofar as strains of bacteria have been detected that were insusceptible to the concentrations normally used, researchers usually attributed this to phenotypic (i.e. non-genetically determined) modifications (IFH00a). Resistance of this type probably disappears when exposure to the disinfectant has ended. However, resistance detected in laboratories and in practice is almost always of a low level. The clinically used high concentrations therefore remain effective and the increased resistance to disinfectants is not a clinical problem at present (IFH00a, Rus99, Rus00ab). However, the implications in the long term of this low-level resistance are not known (Sul00). An obvious comparison can be made here with resistance to antibiotics, which also began with a small reduction in susceptibility (Hei98, Lev98b).

It is unclear whether the extensive use of disinfectant substances by consumers at home is conducive to the development of resistance. The use of antibacterial soap, deodorant or toothpaste for a period of months by test subjects at home did not lead to any demonstrable development of resistance (Cox87, Fin98, Jär93, Vol93, Vos75, Wil76). However, according to Levy, until recently the use of disinfectants was practically limited to hospitals and other places with susceptible patients, and the application in consumer products of substances such as triclosan has expanded enormously only recently (Lev99b). He points out the fact that little research has been conducted into resistance in household conditions. He and other specialists consider it likely that resistant strains of bacteria will emerge (Bam99, Hea99, Lev98a, Lev99b). Levy fears that disinfectants will lose their effectiveness in situations in which they are really necessary (Lev98a). Russell and Maillard share this concern about the increased use of antimicrobial substances in the home (Rus00c) and the IFH sees the risk of resistance developing as a reason for discouraging their indiscriminate household use (IFH00a).

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[a] Methicillin-Resistant *Staphylococcus aureus*, a bacterium that is resistant to a large number of antibiotics and is therefore difficult to control.

The emergence of resistance is mainly facilitated by long-term exposure to low, non-lethal concentrations. Hospitals therefore always use (sufficiently) high concentrations of disinfectants. The improper use of these substances by non-professionals and their slow release from plastics to which they have been added may result in exposure concentrations that are too low, thereby promoting the emergence of resistant strains (Lev99b, Rus00b, Tra00). The likelihood of resistance also depends on the nature of the disinfectant. Traditional general-purpose agents, such as chlorine, alcohol and hydrogen peroxide evaporate quickly, whereas substances such as triclosan and chlorhexidine leave residues for a protracted period and form concentration gradients (IFH00a, Lev98a, McM98b, Sul00). Whether this actually leads to the development of resistance has not been proven. Continuous exposure of *Staphylococcus aureus* to triclosan at a low concentration for a period of one month did not result in reduced susceptibility (Sul00). The American Food and Drug Administration has been requested to study the feasibility and relevance of a 'surveillance' programme to monitor the use of antimicrobial consumer products and bacterial resistance (Jon99).

There is growing concern that the increasing use of disinfectants will also lead to an increase in resistance to antibiotics (Chu01, Lev98ab, Lev00, McM98b, Mok97, RPS97, Rus98c, Rus99, Rus00ac). Various studies have shown that the resistance to both types of substances sometimes go hand in hand with each other (see for example Chu01, Mok97). This may involve various mechanisms: strands of DNA, known as plasmids, carrying both genes for resistance to antibiotics and genes for resistance to disinfectants; changes in the outer cell membrane that interfere with the penetration into the cell of both antibiotics and disinfectants; efflux pumps that remove both types of substances from the cell. Russell considers it not proven that the use of disinfectants in hospitals or in the home promotes the development of antibiotic-resistant bacteria, but he does think extensive research is necessary (Rus00c). The American Medical Association subscribes to this view and considers it one of the reasons why it would be wise to avoid the use of antimicrobial substances in consumer products (AMA00). The association calls for disinfectants against which acquired resistance in bacteria has been demonstrated to no longer be used in consumer products until it has been proven that the resistance does not pose a threat to public health and that such products are effective in preventing infections. The Norwegian National Institute of Public Health also takes this view (Høi00). Others point out that misuse of antibiotics is the main cause for the development of antibiotic-resistant strains of bacteria and that the use of disinfectants plays a negligible role in this (Jon99, IFH00a).

All this leads to the conclusion that resistance to disinfectants appears to be increasing in places where these substances are used extensively, such as hospitals and

the food industry. However, the resistance is usually of a low level and the normally used concentrations continue to be effective. It is not certain whether the use of disinfectant substances also promotes resistance to antibiotics, but the possibility cannot be excluded either. It therefore seems advisable to be cautious about adding disinfectant substances to consumer products and about using products with such ingredients in households and for personal hygiene. In particular, this applies to products for which there is no evidence that they are effective in preventing infections, such as antibacterial hand soap, shower gel and disinfectant cleaning agents. Scientific research is necessary to fill the gaps in our knowledge. There is a particular need for greater insight into the extent to which micro-organisms become resistant to disinfectants in conditions that occur in practice, especially in the home, and into the significance of the use of these substances with respect to bacterial resistance to antibiotics.

4.5 Effects on environmental quality

Relatively little is known about the occurrence and behaviour of disinfectants in the environment. The same applies to drugs used in human and veterinary medicine. Nevertheless, this subject has been attracting increasing attention in recent years (see for example Dau99, Küm00, GR01). According to Van Wezel and Kalf (Wez00), disinfectants are among the substances that are wrongly not covered by current (inter)national risk assessment programmes and that deserve more attention in policy-making. Van Wezel and Kalf were unable to find any quantitative data on the occurrence of disinfectants in surface waters and other environmental compartments in the Netherlands, but expect them to be present in measurable quantities, in view of the scale of their use (Wez00). Triclosan and one of its conversion products, triclosan-methyl, have indeed been found in surface water in the Netherlands and abroad (Leo00, Mue00). In Germany, biphenylol, chlorophene, tetrabromine-o-cresol, chloro-m-cresol, PCMX (*p*-chloro-*m*-xylenol) and phenylsalicylate have been found in surface water and sewage treatment plants (Ter98). On the grounds of the toxicological properties of disinfectants and their usually limited bio-accumulating character, Van Wezel and Kalf think that the consequences for the environment will turn out to be limited (Wez00). However, others point out that a substance such as triclosan is toxic to fish, water fleas and algae (Ado00). It is estimated that aquatic organisms are exposed to concentrations between 0.4 and 7.6 times the 'no-effect' concentration (Mue00). It was recently suggested that triclosan has a slight androgenic (resulting in male sex characteristics) effect and that it could disrupt the sex hormone balance in fish (For00). Triclosan-methyl also appears to accumulate in fish (Ado00, Miy84). Quaternary ammonium

compounds are also toxic to aquatic organisms and, moreover, they are difficult to degrade (Küm00). There is some concern about the possibility that disinfectants and antibiotics could have a detrimental effect on biological purification processes in sewage treatment plants and in drinking water production (Küm00). Finally, it is unclear whether the low concentrations of disinfectants that are found in the environment can contribute to resistance development in micro-organisms living in that environment.

Chapter **5**

Policy options

There are different ways in which the government can influence the use of disinfectant substances by people at home and the risks that may be associated with such use. They relate to legislation and regulations, voluntary agreements with the industry, and public information.

5.1 Legislation and regulations

Legislation and regulations offer only limited possibilities for controlling the marketing of disinfectant-containing consumer products. The legislation concerning products containing disinfectant substances is fragmented. Which law covers a product with disinfectant properties depends on its application as defined by the manufacturer. From the consumer's point of view, three laws in particular are of interest:

- The Pesticides Act (Stb98a). This law covers biocides, including multi-purpose disinfectants, i.e. products aimed at controlling or repelling organisms in or on materials, appliances and utensils. It also covers disinfectants for domestic use. The products in question are marked with an N-number.
- The Drug Supply Act (Stb00b). This law covers among other things some products for skin disinfection and mouthwash. Such products are given an RVG-number.
- The Commodities Act (Stb99). This law applies to products including cosmetics and ('hygienic') cleaning agents. These products do not have a number.

Products that contain disinfectant substances may also be covered by the Medical Appliances Act (products specifically intended for disinfecting medical appliances, such as endoscopes, and bearing a CE-mark (Stb97)) or by the Veterinary Medicines Act (products specifically intended for use with animals and having a RegNL-number (Stb98b)). These products have little relevance for consumers in general. Insofar as the legislation in all of these fields is concerned, our country is bound by the relevant European Union directives.

Products covered by the Pesticides Act or the Drug Supply Act require authorisation or registration: they can only be marketed after approval from the competent public authority. This authority's decision is based on information provided by the manufacturer. The information to be provided by the manufacturer depends on the legislative framework that applies (table 2). The most elaborate dossier is required for pesticide (biocide) permits: in addition to information on the product's efficacy - does the product perform as the manufacturer claims? - information must also be provided to enable an assessment of the hazards to human health and the environment. The Pesticides Act does not have provisions for checking whether alternatives exist. Therefore, the argument that proper cleaning usually renders disinfection unnecessary cannot be used in the assessment. However, the Board for the Authorisation of Pesticides recently decided to start setting supplementary requirements with respect to the information on the efficacy of disinfectants for domestic use (CTB00). For the current procedure is mainly keyed to agents intended for professional use and does not adequately guarantee the efficacy of products used by non-professionals in the home.

Medicines are only assessed as to their efficacy and the risks they entail for human health (side-effects). The Drug Supply also does not provide for an assessment of alternatives.

The trade in products covered by the Commodities Act is free, so these products cannot be kept out of the market beforehand. Pursuant to the Commodities Act's Cosmetic Products Decree (Stb00a) manufacturers of cosmetic products must afterwards and if so requested be able to demonstrate to the authorities that their product has the promised effect and that, when used normally, it is safe for the user. To counteract decay, cosmetic products are permitted to contain 'antimicrobial substances' up to a specific maximum. These substances have to be included in a list of permitted substances that have been tested as to their efficacy and safety (EU76). In a number of cases, higher concentrations are allowed for specific purposes, which must be apparent from the form under which the product is marketed; such purposes include dental plaque or odour control. The Norwegian Food Control Authority, together with the Swedish and Danish authorities concerned, is currently considering to request the European Commission to re-assess the use of triclosan in cosmetic products (SNT01).

Table 2 Summary per law of the information to be provided by the manufacturer

Product information	pesticides (biocides)	medicines	cosmetic products	other products
efficacy	+	+	(+)	-
risks for humans	+	+	(+)	-
risks for the environment	+	-	-	-

+ dossier required, - no dossier required, (+) dossier to be provided afterwards and only if so requested by the authorities

There is no sharp distinction between the different areas of jurisdiction. A lot depends on the way in which the manufacturer describes the application the product is intended for. Cleaning agents that 'disinfect' require approval under the Pesticides Act. On the other hand, products that 'clean hygienically' come under the Commodities Act. The boundary between medicines and cosmetic products also can be difficult to draw[a]. Surgical skin disinfectants must be registered pursuant to the Drug Supply Act, whereas hygienic skin disinfectants, such as antibacterial hand soap and shower gel, are covered by the Commodities Act. Within the European Union, a better demarcation of the different legal frameworks is being worked upon.

The unclear distinction can result in manufacturers - for reasons of costs - formulating their product claims in such a way as to minimise the amount of information they have to provide. For reasons of safety for man and environment, it would merit consideration to make the nature of the information that has to be provided less dependent on the product's classification and to gear it more than is currently the case to the possible risks for man and environment. Amongst other things, this would mean that cosmetic products would also require assessment in terms of their environmental safety, if it is suspected that their use will put a burden on the environment. However, the necessary legislative and regulatory adjustments, as well as the development of assessment procedures and instruments, can only take place on an international level.

5.2 Voluntary agreements with the industry and public information

Agreements with manufacturers are another way of limiting the use of products containing disinfectant ingredients. In Sweden, the industry has voluntarily agreed to stop using triclosan in detergents and cleaning products (Ano00).

[a] See the statutory definitions of both terms in annex C.

Finally, informing the public is an important alternative. The public must be made aware that proper hygiene is the best way to limit the burden of disease by infections. The ‘Hygiene code for the private household’ published by the Netherlands Nutrition Centre provides clear information on how people should ensure proper hygiene when preparing food, with personal care and household work (Voe99). However, the code is primarily intended for social workers, information officials, industry and trade. It is essential that they pass on their knowledge to the population. The information provided should also be aimed at children, as 'what's learnt in the cradle lasts till the grave'. The government can help parents and schools by providing information materials. People should also be made aware that the use of disinfectants is not an alternative to normal hygiene and that for many products containing disinfectants it has not been proven that their use helps to reduce the number of infections. Information about this may stimulate a critical attitude among consumers. Finally, people should be made aware that most bacteria are harmless or even beneficial and that very few micro-organisms cause disease. So in general the fear of micro-organisms is unfounded.

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Stb98b Wet van 27 juni 1985, Stb. 410, houdende regelen met betrekking tot diergeneesmiddelen (Diergeneesmiddelenwet), zoals laatstelijk gewijzigd op 19 oktober 1998, Staatsblad 1998: 629.

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A	Rationale
B	Realisation
C	Statutory definitions

Annexes

Annex **A**

Rationale

The Health Council of the Netherlands has the statutory duty (Health Act of 1956, revised in 1997) “To inform our Ministers and both houses of the States General about the current level of knowledge with respect to public health issues”. This duty extends to calling attention to developments that are important for government policy. The present advisory report is an instance of such calling to attention of developments.

Annex **B**

Realisation

This advisory report was prepared by dr. HFG van Dijk, scientific secretary to the Health Council of the Netherlands, after consulting the following experts:

- dr. RR Beumer
  food microbiologist; Wageningen University
- MAJ Bilkert-Mooiman
  Ministry of Health, Welfare and Sport, the Health Care Inspectorate
- dr. CAFM Bruijnzeel-Koomen
  professor of dermatology; University Hospital Utrecht
- dr. CJW van Ginkel
  dermatologists and chemist; University Hospital Utrecht
- dr. B van Klingeren
  microbiologist; National Institute of Public Health and the Environment, Bilthoven
- dr. CMJE Vandenbroucke-Grauls
  professor of medical microbiology and infection prevention; University Hospital, Vrije Universiteit, Amsterdam

The advisory report was assessed by the Standing Committee on Health and the Environment and the Standing Committee on Infection and Immunity.

Secretarial assistance: J Hoorens van den Berg-de Vlieger
Editorial assistance: dr. YA van Duivenboden
Layout: J van Kan

Annex **C**

Statutory definitions

Medicines (Stb00b)

Substances or composition of substances that are intended for use or that are in any way designated or recommended as suitable for:

1 curing, alleviating or preventing of any disorder, disease, symptom, pain, injury or ailment in humans,
2 the restoring, ameliorating or modifying of the functioning of human organs,
3 the making of a medical diagnosis by the administration or application to humans.

Cosmetic products (Stb00a)

All substances and preparations that are intended to be brought into contact with the various parts of the surface of the human body (epidermis, hair, nails, lips and external genitals) or with the teeth and mucous membrane of the mouth, with the exclusive or primary intention to clean, perfume, modify the appearance of, or keep in good condition the aforementioned parts of the body, or to correct body odours.