EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

# The Safety of Reprocessed Medical Devices Marketed for Single-Use

Scientific Committees
- on consumer safety
- on emerging and newly identified health risks
- on health and environmental risks

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SCENIHR

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http://ec.europa.eu/health/scientific_committees/emerging/members_wg/index_en.htm

## ABSTRACT

One of the Directives regulating the placing on the market of medical devices in the EU is Directive 93/42/EEC on medical devices. This Directive distinguishes between those devices that are intended by the manufacturer to be reused and those which are intended for single-use. Both types of devices must comply with the essential requirements of this Directive. The use of single-use medical devices (SUDs) has considerably increased for a variety of reasons. However, some medical devices have continued to be reprocessed despite the fact that they were intended for single-use. The use of reprocessed SUDs may not be without risk. In this opinion the possible risks involved in the reprocessing and reuse of single-use medical devices have been evaluated.

Several potential hazards have been identified that may eventually lead to a risk for patients on whom a reprocessed SUD would be used. As is the case for medical devices intended for re-use, the major hazard arises from the inadequate cleaning, disinfection and/or sterilization that may result in persistence of either a chemical or a microbiological contamination, the former resulting in a risk of toxic reactions, the latter in a risk of microbiological infection. Of specific concern is the hazard of the potential contamination with agents causing transmissible spongiform encephalopathies (TSEs).

In addition, the interaction with the chemicals used during the various procedures may result in changes in the material characteristics which can affect the performance of the device. Other factors that may increase the risk for the patient when using a reprocessed SUD include poor traceability of a reprocessed device, and inadequate educational and training aspects for complex medical procedures.

Data to quantify the risks are however scarce. Some simulation studies have shown that improper cleaning, disinfection and/or sterilization may leave a bioburden on the reprocessed SUD. There is a lack of data specifically dealing with clinical outcomes for patients treated with reprocessed SUDs. There are a few case reports showing persistence of chemical residues of cleaning agents and disinfectants, persistence of infectious agents and modifications in physical-chemical characteristics.

Despite the absence of data, a number of situations in which an increased risk from using a reprocessed SUD may occur have been identified; an increased risk may be present in particular with the use of a re-processed SUD in invasive medical procedures (designated critical use), and with the use of a reprocessed SUD with certain design features that make it unsuitable for reprocessing and re-use.

Some recommendations are made.

Keywords: single-use medical devices, reprocessing, re-use, SCENIHR, hazards, risks.

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## EXECUTIVE SUMMARY

In the EU both reusable and single-use medical devices are available on the market. Both types of devices must comply with the Essential Requirements that are part of the Medical Device Directive (MDD; Directive 93/42/EEC). The use of single-use medical devices (SUDs) has considerably increased in hospitals. These devices are generally made of polymeric materials (plastics) which are poorly resistant to high temperatures and therefore poorly resistant to steam sterilization processes.

For medical devices intended for reuse, the manufacturer must provide information about the appropriate process to allow reuse including cleaning, disinfection, and packaging and, where appropriate, the method of sterilization to be used, and any restriction on the number of reuses. This information is obviously not available for SUDs. The decision to market a reusable or a single-use medical device is the responsibility of the manufacturer.

The reprocessing practice of single-use medical devices is not currently regulated at the Community level and different national legislations regulate this practice throughout Europe. However, the use of reprocessed SUDs may not be without risk. In this opinion the possible hazards and risks involved in the reprocessing and reuse of single-use medical devices have been considered.

Reusable devices have to be designed in such a way that the key characteristics withstand the reprocessing procedure using a validated process established and specified by the manufacturer.

After the first use, the device has to be considered to be contaminated. Cleaning, disinfection, and sterilization processes (depending on the type and use of the device) are important aspects of the reprocessing. Several steps need to be taken for the reprocessing of a used SUD, each of which may introduce a potential hazard for the reuse of the SUD. The device has to be handled during transportation to the location where the reprocessing will be carried out. This includes immersion in a disinfectant and/or packaging to avoid further contamination and to avoid infection of the staff handling these devices. Improper handling introduces a hazard for subsequent reuse of the device.

The chemicals and procedures used for cleaning, disinfection and sterilization may interact with the device which may result in changes in the physicochemical properties of the material of the device. Such changes may result in a reduced performance of the device, for example, loss of flexibility due to changes in the plastic materials, reduced smoothness by altered surface coatings, etc. In addition, after each procedure, chemical contaminants may remain in the device posing a toxic hazard for reuse. Improper cleaning, disinfection, and/or sterilization may introduce a serious hazard for the next use of the devices such as a microbial infection in the patient on which the device is used. A specific hazard is the possible contamination with agents that cause transmissible spongiform encephalopathy (TSE) as they are particularly resistant to commonly used physical and chemical methods of cleaning, disinfection, and/or sterilization.

For SUDs there may be certain design features hampering reprocessing after their use. In order to prevent the potential hazards associated with the reprocessing of SUDs the whole reprocessing cycle starting with the collection of the SUD after first use until the final sterilization step should be evaluated and validated for its efficacy.

Published data on the hazards and risks are very limited. Some simulation studies and a few clinical studies have shown that reprocessing of SUDs may result in inadequate cleaning, disinfection and/or sterilization leaving a bioburden on the reprocessed SUDs.

In general, there is a lack of data specifically dealing with clinical outcomes for patients associated with reprocessed SUDs particularly with regard to possible delayed effects, for example, infectious diseases and/or immunological complications. There are a few case reports showing persistence of chemical residues of cleaning products and disinfectants,

persistence of infectious agents and modifications in physico-chemical characteristics of the devices.

In addition to the possibility of chemical and microbial residues remaining in the devices as a result of improper cleaning, disinfection, and/or sterilization, as well as alteration of the material characteristics of the devices after reprocessing, there are some other aspects that may introduce a potential hazard and thus a risk for each subsequent use of the reprocessed SUD. These include: possible loss of documentation and information; problems of traceability during the lifetime of a particular device; possible errors in re-assembling of devices (some devices need to be assembled on location); and educational and training issues for complex medical procedures.

Due to the scarce reports of incidents linked to the use of reprocessed medical devices and the absence of quantitative data related to the eventual residual biological and chemical contamination after reprocessing, it is not possible to quantify the level of risk associated with the use of reprocessed SUDs.

Despite the absence of data, a number of situations in which an increased risk from using a reprocessed SUD may occur have been identified; in particular an increased risk may be present with the use of a re-processed SUD in invasive medical procedures (designated critical use), and the use of a reprocessed SUD with certain design features that make it unsuitable for reprocessing and re-use.

Some recommendations are made.

## 1. BACKGROUND

Historically, before the 1980s medical devices were usually developed as reusable medical devices. Their reuse was facilitated by their shape, design, size and the fact that they were usually made of resistant materials like glass, metal or rubber, and reprocessed by steam sterilization processes. At this time, the evidence for cross contamination or transmission of infection between patients by the reuse of medical devices was rather limited. The emergence of blood transmitted diseases like hepatitis as major public health concerns in the early 1980s and the risk of nosocomial transmission by reuse of contaminated syringes heightened interest in the development of single-use injection medical devices. Later on, the discovery of HIV and its transmission by contaminated blood, among other mechanisms, put more pressure on the medical profession to use single-use[1] medical devices, and accelerated the development of these devices.

In addition to these major public health concerns, the advancements in technology led to the development of more sophisticated and complex medical devices. These devices were generally made in novel plastics which are not resistant to high temperatures and therefore not resistant to steam sterilization processes. New instruments were developed for mini-invasive procedures, particularly in cardiology, with smaller lumens and more intricate, delicate working mechanisms. Therefore, these devices were not as easy, or even impossible, to clean or sterilize properly. It was therefore impossible for the manufacturer to demonstrate that these devices were safely reusable and because of this, these products were labelled as "single-use".

The use of single-use medical devices has considerably increased in hospitals in particular to reduce the risks of cross contamination between patients.

Directive 93/42/EEC on medical devices[2], adopted on 14 June 1993, distinguishes between those devices that are intended by the manufacturer to be reused and those which are intended for single-use.

- For medical devices intended, by the manufacturer, to be reused according to the essential requirements, the manufacturer must provide information on the appropriate process to allow reuse including; cleaning, disinfection, and packaging and, where appropriate, the method of sterilization to be used, and any restriction on the number of reuses. The decision to market a reusable or a single-use medical device is the responsibility of the manufacturer.
- Medical devices intended for single-use must bear on their label an indication that the device is for single-use.

During the years following the implementation of the Medical Devices Directive (MDD), the shift of some categories of medical devices from reusable devices to single-use was progressive. Therefore, reusable and single-use medical devices intended for the same use have been coexisting on the market. This was misleading for hospitals, and sometimes in order to face increasing pressures to implement cost control, some medical devices have continued to be reprocessed (either at hospitals or via third party reprocessing providers) despite the fact that they were intended for single-use. In that context several concerns began to be raised, including patient safety.

The reprocessing practice of single-use medical devices is not currently regulated at the Community level and different national legislations regulate this practice throughout Europe. Few countries allow the reprocessing of single-use medical devices and have

[1] Directive 2007/47/EC defines a "single-use" medical device as "a device intended to be used once only for a single patient"
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:247:0021:0055:EN:PDF

[2] Directive 93/42/EEC concerning medical devices (OJ L 169, 12.7.1993)
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31993L0042:EN:HTML

developed guidelines, some countries prohibit it, and some Member States do not have any specific regulations on this aspect.

To address the concerns about patient safety and to clarify the notion of single-use, Directive 2007/47/EC, adopted on 5 September 2007, amending Directive 93/42/EEC, provided further clarification on the definition of the term "single-use", and introduced new requirements for single-use medical devices. Firstly, the manufacturer's indication of single-use must be consistent across the Community. The Directive also introduced the requirement that if the device bears an indication that it is for single-use, information on characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used must be provided in the instructions for use.

In addition to these new requirements and to ensure that the reprocessing, and in particular the reprocessing of single-use medical devices does not endanger patients' safety or health, the Commission should engage in further analysis in order to determine whether additional measures are appropriate to ensure a high level of protection for patients.

In that context, Directive 2007/47/EC inserted the following provisions as regards the reprocessing of medical devices:

*"Article 12a*

***Reprocessing of medical devices***

*The Commission shall, no later than 5 September 2010, submit a report to the European Parliament and to the Council on the issue of the reprocessing of medical devices in the Community.*

*In the light of the findings of this report, the Commission shall submit to the European Parliament and to the Council any additional proposal it may deem appropriate in order to ensure a high level of health protection."*

In order to prepare the above mentioned report, the Commission services launched a public consultation[3] on the reprocessing of medical devices, focussing on the reprocessing of single-use medical devices.

Based on the findings of the above mentioned consultation and further to bilateral meetings with various stakeholders, the Commission services organized a workshop[4] in December 2008. The aim was to collect further data in order to get a clearer picture of the reprocessing practice of single-use medical devices, and to assess which policy options might be appropriate for the reprocessing of single-use medical devices in Europe.

[3] http://ec.europa.eu/enterprise/medical_devices/guide-stds-directives/synthesis.pdf

[4] http://ec.europa.eu/enterprise/medical_devices/pdfdocs/summary_5_12_2008_workshop.pdf

http://ec.europa.eu/enterprise/medical_devices/reprocessing.htm

## 2. TERMS OF REFERENCE

The SCENIHR is requested to assess the following:

1. Does the use of reprocessed single-use medical devices constitute a hazard for human health (patients, users and, where applicable, other persons) causing e.g. infection/cross contamination and/or injury?
2. If yes in ToR 1, please characterize the risk for human health.
3. If yes in ToR 1, under which conditions or uses does the reprocessing of single-use medical devices pose a risk? Please consider, in particular, the following:
    - Intended use of the device;
    - Reprocessing method used: cleaning, sterilization and/or disinfection (depending generally on the material of the device) and lack of instruction on the reprocessing method to be used; and
    - Other characteristics such as functionality, handling, raw material or design of the device.

## 3. LEGAL FRAMEWORK

Based on the New Approach, rules relating to the safety and performance of medical devices were harmonised in the EU in the 1990s. Beginning in 1990 with Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices, this was later followed in 1993 by Council Directive 93/42/EEC of 14 June 1993 concerning medical devices and in 1998 by Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices.

The three above-mentioned legal texts form the core legal framework for medical devices. Their aim is to ensure the functioning of the internal market and a high level of protection of human health and safety. They have been supplemented over time by six modifying or implementing Directives, including the last technical revision brought about by Directive 2007/47/EC which amended Directive 93/42/EEC and Directive 90/385/EEC.

**Directive 93/42/EEC**[5] on medical devices foresees a risk based classification with four classes; Class I (lower risk), IIa, IIb and III (higher risk), based on the vulnerability of the human body, and taking into account the potential risks associated with the technical design and manufacture of the devices. Annex IX of this Directive sets out the rules for classification depending on the duration of use, part of the body concerned and characteristics of the device (e.g. invasiveness, active device, etc.). The classification of a device has an impact, among others, on the conformity assessment procedure to be followed prior to placing it on the market.

The conformity assessment procedures for Class I devices can be carried out, as a general rule, under the sole responsibility of the manufacturers in view of the low level of vulnerability associated with these products.

For Class IIa devices, the intervention of a notified body is compulsory at the production stage.

For devices falling within Classes IIb and III, which constitute a potentially higher risk, inspection by a notified body is required with regard to the design and manufacture of the devices. Class III is set aside for the most critical devices for which explicit prior

[5] OJ L 169, 12.7.1993, p. 1

authorization with regard to conformity is required in order for them to be placed on the market.

**Directive 90/385/EEC**[6] on active implantable medical devices establishes the specific rules that a manufacturer has to follow for active implantable medical devices. There are no classification rules laid down in this Directive as it is concerned with a more homogeneous group of devices.

**Directive 98/79/EC**[7] on *in vitro* diagnostic medical devices foresees two main product classes. The large majority of devices do not constitute a direct risk to patients and are used by competently trained professionals, and the results obtained can often be confirmed by other means. Therefore, the conformity assessment procedures can be carried out, as a general rule, under the sole responsibility of the manufacturer. Taking into account the existing national regulations, the intervention of notified bodies is needed only for defined devices, the correct performance of which is essential to medical practice and the failure of which can cause a serious risk to health.

[6] OJ L 189, 20.7.1990, p. 17

[7] OJ L 331, 7.12.1998, p. 1

# 4. SCIENTIFIC RATIONALE

## 4.1. Introduction

Reusable and single-use medical devices (SUDs) coexist on the European market. In order to minimize the risk of health-care-associated infections, rules were progressively put into force for the use of medical devices. These include the obligation for manufacturers of reusable devices to provide instructions on how such reusable devices should be handled and treated (re-processed) in order to be reused (EN ISO 17664:2004).

For economic and environmental reasons reprocessing of SUDs might be considered as useful and is practiced officially or unofficially according to the legislation in different Member States. In some Member States this practice is strictly forbidden, while in others it is regulated under certain conditions of control. There are also countries where the situation is not addressed by any regulation.

Financial considerations are probably the main reason for the reprocessing of single-use medical devices. It is assumed that cost savings can be achieved by reprocessing of single-use medical devices. The degree of those savings depends on a number of factors such as the purchase cost of a new device and the cost of an adequate reprocessing process including an appropriate quality management system.

It is estimated that 72.6 billion euros per year are spent on medical devices in Europe (Spielberg 2009). A national survey in Canada investigating the current practices of reprocessing and reusing SUDs in Canadian acute-care hospitals indicates that 28% of hospitals participating in the survey reprocess single-use devices (Polisena et al. 2008), and gives an overview on the types of SUDs most frequently reprocessed at acute-care hospitals in Canada. Although reports demonstrate cost saving effects of reprocessing SUDs by around 50% when concentrating simply on unit costs (Prat et al. 2004), it has been stated (Jacobs et al. 2008) that the published literature does not provide sufficient evidence to solidly assess cost savings by reprocessing SUDs within complex medical processes, and that sound data on clinical outcomes of using reprocessed SUDs are missing.

The reuse of single-use medical devices (see glossary) raises issues of product performance and quality, but also the issue of legal responsibility. One question that has been raised in the literature is whether or not the original manufacturers are liable for any reduction or failure in the performance of a particular single-use medical device that has been reprocessed. The reprocessing may have been carried out without any recommendation, and maybe even without permission, from the original manufacturer, which raises the question of how the legal responsibility has to be identified for such reprocessed SUDs.

Although these issues are clearly important and need to be addressed, they are not within the remit or area of expertise of the SCENIHR. Consequently they cannot be addressed in this opinion. Rather the opinion is focussed on a scientific risk assessment of the reuse of various medical SUDs.

Aspects of reuse that are addressed in this opinion are:

i) Nature of the use and risks to patients, users and other individuals that might be associated with residual contamination of particular categories of medical devices after each use in individual patients.

ii) Changes that may occur in the physical performance of a particular category of medical devices, e.g. due to some loss of material characteristics with potential consequences for the patient and/or the user.

iii) Health implications of the reprocessing.

iv) Quality control aspects of reuse (e.g. what is an acceptable number of reprocessing and reuse cycles and how can these be controlled in practice).

Aspects which are not addressed in this opinion are:

i) The economic impact of reprocessing;

ii) The environmental impact;

iii) Ethical issues; and

iv) Legal issues.

### 4.2. Hazard considerations

In the EU both reusable and single-use devices (SUDs) are available on the market. The use of SUDs has considerably increased in hospitals in particular to reduce the risk of cross contamination between patients. These devices are generally made of novel polymeric materials (plastics) not resistant to high temperatures and often complex in terms of geometry (shape).

Most countries have experienced rising costs of health care due to a number of factors including the increasing complexity of medical procedures and devices. This has resulted in considerations on possible reuse of certain SUDs. Reduction of plastic waste has also been advocated as an argument for reprocessing of devices intended for single-use. On the other hand, appropriate reprocessing procedures, including a quality management system and validation of the safety and functionality of reprocessed SUDs, may be expensive. In addition, proper cleaning and sterilization of the devices may also have an impact on the environment which is difficult to evaluate.

It should be realised that reprocessing and reuse are common practices for reusable medical devices and the processes to be applied before reuse can occur are included in the manufacturer's information about the device. The reusable devices have to be designed in such a way that the key characteristics allow and withstand cleaning, disinfection and/or sterilization using a validated process established and specified by the manufacturer (see also EN ISO 17664:2004). The information supplied by the manufacturer shall also contain information on any restriction on the number of reuses.

The principal concern of health care must be the safety of both patients and health care professionals.

#### 4.2.1. Design characteristics of the SUDs

Many SUDs are made from polymers (e.g. plastic) allowing them to be mass produced at limited costs and/or giving them specific qualities (e.g. the flexibility of long catheters for stent placing). Although polymers have specific properties, allowing the production of complex SUDs, they may not be durable. While this is perfectly acceptable if the device is used only once, it might be a problem when it is reused, since the properties of the material might deteriorate rapidly once the device is reprocessed. Since SUDs are not designed to withstand any reprocessing, some types may be damaged easily when handled without care.

Contrary to reusable medical devices, reprocessing is not considered during the design of a single-use device and therefore complex design features hampering reprocessing can be incorporated in a SUD. Examples include long and narrow lumens, and moving parts. In view of this, subsequent reuse introduces the hazard of device failure or suboptimal effectiveness of the device.

The number of reprocessing cycles and how often a particular type of SUD can be reprocessed are important considerations. Changes in the device properties and the formation of residues on its surface as a result of its use could lead to dysfunctional

devices after the first cycle of reprocessing. If the changes gradually build up, the number of reuses after which they become unacceptable may limit the number of reprocessing cycles. Many of the materials used for SUDs are not commonly reprocessed and therefore, there is no or only limited information available on the effects of reprocessing on these materials. Therefore, detailed studies are required to establish the compatibility of these materials with the reprocessing procedures.

### 4.2.2. Procedures for removal of pathogenic agents

Within the reuse and/or reprocessing of medical devices the processes of cleaning, disinfection and/or sterilization of the medical devices are of utmost importance. If reprocessing is not properly carried out, it may introduce serious hazards in subsequent applications.

Pathogenic agents/substances include:

- Bacteria in vegetative or spore form (the spore form has a high resistance to disinfection or sterilization processes);
- Microscopic fungi, essentially yeasts and aspergillus;
- Viruses;
- Microscopic parasites; and
- Prions which are agents responsible for transmissible spongiform encephalopathies (TSEs).

Furthermore, endotoxins (which are part of the bacterial cell wall of Gram-negative bacteria and can be responsible for septic shock) may remain on a SUD even after sterilization as they have a very high resistance to disinfection or sterilization processes.

A medical device which has been used for an invasive or non-invasive medical procedure is contaminated by the biological liquids or tissues which were in contact with the medical device used and potential disease-causing agents which any individual is carrying.

The FDA has adopted a classification system based on the definition by Spaulding, reviewed by Alvarado (1994) (see Table 1).

For the purpose of this opinion, the following terminology, which is an adaptation of that proposed by Alvarado (1994), has been used:

**Device for critical use**: A device that is used for surgically invasive medical procedures. These devices should be sterilized.

**Device for semi-critical use**: A device that comes into contact with intact mucous membranes and does not penetrate tissues. These devices should receive at least high-level disinfection.

**Device for non-critical use**: A device that does not touch the patient or touches only intact skin. These devices may be treated with low-level disinfection.

Some examples are presented in Table 1 (based on Alvarado 1994).

**Table 1 Classification of devices, processes, and germicidal products according to Spaulding Classification System**

| Device classification | Device (examples) | Spaulding process classification |
|---|---|---|
| Critical (enters tissues or vascular system) | Implants, scalpels, needles, other surgical instruments, etc. | Sterilization – sporicidal chemical prolonged contact |
| Semicritical (touches mucous membranes [except dental]) | Flexible endoscopes, laryngoscopes, endotracheal tubes | High-level disinfection – Sporicidal chemical: short contact |
| Non critical (touches intact skin) | Thermometers, hydrotherapy tanks | Intermediate level disinfection |
| | Stethoscopes, bedpans, etc. | Low level disinfection |

The entire process of preparing a used medical device for a new episode of use consists of several steps, some of which can be performed in one procedure (e.g. cleaning and disinfection).

### 4.2.3. Treatment after use

Improper handling after use may introduce hazards for the subsequent use of the reprocessed medical device. Used medical devices should be reprocessed as soon as possible. However, it is not always possible to do this due to transportation logistics or because the medical procedures were conducted outside the working hours of the sterilization department. Therefore, preliminary treatment near the point of use should be carried out in these cases.

Currently, immersion and/or packaging are carried out prior to transportation to the place of sterilization.

Immersing medical devices immediately after use in a container with a solution having detergent and disinfecting properties and meeting specific standards aims to:

- Avoid the desiccation of the biological liquids or pieces of fabrics present on the instruments. This facilitates cleaning the devices;
- Avoid the creation of a biofilm;
- Protect personnel; and
- Protect the environment during transportation to the place of cleaning and sterilization.

Packaging consists of placing the devices in a (preferably sealed) container. The main purpose is to prevent desiccation of the product, but it also protects the personnel and the environment during transportation.

Avoiding desiccation is a constant concern as dried contaminants, particularly prions, are more difficult to remove (Lipscomb et al. 2007).

### 4.2.4. Procedures for cleaning

Proper cleaning of a used medical device is necessary to allow effective disinfection and sterilization. This operation is preferably automated at controlled temperatures ranging from 20-65°C, allowing for better effectiveness and reproducibility than manual cleaning. Gross contamination is often removed prior to automatic cleaning by manual action

and/or treatment in an ultrasound bath. During the last decades there has been considerable progress in cleaning which can be attributed to the following:

- A better knowledge of the tension-active products and the effect of pH of the detergent.
- Introduction of automated washer disinfectors.
- The development of standards for automated washer disinfectors, including standardized test methods for the cleaning efficacy.
- An increase in the use of alkaline detergents.

The automatic washing machines should be subject to a validation according to the standards of series EN ISO 15883. Validation should consist of both physical tests and testing of the cleaning efficacy including the use of test contaminations. The latter is hampered by the absence of standardized test contaminations.

The cleaning of devices containing a lumen is challenging. These devices should be connected to equipment to be flushed. If the lumen is only open at one end, flushing is not possible and other ways to clean the lumen have to be used.

The cleaning of the device is influenced by the materials used and the accessibility of the surfaces to be cleaned. Potential problems occur with devices containing internal or moving parts which cannot be adequately cleaned using standard equipment. As the remaining contamination is not visible from the outside, this is only noticed when the functionality of the product deteriorates and the cause of this deterioration is investigated.

Standard washer-disinfectors used for cleaning and disinfecting surgical instruments are not designed to deal with the design features of complex medical devices, such as a long narrow lumen, which is frequently encountered in SUDs.

The mechanical, thermal and chemical impact of reprocessing procedures may influence the properties of the materials and the construction of the device. This can influence the mechanical strength of the product and its biocompatibility. Surface coatings may disappear when the device is cleaned. Special attention should be given to the joints between the different parts of a product. The materials used to create the joints are often different from the other materials used to construct the rest of the device. Weakening of these joints can jeopardize the safety and functionality of the product, as parts of the device may detach during use and remain in the patient.

### 4.2.5. Procedures for disinfection

After cleaning, particularly when using a washer-disinfector, the devices are disinfected to remove potential microorganisms. Improper disinfection may result in hazards of contamination. Disinfection can be performed by chemical or thermal processes. For thermostable materials, water at 80-96°C for less than 1-10 min may be used. This destroys the vegetative forms of bacteria, microscopic fungi, viruses and parasites. Disinfection corresponds to a decrease in the populations of bacteria, spores and viruses. In order to achieve this, a thermal or chemical process with a disinfectant is necessary. A disinfectant is defined in the standard ISO 13408-1:2008 as "a chemical or physical agent that kills most infectious or other undesired microorganisms, but not necessarily highly resistant bacterial or fungal spores".

Similar to cleaning, automated disinfection is preferred over manual disinfection.

For thermolabile materials such as those used in flexible endoscopes, disinfection is performed using an aqueous chemical disinfectant at relatively low temperatures (room temperature up to 60°C). Chemical disinfectants that are widely used are glutaraldehyde and peracetic acid. To remove residues of the chemical disinfectant, a final rinse with

water of high microbiological quality is necessary. The use of a gaseous disinfectant is very rare.

At the end of the cleaning/disinfection step, the medical devices must be dried. If drying is insufficient, additional drying must be performed by using a cloth, filtered air or a drying cabinet. An incompletely dried device cannot be assumed to remain disinfected for a long time-period.

According to the classification of Spaulding, three levels of disinfection can be defined depending on the infectious risk during subsequent use of the medical device (high, intermediate and low-level disinfection).

For certain medical devices, e.g. flexible endoscopes, disinfection is considered to be adequate and constitutes the final step before the device is used again.

For devices to be sterilized, intermittent disinfection is mainly performed for the safety of the personnel preparing the device for sterilization.

The products and procedures used must be in conformity with the standards in force (EN 1040:2005, EN 1275:2005, EN 13624:2003, EN 13727:2003, EN 14347:2005, EN 14348:2005, EN 14476:2005+A1:2006, EN 14561:2006, EN 14562:2006, EN 14563:2008).

### 4.2.6. Inspection, assembly and packaging

After cleaning and disinfection, the devices are re-assembled if they were taken apart for cleaning and disinfection. In many cases, a set of instruments is assembled for specific medical procedures. At this stage, the users of the device should perform a check on the device to confirm the proper functionality of that particular device.

The aim of packaging for devices to be sterilized is to allow sterilization, provide physical protection, maintain sterility up to the point of use and allow aseptic presentation. The design of the packaging system and the choice of materials is influenced by: the specific nature of the medical device; the intended sterilization methods(s); the intended use; the required expiry date; and transport and storage conditions.

The quality of packaging determines the maintenance of sterility. Technical requirements for packaging are described in the standards EN ISO 11607-1:2006, EN ISO 11607-2:2006, and EN 868-2:2009 to EN 868-10:2009.

Improper inspection, assembly and packaging may result in a hazard for subsequent use due to dysfunctional or non-sterile devices.

### 4.2.7. Procedures for sterilization

After cleaning and disinfection, in order to prevent infection due to contaminated medical devices, sterilization of these devices is necessary depending on the type and intended subsequent use of the device.

To obtain a sterile device, it is imperative that the sterilizing agent can reach every surface of the product under the specified sterilization conditions. If the sterilizing agent cannot reach all surfaces to be sterilized or the required levels of the sterilizing conditions (e.g. temperature and humidity) cannot be obtained and maintained as prescribed, the specified sterility assurance level might not be reached and any residual contamination poses a hazard for the patient. Limitations for both the sterilizing agent and the sterilization conditions may be the packaging and specific design characteristics of the device, for example long narrow lumens, large volumes, porous materials, moving and glued parts. To demonstrate the ability of certain sterilization processes to achieve sterility, extensive physical and microbiological testing may be required. Based on these considerations, sterilization is to be performed in a place dedicated for this purpose,

preferably in a centralized service of sterilization (Council of Europe 1972). This is current practice in most Member States.

Sterilization methods for medical devices can be divided into three groups:

- High temperature sterilization;
- Gas sterilization; and
- Radiation sterilization.

The choice of treatment depends on several elements: behaviour of the materials under these treatments; cost; and whether the treatment takes place in-house or by a subcontractor.

**High temperature sterilization**

The most commonly used sterilization method is steam sterilization at temperatures ranging between 110°C and 134°C. This method is reliable, easy to control and allows for the sterilization of a hollow and porous material if a properly operated sequence of vacuum and steam pulses system is used to remove the air remaining in the devices. Due to these properties, steam sterilization is the sterilization method of choice for the sterilization of the reusable medical devices in hospitals. The processes must be validated, and routine controls should be performed to release the sterilized devices. Several standards exist for moist-heat sterilization processes (EN ISO 17665-1:2006 and EN ISO/TS 17665-2:2009, EN 13060:2004+A1:2009 and EN 285:2006+A2:2009). However, due to the thermolabile properties of materials used for most SUDs, steam sterilization usually cannot be used to sterilize SUDs.

Dry heat sterilization processes require higher temperatures (160-250°C). Temperatures higher than 250°C can eliminate endotoxins. Sterilization by dry heat is seldom used for the sterilization of medical devices, due to the high temperatures required and the long process time for this procedure, especially if the products are wrapped, as the packaging acts as a barrier for heat penetration.

**Sterilization by gases**

The following agents are used for sterilization by gases (Dusseau et al. 2004) including alkylating agents like ethylene oxide (EO) or a mixture of steam and formaldehyde, and oxidizing gases like hydrogen peroxide, ozone and peracetic acid.

Residues of gaseous sterilizing agents can remain after the sterilization processes. It should be carefully checked that the levels of residues do not jeopardize the safety and functionality of the device. Multiple reuses should be more carefully considered as the residues may accumulate. The sterilizing agent could also react with the materials of the device. This can lead to changed properties of the medical device or bio-incompatibility.

Alkylating agents

- The most commonly used sterilization method after steam sterilization is ethylene oxide (1,2-epoxyethane, EO). Ethylene oxide can be used at low temperatures (40-55°C) and has good penetrating properties. The concentration of EO used ranges between 450 and 850 mg/L. Ethylene oxide is extremely toxic, flammable and explosive. In addition, EO is classified by the WHO in group 1 of substances carcinogenic to humans. Due to these properties, using EO as a sterilizing agent requires extensive safety and environmental measures and precautions. Therefore, the use of this sterilization method is decreasing in European hospitals and is mainly performed in dedicated and industrial facilities. Due to their toxic properties, residues of ethylene oxide and its possible reaction products (ethylene chlorhydrine, or 2-chloroethanol and ethylene glycol) have to be removed after sterilization by aeration. Acceptable levels for residual EO and the reaction products are specified in the

standard EN ISO 10993-7:2008/C1:2009. Chlorinated polymers cannot be sterilized by ethylene oxide after a first sterilization by ionizing radiation because of the formation of highly toxic molecules (ethylene chlorhydrine or 2- chloroethanol). The standards EN 1422:1997+A1:2009 and EN ISO 11135-1:2007 and EN ISO/TS 11135-2:2008/AC:2009 on sterilization describe requirements related to EO sterilization processes.

- Mixture of steam/formaldehyde. Low Temperature Steam Formaldehyde (LTSF) is a sterilization method used uniquely in hospitals. Temperatures range between 56°C and 80°C. Due to recent concerns on the carcinogenicity of formaldehyde, its use as a sterilizing agent is under discussion. The standards EN 14180:2003+A2:2009 and EN 15424:2007 describe requirements related to LTSF sterilization processes and formaldehyde residues.

Oxidizing gases:

- A relatively new sterilizing agent for medical devices is hydrogen peroxide. The advantage of hydrogen peroxide is that is does not leave toxic substances as residues. The temperature for the most frequently used sterilizer is 45°C.
- Ozone: A new development is the use of ozone as a sterilizing agent, but its use is limited and occurs mainly outside Europe.
- Peracetic acid: Gaseous peracetic acid is used as a sterilizing agent on a very small scale. However, it is widely used in a liquid form for disinfection purposes.

In the absence of specific standards on the development, validation and routine controls of sterilization processes, the reference standard is EN ISO 14937:2009.

**Radiation sterilization**

Radiation sterilization is only used in industrial settings. Two types of radiation sterilization are commonly used for medical devices: gamma radiation and beta radiation.

- Gamma radiation sterilization is achieved by exposing the devices to Co-60 rods emitting gamma radiation. This method of sterilization requires extensive safety measures (mainly extensive shielding by concrete) due to the penetrating ability of gamma radiation and the fact the radiation cannot be turned off.
- Beta-radiation (accelerated electron beam). The devices are exposed to an electron beam. This sterilization method has limited penetration. Less safety measures are required, due to the limited penetration capabilities and the fact that the sterilization equipment can be turned off.

Ionizing radiation is known to change the properties of several types of materials, notably certain polymers like plastics. Some can become brittle due to ionizing radiation, which sometimes occurs a long time after exposure to radiation.

Sterilization by ionizing radiation is described in the standards EN ISO 11137-1:2006 to 11137-3:2006.

Although all sterilization methods are developed and validated to achieve the sterility assurance level of a $10^{-6}$ probability of contamination, steam sterilization, in particular, is able to achieve much higher levels. The resistance of a micro-organism to a sterilization process is evaluated by the mean of the D value (time to reduce a population of a specific micro-organism ten times). For steam sterilization, the D value at the reference temperature (121°C = $D_{121}$) of the reference test spore (*Geobacillus stearothermophilus*): 1.5 to 2 min, is dramatically higher than the $D_{121}$ value of the environmental micro-organisms or pathogenic micro-organisms. The $D_{121}$ value of *S. aureus* is about 2 sec, and 0.1 sec for a Salmonella spp, respectively 45 times and 1,600

times lower. A comparison of various low temperature sterilization techniques was published by Alfa et al. (1996) and Rutala et al. (1998).

### 4.2.8. Differences between disinfection and sterilization

Disinfection is a process with limited capabilities for the inactivation of micro-organisms. Since disinfected products are not wrapped, they can be contaminated and do not remain disinfected. The required efficacy of the disinfection process is linked to the intended use and the micro-organisms relevant for that use (e.g. bed pans require a lower level of disinfection than a flexible endoscope). It is not possible for disinfection to achieve sterility. It only decreases the population of micro-organisms by a limited reduction factor (up to $10^5$).

By definition, sterilization processes are able to inactivate all varieties of micro-organisms resulting in a very low probability of persistence. It is therefore possible for sterilization processes to achieve sterility. The process of disinfection is less effective in reducing the number and range of micro-organisms. For disinfectants, the level and intended spectrum of activity is specified in international standards. However, it should be noted that a process of disinfection can never replace sterilization for those medical devices which were initially marketed as sterile devices.

### 4.2.9. Prion inactivation and/or removal

A specific hazard is the possible contamination with agents causing transmissible spongiform encephalopathies (TSEs) as they are particularly resistant to commonly used physical and chemical methods of cleaning, disinfection and/or sterilization. The causative agent of these diseases is thought to consist of the pathogenic isoform of the prion protein (PrP), which is misfolded into the infectious agent PrPSc. It is known that transmission of Creutzfeldt-Jakob disease (CJD) can occur in specific situations associated with medical interventions (iatrogenic infections) (Armitage et al. 2009). The first case of iatrogenic transmission of CJD was identified in 1974 in a corneal graft recipient. In 1996 the National Surveillance Unit in the United Kingdom identified a new form of CJD, which is now known as variant CJD (vCJD) that affected a much younger age group when compared to classical sporadic CJD. In vCJD the prions (PrPSc) are mainly distributed to cells of lymphatic organs and brain tissue of affected individuals while levels of infection vary at different stages of incubation. Thus, medical devices may become contaminated with prions after contact with infected tissues and/or blood, even when there are no clinical symptoms.

Prions are not significantly affected by chemical disinfectants and some disinfectants may act as protein fixatives and may stabilise the agent (i.e. Low Temperature Steam Formaldehyde, LTSF). TSE agents (prions) are known to be resistant to standard methods of sterilization, (ethylene oxide, ionising radiation). Steam sterilization (autoclaving) remains an important method of reducing infection, although different strains of TSE agents are known to vary in their sensitivity to heat. However, it cannot be relied upon to completely eliminate infection. Therefore, effective cleaning is of great importance in the removal of these agents.

Some processes are capable of inactivating prions (Rutala and Weber 2001, Taylor 1999, WHO 1999). Processes ensuring a total inactivation of the TSE agents which have been identified to date are:

- The immersion in a solution of sodium hypochlorite with the concentration of active chlorine of 2% and a quantity of active chlorine of 20.4 g/L (bleach to 20,000 ppm) for 60 minutes at room temperature;
- The immersion in a solution of 1 M sodium hydroxide for 60 minutes at room temperature.

These procedures are relatively aggressive precluding their application to a number of materials used for the production of both reusable and single-use medical devices.

### 4.2.10. Physico-chemical hazards

The most obvious chemical hazard is due to residues of chemical decontaminants that may remain after cleaning either by inadequate washing afterwards or by absorption into the materials of the device (MHRA Device Bulletin 2006). Also, for ethylene oxide sterilization, the remaining EO residues may pose a serious risk. During use and reprocessing, an interaction might occur between the chemicals present in the material used for the medical device, chemicals in the body, and/or the chemicals used during reprocessing. Such interaction may or may not affect the functional properties of the medical device. In addition, after repeated reprocessing, ageing of the device may occur such as an increase in brittleness of polymers such as plastics due to loss of plasticizer. Changes in physico-chemical characteristics of a reprocessed SUD may affect health care professionals as well as patients. Physical characteristics can be described as elasticity, stiffness, roughness, strength, conductivity, amongst others.

The evaluation of potential physico-chemical hazards can be investigated by using the EN ISO 10993 series dealing with the biological evaluation of medical devices, in order to show conformity with the Essential Requirements of the MDD.

Published examples of physico-chemical hazards include:

- The surfaces of used plates and screws for ostheosynthesis were more hydrophilic than new ones, had increased amounts of calcium-phosphates at their surfaces, and possessed a higher number of scratches (Magetsari et al. 2006). However, simple cleaning methods were sufficient to yield elemental surface composition with hydrophobicities similar to those of new ones, although material damage like pitting corrosion could still be observed.
- For coronary angioplasty balloon catheters, the clinical use and reprocessing caused partial modifications of the material properties inducing an overall shrinking effect on the balloons (Fedel et al. 2006). A maximum of about 6% variation of the nominal values was detected which was, however, within the original specifications (±10%) of the manufacturer thus showing conformity of the reprocessed devices. Main changes were noted during the first reprocessing of the devices while a second cleaning and sterilization did not introduce further alterations.
- For PVC catheters successive reuse resulted in increased plasticizer loss, an increase in glass transition temperature and a small decrease in molecular weight (Granados et al. 2001). In addition, an increased surface roughness and surface grooves were noted as indicators of severe damage. The magnitude of the changes of the biomaterial parameters suggested that the reuse may alter the original device performance.
- Endoluminal catheter (i.e. for embolization) is a critical device which is used in a normally sterile environment. The physical configuration lets the tip of the device enter branching vessels which get smaller and smaller until the final destination has been reached. Changed elasticity (increased stiffness) can lead to physical impossibility to reach the targeted vessel part. As a consequence, more invasive techniques (surgery) or death due to unstoppable bleeding may occur.
- King et al. (2006) assessed new and reprocessed arthroscopic shaver blades. Of the 27 reprocessed shaver blades, 13 (48%) had detectable levels of protein and 17 (63%) had detectable levels of nucleic acid on their surface. New shaver blades had no contaminants and no visible damage. Image processing revealed smoothness of the surface of menisci cut with new shaver blades. Menisci cut with reprocessed shavers showed rougher edges than did menisci cut with new shavers. All of the

reprocessed blades visually evaluated showed some level of damage or wear, whereas no new blade had such damage.

- Hypothetically, reprocessing may also affect coatings present on a SUD, resulting in reduced smoothness of the SUD which may limit further use of the device.

#### 4.2.11. Conclusions

After use, all medical devices that have been in contact with patients may contain contaminants including pathogenic microorganisms, the elimination of which during cleaning, disinfection, and sterilization steps may be difficult. If the efficacy of these steps is not properly validated, the resulting persistence of the contamination poses a hazard of infection for the next patient on whom the medical device is used. The use of high-level disinfection instead of sterilization increases the hazard for the persistence of the contamination. A process of disinfection can never replace sterilization for those medical devices which were initially marketed as sterile devices.

For reusable medical devices cleaning, disinfection and sterilization is needed before a device can be reused. From a technical point of view, the same processes apply to single-use devices if they are reprocessed. For reusable medical devices, these procedures and conditions have been evaluated and validated, and must be provided by the manufacturer. This is not the case for single-use devices. This means that before a single-use device might be reprocessed all procedures involved in the reprocessing need to be developed and validated. Due to their material characteristics, most single-use medical devices cannot be sterilized by high-temperature processes and are, therefore, only suited to being sterilized by gas or radiation.

A particular hazard remains with the elimination of prion contamination because only relatively aggressive cleaning methods, not compatible with the commonly used materials, can ensure complete prion inactivation.

In addition to the microbiological hazards, toxic residues and changes of the physico-chemical characteristics of the device as a result of its handling and reprocessing also pose a hazard for the patient.

### 4.3. Risk considerations

#### 4.3.1. Patients and health professionals at risk

Both patients and healthcare professionals may be exposed to reprocessed SUDs during a medical procedure.

Patients at risk as a result of the possible reuse of SUDs are the second, third and any subsequent patients who may come in contact with a pathogenic microorganism able to provoke an infection, or persistent chemical residues provoking toxic responses. Patients as primary targets of the reprocessed SUD represent a heterogeneous group. Specific groups at risk include immunocompromised patients (e.g. HIV infected and organ transplant patients) and prematurely born infants.

Besides the presence of biological and chemical residues, a change in the physical characteristics of the reprocessed SUD might harm the patient, degrade the learning curve of the health-care professionals involved, or add a handling risk during the procedure of use. For example:

- Patients with reduced arterial elasticity might react during a procedure carried out using a reprocessed SUD which has changed its physical parameters (e.g. increased stiffness and increased roughness of the surfaces). The higher shear stress in the vasculature could lead to an increased risk of endothelial damage and rupture. In

theory, a life threatening event such as an apoplectic stroke is possible as result of the maltreated vessel and consecutive thrombosis.

- The change of behaviour of reprocessed SUDs might decrease the learning curve of health care personnel due to changed elasticity, feeding force, stiffness and other factors.

In addition to patients, health care professionals may be at risk when using reprocessed SUDs. However, relatives providing home care for patients may also be at risk when using reprocessed medical devices. During home care disinfection or even sterilization of parts of a medical device or the entire medical device may have to be performed resulting in an additional risk.

### 4.3.2. Medical procedures

Besides the condition of the device itself, the nature of the medical procedure has an influence on the potential risks for the patient. The need and extent of the disinfection/sterilization requirements can be indicated by the Spaulding classification which relates to the risk for the exposed patient. The risk differs in relation to the use of the medical device and can be categorized in three groups (non-critical, semi-critical, and critical medical device use).

1. Topical contact, Non-Critical procedure.

Topical contact on intact skin is generally limited, and a limited area of the skin is affected. Thus, the risk may be considered to be very low. However, two exceptions should be considered: (i) if the dose to start an infection is not known and (ii) if the transmission route is not known, then the associated risk cannot be quantified.

2. Semi critical procedure: device comes into contact with intact mucous membranes and does not normally penetrate tissues.

This section is primarily the domain of endoscopes and their use for medical procedures. There is a worldwide trend to extend the boundaries of the diagnostic and therapeutic procedures. The border with surgical procedures is blurred. While the endoscope remains in the area of intact mucosa, the cutting, grasping and dissection devices may not. In most cases, a device used in the screening procedure will encounter an intact mucosa all the way. However, there are situations in which the device has to pass through inflamed areas or malignancies which will depend on the age, medical history and other factors of the patients.

An upcoming trend in endoscopy in which devices are used inside other devices needs special attention. For example, a standard endoscope is used to find the end of the bile duct which enters the gut, and a second, internal, thinner endoscope may be used for guiding single-use devices for grasping stones in the bile duct or placing stents. This procedure has the danger that biofilms, particles, and remnants remaining in the endoscope from previous uses can be scrubbed off and contaminate the patient.

Malfunction, in general, will remain without severe consequences except for procedures in the bronchial tree, where failure to remove a foreign body by a medical device via the airways would result in a surgical procedure which by itself poses a higher risk compared to endoscopal removal.

3. Critical-invasive procedures.

In this situation the risk is linked to remaining bioburden, toxic or allergic compounds, and technical problems due to modification of the physical properties of the reprocessed SUD.

### 4.3.3. Biological risks

The biological risk for patients exposed to SUDs is especially linked to viruses and non-conventional transmissible agents (prions) with some evidence in the literature of patients infected with Creutzfeldt-Jakob disease after use of contaminated medical devices (Armitage et al. 2009).

There are some publications indicating that SUDs having undergone reprocessing do not meet the same quality standards as new devices delivered by the original manufacturer since reprocessed SUDs may exhibit contaminations by proteins and viral nucleic acids:

- Heeg et al. (2001) investigating single-use and reusable biopsy forceps and papillotomes, as well as a reusable stone retrieval basket, reported that none of the reprocessed single-use instruments were effectively cleaned, disinfected, or sterilized in accordance with the adapted protocol. Cleaning procedures facilitated distribution of contaminants further into the lumens of the disposable forceps.
- Luijt et al. (2001) determined the theoretical risk of virus transmission during reuse of catheters using an *in vitro* study with seeded RNA virus (echovirus-11) or DNA virus (adenovirus-2). According to the procedure used for cleaning, disinfection, and sterilization of the catheter, the percentage of detectable RNA or DNA by PCR was variable but never zero.
- Roth et al. (2002) included in their study single-use laparoscopic dissection devices (n = 3) and a variety of clinically used and reprocessed SUDs (n = 114) for testing their clean-ability. Cleaning could not completely eliminate intentionally added microorganisms, but the devices were effectively disinfected. However, sterilization could not eliminate the intentionally added microorganisms completely. In the examination of the clinically used and reprocessed devices the results were as follows: 11% of the sterile packages were damaged; 33% of the devices were incomplete and parts were missing; 54% did not meet the criteria for functionality. In addition, light microscopy, scanning electron microscopy, and X-ray photoelectron spectroscopy showed contamination on the outside and inside of all devices. Of the tested SUDs, 40% remained contaminated following resterilization.
- Cléry et al. (2003) demonstrated that routine cleaning and autoclaving does not remove protein deposits from reusable laryngeal mask (LMA) devices. Based on their findings, the authors discuss the risk of prion disease transmission from reusable LMAs and present a worst-case scenario on the basis of estimates for the incidence of prion disease (assumed 1 per million), the number of LMA uses per annum (20 million), the frequency of contamination (assumed 100%), the frequency of infection from a contaminated LMA (assumed 100%), and the number of uses of each LMA after contamination (assumed 20 and assuming that the risk of infection does not decrease with each use). The authors thereby demonstrate a probability of 400 infections per annum, or a 1:50,000 chance of infection per LMA use.
- da Silva et al. (2005) performed a safety evaluation of SUDs after submission to simulated reutilization cycles. The reprocessing cycles were simulated after intentional contamination of selected test material such as intravenous catheters, 3-way stopcocks, and tracheostomy tubes with Bacillus subtilis var. niger ATCC 9372 spores ($10^7$ Colony Forming Units/product). After each reprocessing cycle, specimen samples were evaluated by microbial counts, direct and indirect inoculation sterility tests, cytotoxicity evaluation, and scanning electron microscopy. Microbial counts as high as $10^3$ CFU were obtained after the 10th reprocessing cycle, in addition to scratched and damaged surfaces observed by scanning electron microscopy.
- Tessarolo et al. (2006) assessed the sterility of reprocessed non-lumen electrophysiology catheters (n = 73) according to the number of reprocessings. After the second reprocessing, seven of 36 devices showed growth of gram-negative bacteria other than the inoculated strain. The authors conclude that reprocessing

according to the presented reprocessing protocol was insufficient to guarantee device sterility after five reuses.

These studies indicate that the reprocessing protocols described in the studies did not result in sufficient decontamination of the SUDs. It is unclear if the protocols used to reprocess the devices were insufficient or if the devices could indeed not be properly reprocessed. Whether such contaminations introduce for patients a risk of developing infectious diseases and/or immunological complications such as inflammatory or allergic reactions is not sufficiently evaluated by clinical studies. Studies claiming safety of reprocessed SUDs do not cover any form of long-term observation of patients regarding the development of infectious diseases and/or immunological complications following exposure (Buchwalsky et al. 2001).

A government report from the Canadian region Saskatchewan states that in September 2008, Alberta Health released a statement that reuse of single-use syringes had occurred over a five-year period in a medical facility (Saskatchewan Health 2009). There has been no epidemiological indication of a connection between a notified blood-borne viral infection and a health care facility. It was calculated that the population in the geographical region in which hospitals practice the use of reprocessed syringes exhibit a slightly higher risk of acquiring a blood-borne virus than in the general population of Prairie North ($1.86\text{-}3.02\times10^{-6}$ versus $1\times10^{-6}$) (Saskatchewan Health 2009).

There are no reports estimating the risk of contamination after the reuse of either reusable medical devices or reprocessed single-use medical devices. As medical devices may come into contact with blood, the biological risks as assessed for the transmission by blood or untested blood components may currently serve as a rough estimation of the level of exposure to biological agents for patients undergoing procedures involving reprocessed SUDs.

Beltrami et al. (2000) assessed the risk of blood-borne infections in health care workers (HCWs) coming into contact with the blood or body fluids of infected patients due to needlestick and sharp injuries. The average risk for HIV transmission following a percutaneous exposure to HIV-infected blood is approximately 0.3% (95% confidence interval 0.2 to 0.5%), and the risk following a mucous membrane exposure is 0.09% (95% confidence interval 0.006 to 0.5%). The risk after a cutaneous exposure has not been well quantified. With regard to hepatitis B virus (HBV), the authors summarize literature indicating that the average volume of blood inoculated during a needlestick injury with a 22-gauge needle is approximately 1 µL, a quantity sufficient to contain up to 100 infectious doses of HBV. The risk of transmission after a needlestick exposure to a non-immune person is reported to be at least 30% if the source patient is HBeAg positive but is less than 6% if the patient is HBeAg negative. The average incidence of hepatitis C virus (HCV) seroconversion following needlestick or sharp material exposure from a known HCV-seropositive source patient is 1.8% (range: 0 to 7%).

As discussed above, there is a risk of infection from contaminated reprocessed SUDs. Emerging infectious disease agents and their potential to be transmitted by blood were reviewed by a working group of the American Association of Blood Banks (Stramer et al. 2009). Key characteristics of each agent were identified, researched, recorded and documented in a standardized format. Sixty-eight infectious agents were identified and described in detail. This report identifies a wide range of biological agents that may also be relevant for patients undergoing medical procedures involving reprocessed SUDs. The highest priorities were assigned to Babesia species, Dengue virus, CJD and vCJD. Thus the SUDs used in contact with patients suffering from these diseases are to be considered as a particular risk.

### 4.3.4. Physico-chemical risks

Potential changes in physico-chemical characteristics of the material used for the production of SUDs were identified as hazards and thus pose a potential risk to patients.

However, clinical data on the occurrence of such risks are lacking. The consequences of the failure may range from prolongation of the medical procedure to death of the patient.

### 4.3.5. Case reports on incidents with reprocessed medical devices

Reports of cases where the use of reprocessed medical devices intended for single-use have caused harm to patients are scarce. It is thus difficult to estimate the frequency of such incidents and the cases reported should be taken as examples. In general, the personnel involved in incidents are likely to be reluctant to report the incidents for insurance or other reasons. In most European countries, the reporting of incidents is not mandatory. In the United States, reporting of incidents involving medical devices is mandatory and all reported incidents are integrated into a searchable database called MAUDE (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.CFM). However, when analysing the reported incidents, the Government Accounting Office (GAO) did not find any evidence that reprocessed SUDs caused more incidents than other devices (http://www.gao.gov/new.items/d08147.pdf). To date, the number of devices which have been reprocessed and used in the US is around 50 million. It has to be noted that a reprocessed SUD in the US must comply with the same requirements as the original devices[8].

It may be difficult to define an adverse event when using reprocessed SUDs. A prolongation of a medical procedure due to a reduced performance of the reprocessed SUD leading to an increase in hospital days can be considered an adverse effect but would be difficult to identify. Even post treatment infections may be difficult to attribute to the use of a reprocessed SUD as these also may occur due to the treatment itself or other unknown conditions.

**Case reports of incidents with reprocessed SUDs due to:**

Persistence of residues of cleaning or disinfectant agents (allergy, toxicity)

The death of 16 premature infants due to flushing of central venous catheters with water containing benzyl alcohol was reported. Both SUDs and non-SUDs were used. No further incidents were reported after changes in the procedure (MMWR 1982).

Persistence of infectious agents or endotoxins (infections, toxicity or immunological reactions)

The two reports on adverse reactions after reuse of catheters for cardiac use are old and look at SUDs and non-SUDs (Jacobsen et al. 1983, Kundsin and Walter 1980). Another report is concerned with respiratory infections due to the reuse of single-use stopcocks during bronchoscopy (Wilson et al. 2000). Recently, two outbreaks of hepatitis C were reported in the US due to reuse of needles and syringes labelled as SUDs (Olsson 2009).

Modification of physical and/or chemical characteristics (brittleness)

The breaking of a SUD that has been reprocessed has been reported in various media but not in the scientific literature. The tip broke off a reprocessed single-use cardial catheter in a Miami hospital causing lasting disability of a patient (Court decision 1981). In addition, there are a few known incidents with reprocessed single-use medical devices that have been the subject of court rulings in France (Tribunal Grande Instance Paris 1991).

Biocompatibility considerations

Haemodialysis machines are life-saving devices used to treat patients with kidney failure. Originally, cellulosic dialysis membranes were used and it was observed that reuse of the

[8] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ReprocessingofSingle-UseDevices/default.htm

membranes improved the biocompatibility and thus caused less adverse reactions in the patients (Lowrie and Hakim 1980). Later on, synthetic membranes were introduced that were more biocompatible and these dialysis membranes were sold as single-use devices ("dialysers"). In the US, reuse of dialysers resulted in 40% higher morbidity and higher mortality (around 25%) among the dialysis patients (Feldman et al. 1999a, Feldman et al. 1999b). A Canadian meta-analysis of all available data showed also an increased morbidity with reused dialysers (Manns et al. 2002). The lower cost of reusing the dialysers was counterbalanced by an increasing number of hospitalisation days. In Europe, some countries do not permit reuse, and in most other countries reuse of dialysers concerns less than 10% of the patients. A notable exception is Poland where most dialysers are reused (Lowrie et al. 2004). As the dialysers have become cheaper in later years, the economic benefit of reuse is questionable when weighted against the cost of increased morbidity (Manns et al. 2002).

In conclusion, a few cases indicate the possibility for causing harm to patients or users due to reuse of single-use devices. However, only immediate effects are easily observed. Long-term consequences, in particular infections, are rarely proven or even detected.

It should be noted that several of these reports identify effects that are similar for reusable and single-use medical devices.

### 4.3.6. Miscellaneous issues

In addition to hazards and risks associated with the chemical-physical, biological and performance characteristics of medical devices there are some other aspects which need to be considered.

For reuse and sterilization one has to consider two quite different situations:

- The medical device (SUD) has not been used on a patient. The container/packaging of a SUD has been opened during a medical or surgical activity. It might also be that it can be assessed that there is only a breach in the outer layer of the packaging. In these cases it is possible that such SUDs can enter a process of sterilization. In several cases, the manufacturer can provide procedures for the reprocessing of opened but unused devices.
- The SUD has been used and has been in contact with a patient. It should normally be considered as waste and can be discarded because it has fulfilled its one-time function. Sterilization is only one of the steps of the whole reprocessing.

In this context, the major consideration of associated risks of using a reprocessed SUD is the type of re-use of the used and discarded SUDs. The risk can be defined based on actual information on incidents or anticipated potential hazards. If the incidents database is reliable the risk can be estimated based on:

- The number of each type of adverse incident in relation to the total number of uses of reprocessed single-use devices.
- The number of each type of adverse incident with reprocessed single-use devices compared with the number of each type of adverse incident arising from multiple use devices.

In the absence of data concerning incidents, information from simulation studies and hypothetical hazards present indications for potential risks as mentioned above in sections 4.2.1 – 4.2.10 and 4.3.3.

When multiple-use devices are present on the market at the same time as reprocessed SUDs, the differences between the two types of devices must be considered in terms of risk assessment and how these differences can be identified. Therefore, the question is whether it is possible to identify a framework based on hazard characterisation that can

be applied to both reprocessed SUDs and multiple-use devices and which allows a distinction to be made between these two.

Some critical points for reprocessing of a SUD may be:

- The reprocessed SUD must achieve a level of quality and safety which is comparable with the original SUD. It has to comply with the Essential Requirements of the MDD.
- The number of reprocessing procedures allowed for a particular device should be determined. The number of times the device has already been used must also be identified.
- The reprocessed SUD has to be identified.

Other aspects involved with the practice of SUD reprocessing which are of great importance are:

Documentation and information about the devices

Handling instructions and guidance according to the use of the device and the role of a person in a health care team are part of each device. The majority are printed flyers, leaflets or booklets. Not only can this documentation get lost, but it can also become contaminated in various ways during the medical intervention. Moreover the partial or complete loss leading to incomplete or absence of printed instructions may result in an additional source of errors. The procedures of reuse should therefore guarantee that the information shall still accompany the reused device.

Evaluation and validation

Quality controls on the performance of the reprocessing of the medical devices, including the validation and evaluation of the results, are necessary. There are currently no specific requirements for the reprocessing and/or reuse of SUDs.

Traceability throughout the lifetime of a device

Every device has a unique production (lot or batch) number which is normally part of the packaging. This production number can either be printed on the package or can be a separate sticker which is to be applied either to the surgical or intervention's documentation or could be put in the patient's record. Re-use of devices makes it difficult to keep the production number together with the device. Therefore, a traceability system has to be in place.

Identification of (sub)parts of a complex device

Confusion on "what is what" after reprocessing and the use of proper terminology, leading to possible human errors. Considering the situation that some devices need to be put together before use in a medical intervention, the original packaging plays an important role. Intelligent packaging reduces handling errors by forcing the user to get through the process in a guided way. For example, parts of the device can be packed one in another so you cannot change the order of assembling. Additional numbers, terms or markings with pictograms of the "intended next step" can be essential help in the procedure of preparation.

Educational and training issues

The point of training has two main aspects. The device is easily identified by its unique packaging. If it is a simple device, only the handling needs further attention. If it is a complex device, more consideration needs to be given. The primary training will start with original packed devices which have a user guide and intelligent packaging which limits misuse. Any changes in the order of the packaging or different placement in the original packaging are a potential source of error.

The handling and behaviour of devices might change during the (multiple) re-use of SUDs due to changes in the physicochemical characteristics of the materials used for the medical device. While it can be unavoidable or neglectable for certain non-critical uses of

devices, such changes in the behaviour of devices (e.g. reduced flexibility, reduced smoothness) can have an effect on the learning curve of the physician for low frequency medical procedures. If the status of the re-used SUD is not known (how often the device has been used before) non-predictable features might be present.

### 4.3.7. Conclusions

Some simulation studies have shown that reprocessing of SUDs potentially may result in improper cleaning, disinfection and/or sterilization leaving a bioburden on the reprocessed SUD. This presents a risk of infection when using the reprocessed SUD. Toxic reactions may occur when cleaning or disinfectant residues remain on the reprocessed SUD. In addition, changes of physical and chemical characteristics of the devices may eventually have an impact on the performance of the reprocessed SUD.

It is very difficult to identify an adverse incident as a result of the re-use of an SUD. There may be a "grey" area for which the recognition and reporting of incidents is difficult, such as a prolonged surgical procedure due to stiffness of a reprocessed SUD catheter, and a prolongation of hospital days. Furthermore, long-term effects may not be identified and attributed to the use of reprocessed medical devices. Although the potential hazards can be identified, there is no classification system for actual incidents as yet.

The number of documented incidents is very small although it can be speculated that the reporting of incidents is incomplete. A large inventory in the US did not show evidence of a significantly increased risk to patients from reprocessed devices when reprocessing is done under strictly regulated conditions.

## 5. OPINION

### Background

Advancement of technology has resulted in the development of more and more sophisticated and complex medical devices such as devices for minimal invasive procedures, with smaller lumens and with more delicate working mechanisms. The proper cleaning of some devices is difficult or even impossible. These are generally made of polymer materials like plastics, which are not resistant to sterilization processes requiring high temperatures or other aggressive physical or chemical treatments. Furthermore, the emergence of blood-transmitted diseases like hepatitis and HIV infection has accelerated the development and increased the use of single-use medical devices.

The decision to market a reusable or a single-use medical device is the responsibility of the manufacturer. For medical devices intended by the manufacturer to be reused, according to the Essential Requirements of the Medical Devices Directive, the manufacturer must provide information on the appropriate process to allow reuse including; cleaning, disinfection, and packaging and, where appropriate, the method of sterilization to be used, and any restriction on the number of reuses, as described in standard EN ISO 17664:2004. Obviously, for single-use devices such information is not available. Medical devices intended for single-use must bear on their label an indication that the device is for single-use.

The concept of reprocessing single-use medical devices (SUD) is, from the point of view of semantics, a paradox as the meaning of "single-use" excludes reprocessing. However, reprocessing SUDs is propagated mainly by apparent economic considerations.

### Hazards

In principle, there is no difference between reprocessing procedures for multiple-use medical devices and for single-use medical devices. For both categories of devices, cleaning, disinfection and/or sterilization are needed before the device can be reused. For multiple-use devices, the procedures, conditions and number of reuses are already considered at the design stage of the device. The choice of the material and geometry (shape) of the device are also considered at this stage. Information on the reprocessing procedures to be followed must be provided by the manufacturer, and this is not the case for single-use medical devices.

After use, all medical devices that have been in contact with patients may contain contaminants including pathogenic microorganisms, the elimination of which during the cleaning, disinfection and sterilization steps may be difficult. If the efficacy of these steps is not properly assessed, there is a possibility for contamination to persist which may result in the risk of infection during subsequent use in the next patient.

The use of reprocessed SUDs may increase the biological, chemical, and/or physical hazards associated with the reprocessing procedures compared to reusable medical devices or for the one-time use of a SUD.

The biological hazards are associated with the persistence of microbiological contamination or difficulty in removing TSE agents resulting in the risk of infection after reuse. In addition, the persistence of chemical residues after cleaning, disinfection, and/or sterilization procedures poses a hazard for toxic reactions after reuse of the reprocessed medical devices. Interaction of the chemicals used during cleaning, disinfection, and/or sterilization with the medical device may pose a hazard for changes in the physico-chemical characteristics of the device resulting in a reduction of its performance.

**Risks**

The risks are related primarily to the use of the device. Three categories can be identified: (i) non-critical use (in general for skin contact only); (ii) semi-critical use (contact with mucous membranes without penetration of tissues); and (iii) critical use (penetration of tissues or entrance into the vascular system). The highest risk occurs when a reprocessed SUD is used for invasive medical procedures, while the lowest risk is associated with external (skin contact only) use.

Some simulation studies and a few clinical studies have shown that reprocessing of SUDs may result in improper cleaning, disinfection and/or sterilization leaving a bioburden on the reprocessed SUD, which introduces a risk of infection when using the reprocessed SUD. Regarding cleaning, disinfection and/or sterilization, a specific problem that remains is the elimination of prion contamination because only relatively aggressive cleaning methods, not compatible with the commonly used materials for SUDs, can ensure prion inactivation.

Chemical residues as a result of reprocessing may pose a toxic risk when a device is reused. In addition, changes of the physical and chemical characteristics of the devices may occur which may eventually have an impact on the performance of the reprocessed SUD.

It has been shown that a reprocessed SUD can be modified in its structure or functionality and may potentially cause some damage to the patient or health-care workers, e.g. mechanical failure of the device, biological and infectious risks, or chemical risks because of residues.

The number of documented incidents is very small although it can be speculated that the reporting of incidents is incomplete. At the same time, a large inventory in the US did not show evidence of a significantly increased risk to patients for reprocessed devices. This lack of an increased risk may be associated in part with the limitations the US imposes on the reuse of reprocessed medical devices. However, regarding adverse events, there may be a "grey" area for which the recognition and reporting of incidents is difficult, such as a prolonged surgical procedure due to stiffness of a reprocessed SUD catheter, and a prolongation of hospital days. Furthermore, long-term effects may not be identified and attributed to the use of reprocessed medical devices.

**Specific answers to the Terms of Reference**

The SCENIHR was requested to assess the following:

1. Does the use of reprocessed single-use medical devices constitute a hazard for human health (patients, users and, where applicable, other persons) causing, for example, infection/cross contamination and/or injury?

Inadequate cleaning, disinfection, and/or sterilization during the reprocessing of SUDs introduces the hazard of persistence of a bioburden resulting in a risk of infection during subsequent use of the reprocessed SUD for patients and users, as a SUD is not designed to be reprocessed. This hazard which also occurs with devices designed for reprocessing and re-use, is characterized by the presence of contaminants of biological origin on the used SUD including proteins and micro-organisms such as bacteria and viruses. In addition, residues of chemicals used for cleaning, disinfection or sterilization pose a hazard for toxic reactions. Furthermore, alterations in the performance of the device due to reprocessing may pose a hazard such as device failure during subsequent medical procedures. Of special concern is the potential contamination with transmissible agents such as prions for which elimination and inactivation is not possible, or the procedure is not compatible with the materials generally used for an SUD.

2. If yes in ToR 1, please characterize the risk for human health.

In the absence of quantitative data related to the eventual residual biological and chemical contamination after reprocessing, it is not possible to quantify the risk associated with the use of reprocessed SUDs.

Some experimental laboratory simulation studies have demonstrated the risk of both microbiological and chemical residues occurring after reprocessing. The number of documented incidents is very small although it may be speculated that the reporting of incidents is incomplete. In the existing inventory in the US, no evidence of an increased risk was noted for patients from reprocessed devices. This apparent lack of an increased risk may be associated in part with the limitations the US imposes on the reuse of reprocessed medical devices.

3. If yes in ToR 1, under which conditions or uses does the reprocessing of single-use medical devices pose a risk? Please consider in particular, the following:

- Intended use of the device;
- Reprocessing method used: cleaning, sterilization and/or disinfection (depending generally on the material of the device) and lack of instruction on the reprocessing method to be used; and
- Other characteristics such as functionality, handling, raw material or design of the device.

The risk is highest when the reprocessed SUD is used in a critical procedure, i.e. when used for an invasive medical procedure. In contrast, the risk is much lower for non-critical medical procedures in which reprocessed SUDs are used.

The design and choice of material of the SUDs is very important for the outcome of cleaning, disinfection, and/or sterilization and the risk of persistence of a bioburden.

The choice of the method of cleaning, disinfection, and/or sterilization must depend on the chemical composition and nature of the SUD. Inappropriate methods may lead to the introduction of chemical contaminants with adverse biological effects.

Possible changes in the physico-chemical characteristics (e.g. stiffness, brittleness, and surface characteristics) of the material of a reprocessed SUD may pose a risk in terms of performance of the device. Material deterioration resulting in device failure may occur with repeated reprocessing cycles.

Additional critical issues in using reprocessed SUDs may be the identification and traceability of the reprocessed medical device, and for more sophisticated and complex medical devices, the continued availability of documentation needed for proper use of the medical device.

**Recommendation**

Not all SUDs are suited for reprocessing in view of the characteristics or the complexity of certain SUDs. The possibility for reprocessing is dependent on the material used and the geometry of the medical device. In order to identify and reduce potential hazards associated with reprocessing of a specific single-use medical device, the whole reprocessing cycle starting with the collection of these SUDs after (first) use until the final sterilization and delivery step, including its functional performance, needs to be evaluated and validated.

## 6. MINORITY OPINION

None

## 7. LIST OF ABBREVIATIONS

| | |
|---|---|
| **(v)CJD** | (variant) Creutzfeldt-Jakob disease |
| **DNA** | Deoxyribonucleic acid |
| **ECDC** | European Centre for Disease prevention and Control |
| **ECHA** | European Chemicals Agency |
| **EFSA** | European Food Safety Authority |
| **EMA** | European Medicines Agency |
| **EO** | Ethylene oxide |
| **EU** | European Union |
| **FDA** | (US) Food and Drug Administration |
| **GAO** | Government Accounting Office |
| **HBeAg** | Hepatitis B "e" antigen |
| **HBV** | Hepatitis B virus |
| **HCV** | Hepatitis C virus |
| **HCW(s)** | Health care worker(s) |
| **HIV** | Human immunodeficiency virus |
| **ISO** | International Organization for Standardization |
| **LMA** | Laryngeal mask device |
| **LTSF** | Low temperature steam formaldehyde |
| **MD** | Medical device |
| **MDD** | Medical Device Directive |
| **MHRA** | Medicines and Healthcare products Regulatory Agency |
| **PCR** | Polymerase chain reaction |
| **PrP** | Prion protein |
| **PrP(Sc)** | Pathogenic isoform of the prion protein |
| **PVC** | Polyvinyl chloride |
| **RNA** | Ribonucleic acid |
| **SCCS** | Scientific Committee on Consumer Safety |
| **SCENIR** | Scientific Committee on Emerging and Newly Identified Health Risks |
| **SCHER** | Scientific Committee on Health and Environmental Risks |
| **SUD(s)** | Single-use medical device(s) |
| **ToR** | Terms of reference |
| **TSE** | Transmissible spongiform encephalopathy |
| **US** | United States |
| **WHO** | World Health Organization |

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## 10.GLOSSARY

**Single-use medical device (SUD)**

According to Directive 93/42/EEC "single-use device" means a device intended to be used once only for a single patient.

However, in the context of this opinion, the expression "single-use" means that the medical device is intended to be used on an individual patient during a single procedure and then discarded.

**Cleaning** is a validated process used to remove contamination from an item to the extent necessary for further processing or for intended use (ISO/TS 11139:2006).

**Disinfection** is an operation with a temporary result to eliminate or kill the micro-organisms and/or to inactivate viruses on a contaminated surface or object. The result of this procedure is limited to the micro-organisms and/or viruses present at the time of the operation and the reduction of the number of viable microorganisms on the product is achieved to a level previously specified as appropriate for its intended further handling or use (EN ISO 15883-1:2009).

**Packaging** before being sterilized in a sterilizer, the medical devices must be protected from contamination by environmental micro-organisms and particles. Therefore, there is a need for protective packaging (EN ISO 11607-1:2006).

**Reprocessing** of a medical device, for the purpose of this opinion, includes steps needed such as routine maintenance, disassembly, cleaning, disinfection and/or sterilization to allow safe reuse.

**Reusable medical device** is a medical device that is designated or intended by the manufacturer for reprocessing or reuse (EN ISO/TS 11135-2:2008/AC:2009).

**Sterile** For a terminally-sterilized medical device to be designated "STERILE", the theoretical probability that a viable micro-organism is present on/in the device shall be equal to or less than $1\times10^{-6}$ (EN 556-1:2001/C1:2006).

**Sterilization** is a validated process used to render a product free from viable microorganisms. The nature of microbial inactivation is exponential and thus the survival of a microorganism on an individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero, (ISO/TS 11139:2006) and in Europe the accepted level of residual contamination is $1\times10^{-6}$ per item.