

## **EUCOMED INDUSTRY GUIDE**

### **GUIDE FOR MANUFACTURERS TO IMPLEMENT THE REQUIREMENT INTRODUCED BY DIRECTIVE 2007/47/EC FOR INFORMATION ON SINGLE USE MEDICAL DEVICES**

## **INTRODUCTION**

Council Directive 93/42/EEC as amended by Council Directive 2007/47/EC requires additional information for single use devices in Annex I, 13.6 (h).

### **Annex I 13.6 (h) (3)**

13.6 Where appropriate, the instruction for use must contain the following particulars:

(h) If the device bears an indication that the device is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be reused. If in accordance with Section 13.1 no instructions for use are needed, the information must be made available to the user upon request.

### **Objective of this requirement**

Medical devices designated for ‘single use’ may carry a significant risk to patient and users health if reused against the design intent. This requirement to provide information obliges the manufacturer to inform users on known risks if a single use device is reused.

## **DISCUSSION**

The 5<sup>th</sup> amendment of the Directive 93/42/EEC requires informing users of medical devices about known risks, which means available information, must be made known to the user. It is not necessary to conduct testing to identify additional risk factors. This is in line with the understanding of current expectations requiring evidence on any claims made on the performance or uses intended by the manufacturer. A proof of a negative statement is neither technically nor economically feasible, e.g. to document why a device is not suitable for an unspecified or contra indicated use such as the reuse of a single use device.

As specified in the amended Directive 93/42/EEC, Art. 1 (n), "single use devices" are intended to be used once on the same patient. To use the medical device once is understood as usage in one episode as defined in the instructions for use e.g. a single use scalpel can typically be used for multiple cuts during a given procedure on a single patient. The intended purpose of the medical device cannot be changed. When a medical device is intended by the manufacturer to be reused, such reuse activity must be consistent with the manufacturer's instructions and be validated for multiple usages, prior CE marking and before placing the product on the market.

### **When to provide risk statements:**

Essential requirement Annex I, 13.6 reads: “Where appropriate, the instruction for use must contain the following particulars:...”

The term appropriate implies that some of the requirements in section 13.6 may not be required for all medical devices.

Examples where it is not appropriate are cases where there is no known or foreseeable risk such as for single use products that cannot be or are highly unlikely to be reused because of their nature or use, including absorbable products such as hydro gels, adhesive dressings, sutures being consumed during the first usage or cartridges delivering staples or clips with build in self-destruction allowing for one use only.

Such products may not require a warning against reuse. Attachment A provides a decision tree to determine if a risk statement is required for a single use device or not.

### **Reference to standards:**

When assessing the risks inherent in reuse, particular attention should be given to EN ISO 14971 “Medical devices – Application of risk management to medical devices”. Risk assessments carried out according to this standard may have identified the specific risks relative to reuse of single use medical devices. The assessment to define the risk statement may be conducted separately according to this document or fully integrated in the manufacturers risk management processes. If conducted separately the checklist in Annex II may be used to identify risks. Manufactures may use a modular approach to identify product group specific risks according to the various risk factors.

### **Information on known risks in the instructions for use**

In order to ensure the appropriate emphasis of critical information to the user, instructions for use typically contain sections of indications, contraindications, steps for the safe and proper use, warnings, and precautions. Statements providing information on known characteristics and technical factors that could present a hazardous situation if the device is reused will typically be found in the warnings and precautions section of the instructions for use.

## **RISK FACTORS**

The reuse of single use medical devices might lead to increased risk for the patient and the user; the degree of risk is determined by device and use factors. The following list may be used to identify medical device characteristics that could be negatively impacted by reprocessing and reuse. Medical devices may be grouped according to similarities in design and clinical application for the identification of risk factors in reuse.

Input into the assessment may come from complaint data, published literature, health authorities warning letters, design records or reuse studies.

The risk factors associated with the reuse of a single use medical device can be assigned to the following categories:

1. Hygiene
2. Functionality
3. Materials affects (interactions and aging)
4. Packaging and Labelling

Risk statements in the instructions for use should be as specific as possible, in a language understandable by the intended user.

### **Risk Factor 1: Hygiene**

Single use medical devices typically have not been designed to be effectively

- cleaned
- decontaminated
- allow for removal of reprocessing chemicals
- dried or
- resterilized.

Narrow lumen, complex structures may make it difficult or impossible to effectively remove contamination, chemicals and cleaning solutions.

Reuse of single use devices therefore may create a risk of cross contamination of instruments or ineffective cleaning and sterilization and may lead to infection of patients and users.

Consideration must be given to pathogen - patient contacts that are not associated with the original manufacturing process, such as:

- Viral contamination e.g. HIV, Hepatitis
- Bacteria, including antibiotic-resistant strains such as MRSA
- Prions and other abnormal proteins
- Pyrogenes

<b>Risk Statement Hygiene to cover risks related to cleaning and sterilization identified.</b>
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Traces of chemicals used in cleaning or decontamination that remain on or in the device may lead to adverse reactions in the patient.

Additionally, even if an effective re-sterilization method can be identified, a further exposure to a previously used sterilizing agent or exposure to a different sterilizing agent than that used during initial manufacture might lead to a deterioration of the device. For example, where a single use device has initially been sterilized by radiation, a second radiation treatment or steam sterilization may not be compatible with the materials used and ethylene oxide may not be appropriate due to the complex structure of the device.

Even if properly sterilized, the risk of reactions to endotoxins exists. Endotoxins are Gram-negative bacterial cell breakdown products, which can be a significant problem if the device has a heavy bacterial load after use and lead to severe complications like fever, hemorrhage and multiple organ failure with shock symptoms. The sterilization process will not inactivate the toxins, even when decontamination and sterilization is effective in killing the bacteria.

Medical devices such as miniaturized single use devices often do not allow effective cleaning due to complex structure of the device not allowing for the required turbulent flow of water and chemicals to remove contamination and chemicals sufficiently. In such cases, the manufacturer should inform the user by stating that no method is available for sufficient cleaning of the device and inclusion of such a statement in IFU.

Risks to the user should be considered separately. Medical devices may have sharps or other characteristics, which may expose the user to hazardous situations when attempting to clean such devices. Special attention must be given to built-in protective features e.g. safety needles, shielded trocars where inactivation to allow cleaning may increase the risk of injury for the user / operator.

**Risk Statement to cover aspects of user safety including risks when reprocessing devices.**

Additional risk may be present for devices intended for sampling tissues or body fluids for diagnostic purposes, where contamination from previous usage may falsify the results due to residues from previous usage, e.g. tissues in biopsy needles.

**Risk Statement to cover aspects of potential false negative or positive results.**

In conjunction with the Risk Factor Hygiene the level or degree of invasiveness of a medical device may be important in determining risk to the patient.

- External or skin contact
- Mucosal membrane (intact) contact
- Tissue/bone/dentin (or breached skin, mucosal membrane) contact
- Central circulatory or nervous system contact
- Implantation

**Risk Factor 2: Functionality**

Usage beyond the design intent of the single use device may result in unpredictable loss of functionality:

- Reduced accuracy
- Reduced performance
- Altered mechanical properties
- Impaired compatibility with other devices

Some single use devices may experience stress during each cycle of use and reprocessing, leading to fatigue-induced failure and fracturing, e.g. single use drill burrs, saw blades, craniotomy blades.

Some devices will wear out when reused resulting in reduced performance, e.g. knives or scalpels may become dull even after the first use.

Removal of coatings or other substances that ensure smooth functioning of the device such as lubrications or hydrophilic coating for catheters may be removed during the refurbishment process, leading to loss in performance, less patient comfort and reduced safety. Negative outcomes may be patient discomfort, inflammations due to mechanical irritation or negatively impact the clinical outcome in cases where lubricants prevent corrosion, enable (micro)- motion essential for the correct performance of a devices. In some cases lubrication or coatings can not be renewed.

Safety functions may be negatively impacted e.g. shielded trocars or needle stick safety functions may be impaired putting patients and users at risk of injury.

<b>Risk Statement to cover respective areas of loss in functionality.</b>
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Additional risks due to impaired electrical safety or performance for active or energy transmitting devices

- Electrical shock
- Unintended temperature
- Reduced battery life

Electrical safety as defined in the respective harmonized standards e.g. the EN ISO 60601-1 series should be taken into account. Isolations may be impacted by multiple use and reprocessing leading to leakage current. Devices operating by producing heat such as electrosurgical devices may exceed intended temperatures or parts not intended to be active may create burns outside of the active area. For devices containing a battery the impact of reuse should be addressed.

<b>Risk Statement to cover risks related to electrical shock.</b>
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**Risk Factor 3: Material effects (interaction and aging)**

Many single use medical devices are made from materials specifically chosen and often suitable only for the intended single use. Those materials may degrade or change their characteristics when being repetitively used, or when coming into contact with chemicals or being exposed to high temperatures during reprocessing.

Potential risks are:

- Corrosion
- Aging induced stresses, creep and fatigue
- Non compatibility with chemicals changing the biocompatibility
- Absorption of chemicals and release during usage
- Temperature induced material changes
- Sterilization induced material changes
- Absorption of body liquids with impact on functionality of the device

Material Alteration: cleaning, disinfection, sterilization and repeated usage of the device may lead to changes in the material characteristics and to unpredictable break down of the device such as stress corrosion or cracking for metals or polymer crazing of plastics.

Chemicals used during decontamination and cleaning may be absorbed by the device or remain in lumen or complex structures of the device and be released during usage causing sensitization or burns.

Interactions with chemicals or an inappropriate sterilization method may lead to compromised biocompatibility of the materials (e.g. Gamma sterilization for PVC). The respective harmonized biocompatibility standards may be used to identify risks.

The impact of repeated sterilization e.g. multiple gamma sterilization or sequences of sterilization with varying sterilization methods e.g. ETO after gamma sterilization may lead to device fatigue, material alteration or be incompatible with the materials used.

**Risk Statement to cover material specific effects identified.**

#### **Risk Factor 4: Packaging and labelling**

Packaging and labeling are an integral part of the single use medical device and often go beyond a sole function to ensure sterility. Packaging prevents contamination and protects the device against damage.

Labeling and instructions for use provide important information to the user regarding the proper intended use as well as information on the specific device such as the shelf life, which may be reduced due to reprocessing, but should not be exceeded and manufacturing details for the given batch.

Not maintaining information on the packaging poses the following risks

- Usage beyond the shelf life, impacting functionality and material properties
- Loss of traceability (important in case of FSCA's)
- Usage error due to loss of the instructions for use

Changing the packaging configuration to a standard off the shelf packaging or other configuration not covered by the original packaging validation may lead to

- Damage of the product during shipment and storage
- Loss of sterility
- Risk of injury (e.g. missing protective caps)
- Risk of contamination (where packaging prevent contamination during handling / usage)

**Risk Statement to cover potential physical damage and information gaps.**

## **Annex I Decision tree**

The following decision tree should be used to determine if a risk statement is needed for a medical device.

1. Is the device for single use?

Answer is Yes: proceed to 2

Answer is No: STOP

2. Do known or foreseeable risks when reusing exist and is it technically possible to reuse the device?

Some devices cannot be reused as they are 'consumed', or cannot be reused by their design.

Examples:

A single dose eye drop cannot be 'reused' as the eye drop cannot be retrieved from the eye once inserted.

Absorbable sutures

Answer is YES: proceed to 3

Answer is No: Stop

3. Do known or foreseeable risks when reusing exist and is the potential misuse considered to be Reuse?

Reuse versus other types of misuse:

Reuse in this context is understood as: Usage of a device previously used on a different patient and requiring reprocessing which may include cleaning, re-sterilisation and re-packaging to ensure readiness for usage on another patient for the same purpose. Reuse should not be confused with other types of misuse, which is defined as incorrect or improper use (Ref. EN ISO 14971: 2007) including the usage for a different or not intended purpose. Under certain circumstances single elements of reuse may be defined as a different type of misuse and do not meet the reuse definition. The reuse definition therefore implies previous usage on a patient.

Example:

The packaging of a sterile single use device is opened, but the device is not used on a patient. The device is re-sterilised and used later on a patient. This type of misuse is already addressed in appropriate warning statements.

Half the content of a prefilled syringe (in case it is a medical device) is used on a patient. The needle is replaced and the remainder of the content is used on a different patient. This is misuse, as the part of the device that is used on the first patient is 'consumed' and cannot be retrieved to be used on another patient. The remainder of the syringe is not re-sterilised before use on the second patient.

Answer is Yes: Proceed to 4

Answer is No: STOP

4. Known risks of reuse of the single use device or foreseeable risk?

Manufacturers should be aware when their single use devices are being reused based on post marked surveillance activities. For some devices it is highly unlikely that they would be reused, and manufacturers may not have evidence of any risks related to the reuse. Reuse is not a foreseeable risk for most implantable devices such as intraocular lenses, joint replacements or heart valves.

Reuse of single use devices must be considered in any case when devices are available on the market in single and multiple use versions, such as scalpels.

Special attention should be given to devices intended for lay users.

Answer is Yes or a reusable alternative exists: Complete reuse of single use device risk assessment, add to Technical Documentation and proceed to 4

Answer is No: Document conclusion in the Technical documentation and STOP

5. Does the device have instructions for use?

Develop warning statements based on the risk assessment checklist. The warning statements should be as specific as necessary. The wording should be appropriate for the type of user. A device for lay use may require different statements than a device for professional use.

Answer is Yes: Include appropriate statements in the instructions for use.

Answer is No: Keep appropriate statement available for distribution to customers

## Annex II: Sample Checklist

The risk management process outlined in EN ISO 14971 enables the identification and assessment of risks associated with medical devices. This checklist provides guidance on specific aspects that might be appropriate in management of risks associated with reuse of single use devices.

<b>Risk Factors</b>	
<b>1. Hygiene</b>	
Is there a potential that devices are contaminated by previous usage?	
Do the design characteristics include areas that may be difficult to clean such as narrow lumen, complex structures?	
Are there limits of multiple sterilization e.g. gamma sterilization and degradation of plastics? Is the device incompatible to certain sterilization methods e.g. steam sterilization, ETO, gamma?	
Is it essential for the device to be sterile for the intended use?	
Is there a potential that the device becomes contaminated with viruses or bacteria?	
Does a risk of infection exist for the user e.g. when cleaning sharps?	
Is the level or degree of invasiveness may constitute additional risks	
Is the device implanted?	
Does the device contact the central circulatory or central nervous system?	
Does the device contact normally sterile tissue or bone?	
If the device is used to provide samples for diagnostics and the possibility exists that previous samples remain in the device. What is the effect on false negative or positive results or the required accuracy of the device?	
<b>2. Functionality</b>	
Is there a possibility that performance criteria may be altered due to initial usage and refurbishment? Is there a possibility of reduced accuracy, change of mechanical properties, change in compatibility to other devices, removal of coating which in turn may impact the	

performance?	
For active devices: Is there a risk of electrical shock, unintended high temperature, reduced battery life due to repeated usage and refurbishment?	
<b>3. Materials interaction and aging</b>	
Could materials undergo accelerated aging due to usage and refurbishment e.g. stresses corrosion cracking?	
Is there a possibility that the materials used may absorb chemicals used during refurbishment, which may be released during the subsequent usage?	
Does the device include any materials essential for the intended performance of the device that may be removed during repeated usage or refurbishment?	
Does the device include any medicinal substances that may be altered or removed due to usage or refurbishment?	
Does the device come into contact with medicinal products during the intended usage that may not be fully removed, or react over time with the medical device?	
Does the device come into contact with medicinal products during the intended usage and is there a possibility that drugs may be absorbed by the device and released during subsequent usage?	
<b>4 Packaging and labeling</b>	
Is device specific packaging required to protect functionality / sterility of the device? Does the labeling include information required for tracking / tracing the product not repeated on the product itself e.g. lot number?	