International Association for Soaps, Detergents and Maintenance Products

INDUSTRIEVERBAND HYGIENE & OBERFLÄCHENSCHUTZ

A.I.S.E. / IHO GUIDELINES ON REGULATION (EU) 2017/745 ON MEDICAL DEVICES

March 2021

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Disclaimer

This edition of the guidelines is a based on the fully revised version of the December 2017 Guidelines published by IHO (Industrieverband Hygiene und Oberflächenschutz), translated into English and discussed by experts of A.I.S.E. These guidelines do not under any circumstances exempt the user from their obligation to comply with legal requirements. These guidelines have been drawn up with great care. However, neither the authors nor A.I.S.E. or the IHO accept liability for the accuracy of the details, suggestions or advice presented here, nor for any printing errors. Therefore, in no circumstances can claims be made against the authors or against A.I.S.E. or IHO. An exemption applies in the case of damages caused intentionally or as the result of gross negligence on the part of A.I.S.E. the IHO or auxiliary persons.

These guidelines relate to the text of the Medical Device Regulation (EU) No. 517/745 (MDR), which has been in force since 25 May 2017. The MDR refers repeatedly to guidelines and legislative acts which are not yet complete in order to solve questions of detail. The “Guideline” project group will collect new insights from the legislation once it is adopted and from current member state decisions. These will be continuously incorporated into the available guidelines.

These guidelines have been produced for the information of experts in our member companies. Further versions of these guidelines are in the planning stages and will be produced once outstanding issues have been clarified. Comments and suggestions are always welcome and should be directed to the A.I.S.E. offices. The project group have indicated certain outstanding issues which in their opinion should be integrated into future versions.

1. INTRODUCTION

Aims and Target Audience of the Guidelines

The following guidelines were produced by a project team within the IHO's Medical Devices Working Group, then translated into English and discussed/revised by the experts of the A.I.S.E. Medical Device Task Force. They serve as an industry-specific summary and as an interpretation aid for those new to the topic. They are relevant to companies producing cleaning and/or disinfectant products to be used on medical devices.

The European Regulation on Medical Devices (EU) 2017/745 contains amendments to Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repeals Council Directives 90/385/EEC and 93/42/EEC.

The guidance is specifically targeted to industrial and institutional cleaning and disinfectant products.

2. REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL ON MEDICAL DEVICES (MDR)

After over four years of negotiations, the new regulatory framework for medical devices in the EU was revealed in the MDR. The new European medical device legislation is based on the global concept of conformity assessment. Medical devices will continue not to be state-approved in the way that, for example, pharmaceutical products are. Rather, they will fall under the technical harmonisation directives on bringing technical industrial products onto the market. Conformity assessment procedures will be carried out depending on risk classification, with the involvement of notified bodies.

The goal of the regulation is to create a harmonised European medical device legislation which will ensure the availability of safe medical devices as well as fast market access combined with balanced monitoring before and after the product launch.

The Medical Device Regulation came into force on the 26 May 2017, and it will apply on 26 May 2021.

Sell-Off/Transition Period

The MDR replaces the Medical Devices Directive (93/42/EC) and the IVD Directive (90/385/EC) and compliance is obligatory for all medical device manufacturers from 26.05.2021. The transition period began on 25.05.2017 (for details see Article 120 of the MDR).

Since the conformity assessment procedures for Class I medical devices can be completed without the involvement of a notified body, manufacturers of these devices must comply with MDR rules from 26/05/2021. The Medical Devices Coordination Group (MDCG) has produced GUIDANCE NOTES FOR MANUFACTURERS 16 OF CLASS I MEDICAL DEVICES describing how manufacturers can carry out this process in 9 steps.

For manufacturers of medical devices in higher classes, it is possible to delay compliance with certain MDR requirements.

If certification was issued by a notified body in line with the previous directives before 25/05/2017, this remains valid until the expiry date specified on the certificate. Certificates issued by notified bodies after 25.05.2017 remain valid until the end of the period indicated on the certificate, which cannot exceed five years from its date of issue. At the latest, these will expire on 27.05.2024. Using a certificate compliant with the previous guidelines means that after the end of the transition period on 26/05/2021, modifications to this certificate will no longer be possible. From this date onwards, the notified body may not issue any new or edited certificates. If changes are required, manufacturers will have to immediately procure an MDR-compliant certificate.

In order to carry out MDR conformity assessment procedures, notified bodies must undergo renewed accreditation. Notified bodies must apply to be designated for specific product types. Applications had to be submitted in November 2017. Of the current 55 nominated bodies, just 26 have applied to be designated under the MDR (as of October 2018). Since then, the first nominated bodies have been re-accredited. However, the process has shown to be time-consuming and it remains to be seen whether all the nominated bodies will achieve accreditation in time for the end of the MDR transition period. A current overview can be found on the NANDO website.

For companies, the process of finding a new notified body and having them certify all of the company's medical devices is a laborious one. It is therefore advisable to contact the notified body in good time. The situation is exacerbated by the fact that all manufacturers of medical devices in the new risk category (that is, the medical devices to be processed) need a notified body in the first instance to implement their conformity assessment procedures. This issue may be temporarily ameliorated, as the Commission modified the Regulation on 25 November 2019 so that the transition period for these products is extended until the 26 May 2024.

The sell-off and transition periods depend on new accreditation and currently remain open. According to Article 120 of the MDR transitional provisions, devices with valid accreditation will remain valid until 2023 at the latest. This means that the certificate is valid for three years (2021-2024), with a four-year sell-off period.

3. IMPLEMENTATION GUIDES ON RELEVANT TOPICS

Article 1 - Subject Matter and Scope of the Regulation

Once the regulation comes into force, cleaning and disinfectant products which are intended to process medical devices will for the first time also be categorised as medical devices. Under the previous directive, these products were only included in the definition of accessories. The definition of medical devices in Article 2(1) ends as follows:

The following are also deemed to be medical devices:

- devices for the control or support of conception;
- products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.

A.I.S.E. thinks that the use of the phrase "specifically intended" should be clarified. It suggests that a distinction is made between: products with intended purpose of medical devices, which would be in scope of the regulation, versus products with a multiple purpose which may be used occasionally in a medical environment (e.g. general purpose cleaners or disinfectants that are not specific to medical device use) which are not to be considered as medical devices. The intended purpose of a product is defined in Regulation (EU) 2017/745 as:

'intended purpose' means the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation"

Based on this analysis, the below reasoning is provided for products considered borderline by A.I.S.E. members, so as to provide legal clarity to the sector on the scope of MDR. A column has also been added to show any overlap with the biocidal regulation.

Product Category Considered as an Example	In Scope of MDR (EU) 2017/745	In Scope of Biocide Regulation	Additional Comments
Surface disinfectants	Only those that are specifically intended for disinfecting medical devices	Yes	Surface disinfectants which may be used in a medical environment, a mix of general surfaces and medical device surfaces, will not be medical devices
Brushes and sponges for washing/cleaning nails, hands and/or arms in hospitals (prior to surgery)	No	No	Are not intended for a medical device and thus do not meet the definition of Medical Device in the Regulation (EU) 2017/745.

Laundry detergent	Only if there are statements explaining the product is specifically intended for medical devices	No (cleaning product, not biocidal product)	To carry out professional cleaning it is not possible to use one product but need several products. A laundry detergent cannot fall under MDR since you need various products to carry out the cleaning process.
Insect repellents	No	Yes	Not intended to be used principally for medical use. The primary effect of the products would be on insects and not the human body.

1. Classification Rules

In order to understand, then, how these products should be categorised, the classification rules laid out in Annex VIII should be used. However, none of these rules explicitly apply to cleaning products. As such, we can fall back on the so-called catch-all rule 1: All non-invasive devices belong to Class I, unless they are covered by one of the following rules.

This means that cleaning products are Class I medical devices, just as they were under the previous Medical Devices Directive.

Disinfectant medical products, on the other hand, come under classification rule 16. According to this rule, disinfectants are categorised as class IIa or class IIb depending on whether the medical device being disinfected is for invasive or non-invasive use. However, the term “disinfecting invasive devices as the end point of processing” has been added to the definition.

Under the MDR, disinfectants are only assigned to class IIb if they are intended specifically to be used for disinfecting invasive devices as the end point of processing.

All other disinfectants belong to class IIa. In some cases, this may lead to a change in classification.

TABLE 1: Summary of classifications for cleaning and disinfectant products

Product	Classification
Disinfectants for invasive medical devices	Rule 16 - class IIb
Disinfectants for non invasive medical devices	Rule 16 - class IIa
Cleaning products intended for medical devices (Intended specifically for cleaning, rinsing contact lenses)	Rule 16 - class IIb
Cleaning products intended for medical devices (not intended to clean devices other than contact lenses by means of physical action only)	No other rule present – class I
Cleaning products not intended for medical devices	Not medical devices

2. Accessories for Cleaning and Disinfectant Products - Article 2 (2) - Interpretation

'Accessory for a medical device' refers to an item which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s).

2.1 Scope

A.I.S.E. gives the following legal interpretation of the definition of an accessory for a medical device under EU Regulation 2017/745 on medical devices (MDR), in accordance with Article 2 Paragraph 2:

All products which are not themselves classified as medical devices, but which are intended specifically to be used with an actual medical device, should be considered accessories. These accessories must support the use of the actual medical device, that is to say allowing it to operate or ensuring its medical function. A simple positive claim or label has no relevance to the eventual classification of the product. Assessments of scope should be taken on a case-by-case basis, taking into consideration the definitions and intended purpose of a product.

2.2 Central Pumping Units and Decentralised Dosing Equipment

Central pumping units (previously known as dosing units) are not to be classified as accessories to medical devices because they do not possess a dosing function and the use of the actual medical device is not bound to the use of a pumping unit. Decentralised dosing equipment is not an accessory to a medical device unless its defined purpose is described as such, e.g. if the use of a certain piece of dosing equipment is compulsory with a specific medical device.

2.3 Interpretation Help

Generic implements such as pumps, measuring cups, spray nozzles with mixers, or dispensing bottles should not be defined as accessories: they are interchangeable, and not indispensable for the usage of the medical device.

Example for interpretation help - cloth:

The actual medical device is the disinfectant. A system which the manufacturer explicitly states must be used, consisting of the disinfectant and a specific cloth or cloth dispensing system, comes under the MDR because the manufacturer has identified relevant risks of using unspecified cloth materials during the process of development and risk management.

If the manufacturer of the actual medical device has not made any purpose-defining statement on the use of specific cloth materials or cloth products, any industry-standard cloth can be used. According to the MDR, these are not defined as accessories.

3. Responsibilities/Obligations of Distributors

The recitals of the regulation on medical devices demonstrate that legislators intend to place defined obligations on all economic operators involved in the industry. Distributors are also now included in that category.

The obligations of the different economic operators, including importers and distributors, are thus clearly stipulated which will contribute to understanding of and compliance with the regulatory requirements. The role of the distributor involves the acquisition, possession and supply of products.

In Article 2, Definitions, the MDR provides this definition of the term ‘distributor’:

‘distributor’ means any natural or legal person in the supply chain, other than the manufacturer or the importer, that makes a device available on the market, up until the point of putting into service.

Distributors are therefore economic actors under the new regulation on medical devices. The distribution of a medical device is the interaction until the device is put into service, and is comprised of the acquisition, possession and supply of medical devices. When the device passes into the domain of the end user, the distribution is complete.

Alongside these temporal components, the definition of distribution also includes a further component distinguishing distributors from manufacturers, though this separation is not specifically referenced in the definition.

Under MDR rules, the Medical Devices Directive rules on circumstances of ‘parallel distribution’ are no longer in force, although this term does not appear in the MDR. In Article 16, cases are presented in which obligations of manufacturers also apply to importers, distributors or other persons. One of these obligations relates to the modification of a device already placed on the market or put into service in such a way that compliance with the applicable requirements may be affected (Article 16 Paragraph 1). According to Paragraph 2, the provision of necessary information by the manufacturer regarding a product already on the market is not considered a change. This includes changes to the external packaging or to the packaging size, if the change of packaging is necessary for marketing of the device in a member state.

Re-labelling or repackaging of medical devices is therefore possible under certain conditions for distributors, and the distributor does not become, in medical device legislative terms, a manufacturer by doing so.

Now, for the first time, distributors' obligations have been described in the MDR. These can be found in Article 14.

- When making a device available on the market, distributors shall, in the context of their activities, act with due care in relation to the requirements applicable. This is a general, non-specific rule and aims to resemble the principle of 'Good Distribution Practise' (GDP) in pharmaceutical law.
- Before making a device available on the market, distributors shall verify that all the following requirements have been met:
  - the device has been CE marked and the EU declaration of conformity for the device has been drawn up;
  - the device is accompanied by the information to be supplied by the manufacturer in accordance with Article 10(11);
  - for imported devices, the importer has complied with the requirements set out in Article 13(3);
  - that, where applicable, a UDI has been assigned by the manufacturer.

In order to meet the requirements, the distributor may apply a sampling method that is representative of the devices supplied by that distributor. This means that each device does not have to be individually checked.

Questions remain, however, about how distributors should carry out these checks, and of what quality the checks can be. Is it only a matter of checking whether the CE label is present, or should the quality of the manufacturer's conformity assessment procedures be inspected? The distributor will not be in a position to investigate the latter, as they do not have access to manufacturers' records.

The manufacturer-supplied information which is to be checked consists of operating instructions and labelling. This information must be provided in the language of the relevant member state. If the device is only being passed on to another distributor, then the language is of little relevance to the intermediary. However, if the device has reached the end of its distribution chain, the language matters. The elements of the label must be indelible, easily legible and clearly comprehensible to the intended user. At this point, distributors will likely only be able to check whether the relevant information is present.

The obligatory inspection regarding the UDI focuses on whether the manufacturer has allocated a UDI to the device.

- Distributors ensure that storage and transport conditions correspond to manufacturers' requirements for as long as the device is under their responsibility. More detailed specifications are not provided in the MDR.
- If distributors have reason to believe that the device they are making available on the market does not comply with this regulation, they must immediately inform the manufacturer. Distributors work together with manufacturers and with competent authorities in order to ensure that, if required, the necessary corrective measures are taken.

- If distributors receive complaints or reports about a device from health professionals or users, they must immediately inform the manufacturer. They must keep a register of complaints about non-compliant devices.
- Distributors shall, upon request by a competent authority, provide it with all the information and documentation that is at their disposal and that is necessary to demonstrate the conformity of a device.

The distributor obligations mentioned here in relation to market surveillance and vigilance in the MDR are more concrete and far more comprehensive than those previously laid out in national legislation. For example, distributors are now obliged to provide manufacturers and regulatory authorities with information. Distributors must also keep a register of non-compliant devices, recalls and other corrective measures, and complaints, and they must make this available to manufacturers if requested.

Alongside these general distributor obligations, special obligations apply regarding the traceability of medical devices.

These can be found in Chapter III - Identification and Traceability of Devices, Registration of Devices and of Economic Operators, Summary of Safety and Clinical Performance, European Database on Medical Devices.

According to Article 25, distributors have obligations regarding the identification of operators within the distribution chain. They must at all times be able to inform competent authorities which economic operators they have supplied with a device, from which operators they have obtained a device, and which healthcare facilities they have directly supplied with a device.

Alongside the traceability requirements, these record-keeping obligations will lead to significant additional expenditure on documentation.

Article 16 is relevant for manufacturers working with business partners who independently produce translations of labels or usage directions in other member states, as a quality management system is required. This must include processes by which it can be ensured that the translation of such information is correct and up to date. It must be ensured that the device remains in its original condition and that the packaging of the re-packaged device does not contain any errors.

According to Article 30, member states may maintain or introduce national provisions on registration of distributors of devices which have been made available on their territory. The MDR only stipulates registration with the EUDAMED database for manufacturers, authorised representatives and importers, and not for distributors. Here, national laws must be observed.

To sum up, it is apparent that through the MDR, legislators' attention has been drawn to distributors, and that in future, distributors will have to fulfil explicitly defined obligations. These obligations relate to:

+ checking whether devices comply with requirements
+ compliance with manufacturers' requirements for storage and transport of devices
+ identification of distributors within the supply chain

In future, distributors will be subject to monitoring by the authorities, and they will work together with the authorities on market observation.

Manufacturers must exercise a certain diligence when selecting their business partners. Storage and transport conditions, as well as guaranteed traceability, are particularly important criteria which could lead to the end of a business partnership.

4. Clinical Evaluation

For the first time, the MDR defines “clinical evaluation” in more detail in Article 2, 44: "Clinical evaluation’ means a systematic and planned process to continuously generate, collect, analyse and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer".

Clinical evaluation is required in accordance with Article 61 of the MDR. Alongside the rules laid out in this article, further requirements for the planning, execution and documentation of the clinical evaluation can be found in Annex XIV, Part A of the MDR. This annex stipulates that a clinical evaluation plan must be created and updated, and it describes the minimum requirements for this plan. Available clinical data about the device must be investigated, assessed, and if necessary, expanded upon. If there are gaps in the clinical evidence, scientific literature can also be consulted. All relevant clinical data must be analysed in order to draw a conclusion regarding the safety and clinical performance of the device. The results of the clinical evaluation shall be recorded in an evaluation report.

Further details can be found through the chapters below and in MEDDEV 2.7/1 Rev. 4.

In June 2016, the European Commission published a revised version of the Guidance on Clinical Evaluation - MEDDEV 2.7/1 Rev. 4.

The 10 most important changes to this document and the implications thereof for manufacturers of cleaning and disinfectant products for reprocessing medical devices of risk class I, I*, IIa and IIb are:

4.1 Frequency of Updates to Clinical Evaluations

- For Class I devices, an update every 5 years is appropriate.
- Class IIa devices are primarily employed for occupational safety. Their use varies widely according to national and even regional regulations. For example, such types of disinfectants are not used at all in English-speaking countries - with no drawbacks for professionals working with medical devices. For these devices, an update every 3 years is appropriate.
- The most critical devices for patients are the high-level disinfectants in Class IIb. Here, it seems reasonable to update the clinical evaluation every 2 years, even though these are not “high risk” medical devices in the original sense of the regulation.

If updates are necessary based on the results of post market surveillance, recalls, or changes to the device, these should be carried out as and when the need arises.

4.2 Qualifications of Authors and Experts for the Clinical Evaluation

The qualifications for authors of a clinical evaluation have been newly established and explained. The author should have a higher education degree (university or technical college) plus 5 years of relevant professional experience (or alternatively, 10 years of relevant professional experience without a higher education degree). In addition to their scientific knowledge of chemistry, biology and toxicology, the author must also have a good understanding of medicine and technology, and they must understand the use of the medical device to be evaluated. We suggest that an expert

employee of the manufacturer has thorough knowledge of the device's use as well as being familiar with literature research.

In our case, no specifications regarding qualifications should or can be made in accordance with the MDR. In our sector, the responsibility for the job profile must stay with the manufacturer.

The medical device manufacturer must provide in the technical documentation a current CV and an equally current statement of interests for each author of a clinical evaluation, as well as, where necessary, for each person who releases a clinical evaluation.

4.3 Specific, Measurable Goals for Clinical Evaluation

The main goal is to ensure and prove that a product, when used as intended, will at all times perform as it should and will not, in the course of its use, cause harm to patients, users or to the medical device with which it is used.

This is based on state-of-the-art laboratory data (pre-clinical or non-clinical data) from internal or external studies regarding the:

- effectiveness
- stability
- biocompatibility
- material compatibility
- occupational safety
- safety of use

of the product. Unlike most other medical devices, cleaning and disinfectant products do not come into direct contact with patients, either internally or externally. Apart from Class IIb products, their use is moreover doubly secured by the further process of ensuring that the processed device is safe before its use with the next patient. Further explication of the goals of clinical evaluation is therefore not necessary.

4.4 Establishing Current Knowledge/the State of the Art in Science and Technology

The state of the art (medical background) regarding a device or a class of devices can be described in the clinical evaluation plan. Relatively few journals provide a source of literature related to our products and their use (e.g. Central Services, Journal of Hospital Infection), and their dissemination is often locally restricted, with only a few available through databases such as www.ncbi.nlm.nih.gov/pubmed.

The simplest way to gauge the state of the art in the field of cleaning and disinfectant products is by gathering information from the brochures, product leaflets, usage directions, and safety data sheets produced by competitors. Available national guidelines and guidance documents can also be used.

4.5 Scientific Validity of Data

Since our products are not used on patients, patient data and statistics are not available. Most of the data comes from tests carried out by certified laboratories in accordance with national or international standards. Individual companies have performed internal investigations which were carried out according to specific, self-developed methods. Currently, the clinical evaluation focuses primarily on checking the completeness of the pre-clinical or non-clinical data, as mentioned in Point 3.

4.6 Equivalence of Medical Devices

It has always been the case that the products and product types discussed here possess a fundamental clinical, technological and biological equivalence, and in many cases even a chemical equivalence (active substances). Likewise, biological equivalence is a given if looked at not in terms of the biocompatibility of the undiluted product, but rather that of the traces actually left on the disinfected medical device.

However, formula details are confidential and therefore competitors' product formulations are not accessible. As a rule, all relevant performance parameters of a new product are checked based on the formulation and compared with benchmarks (see also Point 7). For the efficacy of disinfectants, the norm-based standards for manufacturers are paramount. The standard EN 14885:2018 "Chemical disinfectants and antiseptics - Application of European standards for chemical disinfectants and antiseptics" is listed in the draft standardisation request, therefore can be used for efficacy study purposes. IHO also provides a list for efficacy measures of products (www.desinfektionsmittelliste.de).

4.7 Access to Data on Equivalent Medical Devices

For the cleaning and disinfectant product industry, databases do not serve as information sources, meaning that competitor data cannot usually be obtained. A company's own, existing products, with which a new product can be compared across all relevant parameters, are key. It's also customary for companies to carry out their own investigations into competitor products.

4.8 When is a Clinical Investigation Required?

Cleaning and disinfectant products are not used directly on patients.

4.9 Risk-Benefit Assessment

A short examination of the risk-benefit analysis should be recorded in the clinical evaluation. This should also include cross-references to documents on risk management under ISO 14971 and on usability under EN 62366.

4.10 Post Market Surveillance

If post market surveillance provides critical information about a company's own product or a competitor's product, quality management should decide on the necessary measures - including adjusting the clinical evaluation.

4.11 Contents of a Clinical Evaluation

There is currently still some flexibility to meet the requirements laid out in Annex XIV of the MDR for the creation of a clinical evaluation plan. It is possible to create a device-specific plan, but plans can also be non-specific and apply to a group of devices (e.g., if products are of the same risk category or have a similar intended use). Thus, the planning of the clinical evaluation and the systematic literature search for several similar products can be brought together in a single document, while separate clinical evaluation reports (CER) are produced for individual products. A conceivable approach would be to work with a document containing elements of planning or of the plan as well as of the evaluation. Article 61 (13) of the MDR offers the possibility of adopting implementing acts in order to ensure consistent application of Annex XIV of the MDR.

In Annex XIV Part A (bullet points 1-6), the following points are presented as the most important elements of a plan for clinical evaluation of cleaning and disinfectant products:

- identification of the general safety and performance requirements that require support from relevant clinical data
- specification of the intended purpose of the device
- clear specification of intended target groups with clear indications and contra-indications
- detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters
- specification of methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and side-effects
- an indicative list and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device

For products in A.I.S.E.'s portfolio, different considerations must be made compared to most Medical Devices to detail proof of effectiveness, e.g., the main proof of effectiveness for disinfectant products is through efficacy testing.

5. Post-market Surveillance/Vigilance

Post-market surveillance as defined in Article 2(60) of the MDR refers to all activities which manufacturers undertake in cooperation with other economic operators (manufacturers, authorised representatives, importers, distributors) where a potential need for immediate implementation of corrective or preventative measures can be identified. Regulations on post-market surveillance can be found in the following guidelines and legal texts, among others. In future, national laws will have to be observed, meaning that it will be necessary to wait for country-specific implementation.

- MEDDEV 2.12-1 Rev. 8 Guidelines on a Medical Devices Vigilance System
- MEDDEV 2.12-2 Rev. 2 Guidelines on Post Market Clinical Follow Up (PMCF)

Definition of 'incident' according to Article 2 (64-66) of the MDR:

'incident' means any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect;

'Serious incident' (corresponds to the previous MDD definition of 'incident') means any incident that directly or indirectly led, might have led or might lead to any of the following:

a) the death of a patient, user or other person,
b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,
c) a serious public health threat;

'Serious public health threat' means an event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time.

Reporting obligations:

All manufacturers of products placed on the European Union market are obliged to report serious incidents and field safety corrective actions under Article 87 of the MDR.

These reports must be submitted via an electronic system.

The reporting period depends on the severity of the incident and is defined as follows:

- 'Serious incident' - must be reported within 15 days at the latest after a causal relationship has been established between the incident and the device
- 'Serious public health threat' - must be reported immediately, or at the latest, two days after the manufacturer finds out about the threat

All time limits for report submission, depending on the severity of the incident, are laid out in Article 87 Paragraph 2-11 of the MDR.

Urgent action is required when it cannot be guaranteed that continued use of the medical device will not present serious risk to patients, users and third parties.

For example:

- Recall / stop-sale order / stop-use order
- Corrective measures taken by the manufacturer
- Suspected non-sterility
- Fatal incident (unless a causal relationship can be conclusively ruled out)
- A new, previously unheard-of incident with life-threatening consequences
- A serious risk to people in vulnerable groups
- A reasonable suspicion of systematic problems with a batch or a product
- A conspicuous increase in serious incidents

Market observation:

According to Article 83 of the MDR, manufacturers of medical devices must implement post-market surveillance (PMS) as part of their quality management system. This involves creating a plan[1] and writing a report[2] on surveillance, as well as regularly updating these (Article 83-36 of the MDR).

The clinical effectiveness of the device should be routinely checked, in order to record rare complications which can only be observed through widespread, long-term use of the registered device.

The aim is to verify the effectiveness and safety of the medical device over the course of its expected lifespan, confirm that identified risks are reasonable, and to discover previously unrecognised risks.

[1] Guidance on PMCF plan template: https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2020_7_guidance_pmcf_plan_template_en.pdf

[2] Guidance on PMCF evaluation report template: https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2020_8_guidance_pmcf_evaluation_report_en.pdf

Based on the German Medical Technology Association, BVMed, 11/03/2014, a business' post market surveillance (PMS) should consist of the following elements. There may be some variation by member state:

- Post Market Clinical Follow-up (PMCF) in compliance with MEDDEV 2.12/2, other studies
- Production monitoring
- Quality management
- Vigilance system/incident reporting (Entity responsible is Member State dependent)
- Monitoring of competitors
- Customer contact
- Service, maintenance, repairs, safety checks and metrological checks
- Literature surveillance
- Market analysis
- Batch testing/sample testing
- Evaluation and measures with regards to possible off-label use
- Ongoing review and updates to the clinical evaluation
    - Post-market surveillance plan
    - Report after a Class I device is put on the market (template planned for the end of 2019)
    - PSUR, Periodic Safety Update Report (template planned for the end of 2019)
    - Trend reporting

6. Division of Labour/Cooperation between Manufacturer and Marketer

Here, OEM (Original Equipment Manufacturer) is used to mean the "physical manufacturer", who produces a device under the name of the PLM (Private Label Manufacturer) which is completely identical to the device placed on the market by the OEM under their own name.

The terms PLM and OEM are found neither in the previous Medical Devices Directive (RL93/42) nor in the MDR. However, these terms are key to the industrial and institutional cleaning and disinfectant products thus A.I.S.E. deems it relevant to support members by clarifying obligations for these stakeholders. The terms are referenced from explanatory documents. As an example, the one relevant to the German Medical Device Act is "Answers and Resolutions by EK-Med" (3.9 B 16)[3] , and could be relevant for other member states. This document is no longer applicable under the MDR. However, its terminology will be used for the observations made in this chapter, as these terms have proven useful for precise description of the facts.

The definition of a manufacturer is more broadly defined in the Medical Devices Regulation than in Directive 93/42.

'Manufacturer' is used to describe any natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under their own name or trademark (Article 2 No. 30).

So here, the PLM and the actual manufacturer (OEM) have the same legal standing.

The biggest difference between the definition of the manufacturer in the MDR and that in Directive 93/42 relates to the detailed information on manufacturing devices under an own brand label.

[3] [3] EK-Med documents: mdc medical device certification GmbH - EK-Med documents (mdc-ce.de)

The PLM may wish to be seen only as a distributor, selling a device developed and produced by the OEM under their own name or brand. However, in Article 16, this is rejected. Here it is specified that any distributor who carries out the following actions, if they bring a device onto the market under their own name or their own brand, has all the responsibilities of a manufacturer (Article 16 No. 1a):

"A distributor, importer or other natural or legal person shall assume the obligations incumbent on manufacturers if it does any of the following:

makes available on the market a device under its name, registered trade name or registered trade mark, except in cases where a distributor or importer enters into an agreement with a manufacturer whereby the manufacturer is identified as such on the label and is responsible for meeting the requirements placed on manufacturers in this Regulation."

Article 10 of the MDR (General Obligations of Manufacturers) does not distinguish between the OEM and the PLM. Therefore, the PLM carries full responsibility for their PLM device, just as the OEM carries full responsibility for the OEM device which they place on the market themselves.

This relates in particular to the creation, use, maintenance, documentation and implementation of:

- a risk management system (Article 10 No. 2 and Annex I Section 3)
- clinical evaluation (Article 61 and Annex XIV)
- market surveillance (Article 83)
- technical documentation (Annex II)
- verification and validation of devices (Annex II Section 6)
- a risk management system (Article 8 No. 2 and Annex I Section 3)

Every manufacturer must implement a risk management system, whether they are an OEM or a PLM. Since risk management also includes the design and manufacture of the device, cooperation between economic actors is necessary, as only the OEM can assess the details of design and manufacture. In practise, this could mean that the PLM passes on their findings to the OEM, who then includes this information in their risk management files, which in turn must be available to both partners.

- Clinical evaluation requirements (Article 61f)

Like the OEM, the PLM must have a clinical evaluation of their current devices at their disposal. The PLM can only produce this evaluation if the OEM provides them with the necessary data or with their own clinical evaluation to use as a basis.

The clinical evaluation should not be confused with clinical trials.

Here, the (PLM) manufacturer has the option to forego clinical trials, if the device they are placing on the market can be proven to correspond to a device already on the market. The device already on the market could be, for example, the OEM device in question. The two manufacturers are required to enter into a suitable contract (Article 61 Paragraph 5). This option is only available, however, for clinical trials on implantable medical devices and Class III medical devices.

- Market surveillance (Article 83)

It is fundamentally necessary that PLM and OEM cooperate after the product is placed on the market, since market data collected to assess the device is relevant for both actors. Like the risk management system, the TD must draw on the experiences of all businesses involved with the device in question in order to aim for consistency.

- Technical documentation (Annex II of the MDR)

The technical documentation (TD) is required to include comprehensive information and specifications about the manufacturing processes and their validation, including use of adjuvants. It must also contain continuous monitoring and evaluation of the final product. Such extensive documentation can only be found in the OEM's own TD. The PLM is only able to fulfil these requirements if the OEM makes their TD available to the PLM or if the PLM has complete access to the OEM's TD. However, since the TD contains highly sensitive data such as quantitative formulation details or information on raw materials and suppliers thereof, making these documents wholly available to the PLM runs counter to the OEM's legitimate confidentiality interests. It cannot yet be conclusively determined whether, for example, the TD could be stored by a neutral service provider or in a cloud system in order to protect both parties' legitimate interests. As things currently stand, these cloud-based solutions are viewed critically since the PLM does not engage independently with the data. Storing data in such a way that only notified bodies can access it for inspection (e.g. during an audit) without allowing the PLM access will certainly not be a viable option.

In comparison, cooperation between PLM and OEM on technical documentation regarding post-market surveillance appears logical and relatively straightforward (e.g. evaluation of scientific and/or technical literature, databases/registers, comparison with similar devices on the market).

- Verification and validation of devices (Annex II Point 6)

The PLM manufacturer will have to fall back on OEM data, since the PLM is unlikely to collect their own data on, for example, biocompatibility, stability, or shelf life.

Whichever manufacturer is named on the label must fulfil the requirements applied to the manufacturer under the MDR. Here, no explicit distinction is made between PLM and OEM. Paths by which the PLM can consult OEM data can only be interpreted in very limited ways. However, the PLM will have no alternative: they must have comprehensive technical documentation at their disposal, which must in the end be provided by the OEM.

Cooperation in the form of an exchange of the data and documents required under the MDR is necessary in order for PLM and OEM, together, to effectively deal with the amount of documentation needed.

7. Reporting Obligations/Unique Device Identifier (UDI)

By using a unique product number system (Unique Device Identification - UDI) based on international guidelines, legislators aim to significantly improve the effective safety of medical devices after their release onto the market, and to enable traceability. This will also facilitate better incident reporting, targeted field safety corrective action, and better monitoring by competent authorities. It could help to reduce medical errors and to combat counterfeiting. Additionally, use of the UDI system is intended to improve procurement policies, waste disposal and stock management by healthcare institutions and other economic operators. Where possible, it will be compatible with other authentication systems already in place in these settings.

The UDI system will apply to all devices available on the market, except custom-made devices. The system will be based on internationally recognised principles, including definitions, that are compatible with those used by key trade partners.

Furthermore, transparency and adequate access to information prepared specifically for the intended user will be ensured. This is essential to the public interest in order to protect public health, to empower patients and healthcare professionals, and to enable them to make informed decisions.

UDI (Article 2) is a "unique device number" (Unique Device Identification - UDI), a series of numeric or alphanumeric characters that is created by means of a globally accepted device identification and coding standard. It allows the unambiguous identification of a specific medical device on the market.

Annex VI of the MDR contains detailed guidelines on the registration of devices and economic operators in accordance with Article 29. In future, every medical device must receive and be labelled with a unique product number. UDI allocation, including the addition of data to the UDI database which will contain comprehensive, product-specific information, will be performed by a notified body which has not yet been designated. Data retention requirements will apply to all economic operators, which will make risk reporting and risk responses more efficient.

The system consists of three parts:

- actual product data, consisting of static product identification data as well as variable data
- data carrier
- database with information on 24 core features

The UDI identifier consists of two types of UDI: The UDI-DI, or "Device Identification", and the UDI-PI, or "Product Identification". The UDI-DI is a code that is specific to a model of device and that is also used as the 'access key' to information stored in a UDI database. The UDI-PI is a code that identifies the unit of device production and also includes the lot number and manufacturing or expiry date.

These should be distinguished from the Basic UDI-DI. The Basic UDI Device Identifier (Basic UDI-DI) is the primary identifier of a device model. It is the main key for records in the UDI database and appears in the EU declaration of conformity under Article 19.

The European Commission has already created and published several documents on the Basic UDI-I, such as the paper "MDI-UDI and device data sets to provide in EUDAMED", which describes the attributes of master data according to their dataset (https://ec.europa.eu/docsroom/documents/35241) and the "EUDAMED UDI Device Data Dictionary" (https://ec.europa.eu/docsroom/documents/35243). The notified body for the UDI, GS 1 (Global Standards 1) has published documents such as a Basic UDI-DI generator.

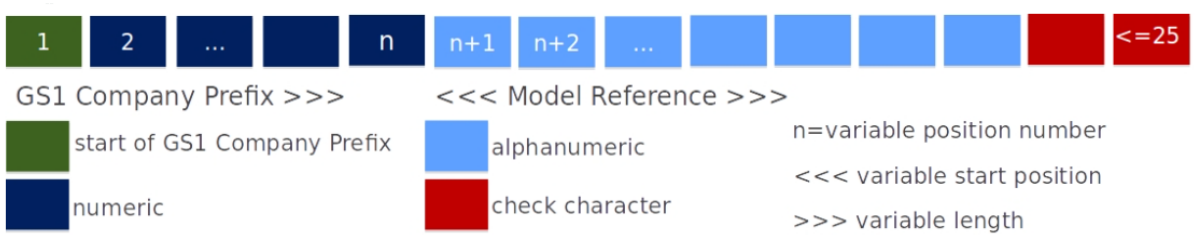
Since devices with shared characteristics (intended use, risk category, basic construction and manufacturing characteristics) can be grouped under a single Basic UDI-DI, manufacturers of cleaning and disinfectant products can, in the simplest case, use 3-5 different Basic UDI-DIs.

So a company of this type could group the following products together:

- Cleaning products for processing medical devices
- Rinsing products for processing medical devices

- Maintenance products for processing medical devices
- Disinfectant products for non-invasive medical devices
- Disinfectant products for invasive medical devices

The Basic UDI-DI can consist of a maximum of 25 characters, including two check characters. The Basic UDI-DI Generator from GS 1 (https://www.gs1.org/services/check-character-calculator) offers the following:



Not all 25 characters have to be used, so the basic UDI-DI for a manufacturer of cleaning and disinfectant products could look like this:

4 xxxxxx000018U

4 for the member country, Germany

Xxxxxx for the company's GTIN[4] identifier

00001 for cleaning products for processing medical devices

8U check characters set by the generator

In this example, rinsing products would be given the serial number 00002, maintenance products would be given 00003, etc.

There is no numerical relationship between the basic UDI-DI, the individual UDI-DIs on packaging units, and the UDI-DIs on multi-packs. The codes are completely different.

The UDI carrier is placed on the label of the device and on all higher levels of packaging. Shipping containers are not considered higher levels of packaging.

As well as being listed on the EU declaration of conformity, it is expected that the basic UDI-DI will also be found on accreditation certificates. As part of the technical documentation referred to in Annex II, the manufacturer must keep an up-to-date list of all UDIs that it has assigned. This means that the quality management system under DIN EN ISO 13485:2016 must create and direct the requisite processes for UDI generation and control (e.g. a system which assigns a unique identifier to each medical device). The quality assurance department of the manufacturing company is responsible for safeguarding.

[4] Global Trade Item Number

Implementation deadlines:

UDI usage is obligatory from the 26/05/2021. By this time, the Basic UDI-DI and the UDI-DI, must have been created and must have been incorporated into the technical documentation for the individual devices. Conformity declarations and certificates must display the UDI.

Different deadlines apply to the placement of the carrier on devices:

- for implantable devices and Class III devices, this is implemented when the regulation comes into force (26/05/2021).
- for Class IIa and Class IIb devices, this is implemented 2 years after the regulation comes into force (26/05/2023).
- for Class I devices, this is implemented 4 years after the regulation comes into force (26/05/2025).

See Unique Device Identification (UDI) System – FAQs:
https://ec.europa.eu/docsroom/documents/42641?locale=en

Until the commission has designated the bodies that will assign UDIs, GS1 (Global Standards 1), HIBCC (Health Industry Business Communication Council) and ICCBBA (International Council for Commonality in Blood Banking Automation) will be considered notified bodies.

In future, medical device manufacturers who supply to the USA as well as to countries in Europe will have to contribute to two databases. In the USA, the UDI has already been implemented. Although the European committees do refer to the guidance papers of the IMDRF (International Medical Device Regulators Forum), there are still differences between UDI in the USA and UDI in Europe. Eudamed contains far more information since it is intended to fulfil further regulatory functions beyond the specific goals of the UDI, such as comprehensive registration of market participants and the provision of rapid access for market surveillance authorities.

Conclusion:

- Companies should make intensive use of the transition period and should carefully implement UDI procedures.
- the identification number should be unique worldwide and it should be possible to integrate the global item number
- if changes are made to fundamental characteristics of a device, it must be possible to assign a new item number
- the devices must be correctly labelled, including placing the correct barcode on the correct packaging, using sufficient barcode quality, and ensuring readability against the background colour
- electronic data exchange in Eudamed (and GUDID), data availability, online access, manual or automatic data entry

Further information on the UDI can be found via the Medical Device Coordination Group, who have published - and in some cases already revised - several documents on the subject (https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/guidance_en). The European Commission has revised its question and answer document on UDI to reflect the postponement of the MDR start date.

8. Qualification Art 15 MDR: Person responsible for regulatory compliance

The MDR places significantly expanded substantive demands on the persons who previously occupied the role of safety officer for medical devices.

Previously, only national rules required a safety officer, but Article 15 of the MDR has made this a European requirement. By the 26 May 2021, every manufacturer must designate at least one person responsible for regulatory compliance within their organisation.

Their registration with EUDAMED remains unnecessary, however, since EUDAMED is not yet accessible.

The EU MDR requires the following qualifications:

- a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognised as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to medical devices
- four years of professional experience in regulatory affairs or in quality management systems related to medical devices
- Responsibilities of the person responsible for regulatory compliance: checking device conformity in accordance with the quality management system before a device is released
- Technical documentation and EU declaration of conformity creation and ongoing maintenance
- Article 10(10): compliance with post-market surveillance obligations
- Articles 87 to 91: fulfilling reporting obligations
- Investigational devices: issuing the statement referred to in Section 4.1 of Chapter II of Annex XV

If a number of persons are jointly responsible for regulatory compliance, their respective areas of responsibility shall be stipulated in writing.

Micro and small enterprises can contract an external person for this role, but must have that person permanently at their disposal.

There is a MDCG 2019-7 Guidance on Article 15 of the Medical Device Regulation (MDR) and in vitro Diagnostic Device Regulation (IVDR) regarding a "person responsible for regulatory compliance" (PRRC)

9. Dual Use Claim

Some association member products are so widely used as disinfectants that they come under both medical device legislation and biocidal products legislation (dual use claim).

According to the MDR (Recital 8), it will remain the responsibility of the Member States to decide on a case-by-case basis whether or not a product falls within the scope of this Regulation. In order to ensure consistent qualification decisions across all Member States, particularly in borderline cases, the Commission should be allowed to, on its own initiative or at the duly substantiated request of a Member State, decide on a case-by-case basis whether or not a specific product, category or group of products falls within the scope of this regulation, after consulting the Medical Device Coordination Group (MDCG).

According to Chapter 4, the Commission shall ensure that Member States share expertise in the fields of medical devices, in vitro diagnostic medical devices, medicinal products, human tissues and cells, cosmetics, biocides, food and, if necessary, other products, in order to determine the appropriate regulatory status of a product, or category or group of products.

The competent authorities on biocidal product legislation have indicated their approval of a dual use claim which would be valid throughout Europe[5] . Accordingly, such products would fall within the scope of both the Biocidal Products Regulation (BPR) and the Medical Devices Regulation (MDR). In order to be placed on the market, these products must go through both approval procedures.

More information on labelling of dual use products is in chapter 4 of this guidance.

10. Nomenclature

The information presented here is a summary drawn from a range of publicly available sources. It should be of use to all interested parties as a guide to the planned future nomenclature for medical devices.

According to Article 26 of the EU Medical Device Regulation (2017/745), a nomenclature for medical devices must be introduced which will be available free of charge to all economic operators and which will support the functioning of the European database, Eudamed:

“To facilitate the functioning of the European database on medical devices (‘Eudamed’) as referred to in Article 33, the Commission shall ensure that an internationally recognised medical devices nomenclature is available free of charge to manufacturers and other natural or legal persons required by this Regulation to use that nomenclature. The Commission shall also endeavour to ensure that that nomenclature is available to other stakeholders free of charge, where reasonably practicable.” (MDR, Article 26)

In the EU Commission document “Medical Device Nomenclature” (04/03/2019), the decision that the Italian CND system would be adopted for use as nomenclature and would be mapped to the GMDN was published. This should mean that when operators register a medical device, they are able to find a CND equivalent to the GMDN code. In addition, a subgroup of the MDCG has been established to facilitate regulatory oversight of the EU nomenclature system. In conclusion, document MDCG 2018-2 was approved/adopted. This document describes the future nomenclature system and lays out the requirements.

According to document MDCG 2018-2, names and codes will be available to all operators and to the public via the Eudamed database. As the nomenclature will be internationally recognised, WHO (World Health Organisation) and IMDRF (International Medical Device Regulators Forum) principles will be taken into consideration during the creation of the nomenclature.

As a regulatory benefit of the nomenclature, effective market surveillance and medical device traceability will be required throughout the entire supply chain.

Clearly, economic operators can and should also raise questions and suggestions regarding the nomenclature, in order to ensure the necessary expertise in the complex and heterogeneous field of medical devices

[5] Document CA-Feb13-Doc.5.1.r/ CA-May13-Doc.5.1.k discussed and endorsed at the 50th/51st meeting of representatives of Members States Competent Authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market

An EU nomenclature team (potentially as an MDCG subgroup) will review and assess the nomenclature rules according to a defined process before these rules come into force. This MDCG subgroup will also perform an advisory function with regards to nomenclature, particularly as regards the suitability of suggested terms and descriptions.

In addition, it is stipulated that the terminology structure should not be unnecessarily detailed or granular, and should not make use of terms that are only used by a few users/economic operators.

The nomenclature should facilitate links with codes used for notified bodies (competence or designation scope), for the scope of QMS/SA certificates, and for economic operators' product portfolios. Furthermore, the nomenclature should have hierarchies by which terms and codes can be meaningfully grouped into categories and subcategories.

The nomenclature provider must have procedures in place which allow EUDAMED entries to be kept continually up-to-date, and must be a legal person of either one of the EEA countries, Switzerland, or Turkey.

Processes must be in place for periodic review of the terminology structure and content in order to incorporate new knowledge and technological developments. It is essential that names and descriptions are made available in all the official languages of the EU.

For information on the current state of the CND system as regards medical device nomenclature in Italy, a presentation made by the Ministero della Salute and the 2018 CND database were drawn upon.

The presentation emphasises that the CND code is useful for market overview as well as market surveillance (by means of comparison between the medical device database and the vigilance database). Successful updating and maintenance of the CND codes will clearly involve the participation of all stakeholders.

In addition, the structure of the CND database is explained. In total, three hierarchical levels are planned: The first level relates to the category of the medical device, the second level represents which group the device belongs to, and the third level describes the type of the medical device.

A CND code is an alphanumeric code with up to 13 characters. The first character is a letter and stands for the category. The 2nd and 3rd characters are figures and stand for the group. The final 10 figures are intended to show the type of the medical device.

In the extract from the 2018 CND database provided as an example in the appendices, it can be seen that Category D stands for “DISINFECTANTS, ANTISEPTICS AND PROTEOLYTICS FOR MEDICAL DEVICES”. Groups 01 to 07 relate to different active chemical substances. Group 08 is for proteolytic substances and Group 99 stands for other disinfectant products and medical devices. In the disinfectants category, there are apparently no codes with more than 9 characters. Therefore, according to the information presented here, another four figures could conceivably be used for more detailed classification of disinfectant products.

It seems worthwhile to work towards further classification based on usage, with reference to an up-to-date risk assessment and a logical division of products within an active substance group.

11. Website Requirements

MDR Annex I, Paragraph 23.1 requires that: *“Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate. Such*

information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following: […]"

This means that if the manufacturer has a website, they are required to provide the information supplied alongside the device to identify the device and its manufacturer, as well as relevant safety and performance information, on that website.

The manufacturer can decide for themselves how best to make this available. For example, the manufacturer could supply the "label" (see MDR Article 2(13)) and, if they are available, the "instructions for use" (see MDR Article 2(14)) on their website.

If the "instructions for use" are made available online, reference should be made to Regulation (EU) No 207/2012[6] on electronic instructions for use of medical devices. This regulation sets out the conditions under which the instructions for use of medical devices can be made available in digital, rather than paper, form (in accordance with the MDD, among others). In addition, the Regulation details requirements which apply specifically to electronic usage directions that are supplied in addition to comprehensive instructions for use in paper form.

According to Regulation (EU) No 207/2012, instructions for use in paper form can only be replaced by electronic instructions for use for certain medical devices. This is not possible for cleaning and disinfectant products. Here, the requirements laid out in Regulation (EU) No 207/2012 Article 9 apply. This means that electronic instructions for use which are provided in addition to comprehensive usage directions in paper form must correspond to the content of the paper instructions. The website must also fulfil the following conditions:

- the website must be protected, by means of hardware or software, against unauthorised access
- the website must comply with the requirements of Directive 95/46/EC [7]
- all previous versions of the instructions for use published in electronic form must be made available on the website, as well as the respective dates of publication.

12. Assessment of Residues

The Regulation (EU) 2017/745 (Medical Device Regulation, "MDR") establishes the regulatory framework for medical devices. One of the aims of the MDR is to guarantee increased safety and health protection. As such, medical device manufacturers are obliged to ensure the safety of their devices and to minimise risk wherever possible. This also applies to biological risks, which are defined as follows in the Requirements Regarding Performance Design and Manufacture (Annex I, Chapter II, Paragraph 10.2):

"Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure."

[6] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:072:0028:0031:DE:PDF

[7] https://eur-lex.europa.eu/legal-content/DE/ALL/?uri=celex%3A31995L0046

The medical device manufacturer must record their fulfilment of these conditions in the Technical Documentation produced for the medical device (Annex II, Paragraph 6):

“The documentation shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of this Regulation and in particular the applicable general safety and performance requirements.”

This is further specified as follows (Chapter II, Paragraph 6.1 b):

"Detailed information regarding test design, complete test or study protocols, methods of data analysis, [...], test conclusions regarding in particular: the biocompatibility of the device including the identification of all materials in direct or indirect contact with the patient or user; physical, chemical and microbiological characterisation [...]. Where no new testing has been undertaken, the documentation shall incorporate a rationale for that decision. An example of such a rationale would be that biocompatibility testing on identical materials was conducted when those materials were incorporated in a previous version of the device that has been legally placed on the market or put into service [...]”.

This system is supported in regulatory terms by the normative requirements laid out in ISO 15883-1:2009 regarding process chemical residue in the mechanical reprocessing of medical devices. This standard requires manufacturers of process chemicals for use in washer disinfectors to indicate an acceptably determined, maximum permissible residual concentration of these chemicals in the medical device, i.e. a limit value (Point 4.4.1). The standard allows the manufacturer to select the criteria used to determine this limit value, the range in which the limit value is situated, and the methods of analysis. A corresponding requirement also applies to manual reprocessing.

When dealing with endpoints which are necessary for the assessment of biological safety, most medical device manufacturers orient themselves according to ISO 10993-1. This standard was harmonised under the Medical Device Directive (MDD) and will remain valid under the MDR (as will the whole family of standards). This standard describes the general principles governing the biological evaluation of medical devices within a risk management process, as well as the evaluation of the biological safety of the medical device itself.

The systematic approach to the biological evaluation of medical devices as part of a risk management process, as described in the standard, begins with the question, “Does either direct or indirect contact with patients fall under the ‘intended use’ of the device?” If the answer is no, then this standard does not apply. ‘Direct contact’ is defined here as a term used for medical devices or device components which come into physical contact with body tissue. ‘Indirect contact’ is defined as a term used for medical devices or device components through which a fluid or gas passes prior to the fluid or gas coming into physical contact with body tissue (in this case the device or device component itself does not come into physical contact with body tissue).

The standard calls for procedures for the reprocessing of medical devices, which involve a final rinse as part of both manual and mechanical reprocessing in order to ensure that process chemicals are sufficiently rinsed away. Where cleaning and disinfectant products are used in this intended way, the products and their components can no longer come into direct or indirect contact with body tissues. This means that the initial question of ISO 10993-1 can be answered with ‘no’, concluding the biological evaluation process as defined in the standard.

Of course, the medical device manufacturer is nevertheless free to use the systematic approach detailed in ISO 10993-1. However, they are equally free to take a different approach, e.g. calculating a possible endpoint for rinsing based on assessment of toxicological information regarding the ingredients contained in the medical device. This procedure also ensures that residues from process chemicals which remain on the reprocessed medical device are harmless, and thus fulfils the fundamental requirements of the MDR on this issue.

Biological evaluation of rinsing agents and maintenance products used in reprocessing should be viewed as an exception to this approach. Rinsing agents can be added to rinse water used in mechanical reprocessing in order to facilitate better and faster drying. Since no further rinsing follows, it must be assumed that components of the rinsing agent could remain on the medical device. When the device is in use, these could then come into contact with patients' body tissue within the bounds of "intended use". For these products, a biological evaluation should be carried out as detailed in ISO 10993-1 and recorded in the technical documentation.

As a final important point for companies. It is key for a manufacturer to be aware that in each country there are specific rules for residues, include those form MD. Companies must check national legislation on residues before placing a product on the market.

4. LABELLING OF DISINFECTANTS & DETERGENTS FALLING UNDER THE MEDICAL DEVICE REGULATION (EU) 2017/745

Cleaning and disinfecting products used in the hospitals for cleaning and disinfection of medical inventory or medical instruments, e.g. endoscopes in a surgery room, are classified as Medical Devices in conformity with the Medical Devices Regulation (MDR). Products used in hospitals for disinfection of general surfaces, e.g. walls in a surgery room, are classified as Biocidal Products and require an authorisation according the Biocidal Products Regulation (EU) 528/2012 (BPR). Cleaning products instead are in scope of the Detergent Regulation (EU) 648/2004. In addition, disinfectants and detergents must be labelled according to the Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation).

Under the MDR, products specifically intended for the cleaning, disinfection or sterilisation of devices are deemed to be medical devices and so should comply to the requirements of the Medical Device Regulation (EU) 2017/745.

This chapter seeks to provide guidance as to the applicable regulations for labelling of disinfectants and detergents falling under the Medical Device Regulation.

1. Products specifically intended for disinfection of Medical Devices

Disinfection is the targeted use of a disinfectant to help prevent the spread of infection in situations where there is high risk of transmission of harmful microbes (e.g. when someone is infected or is vulnerable to infection). These products prevent the spread of infection by deactivating or killing harmful organism and are already in scope of the Biocidal Products Regulation (BPR).

Especially for disinfectants there are various cases of products with **the exact same formulation** and **the exact same action**, which differ only between the regulatory process for placing them on the market. The result however will be that they will be evaluated in parallel, using different legislative paths, by relevant Notified Bodies/Competent Authorities (medical/biocidal).

Building on the above example, it is possible for cleaning staff at the hospital to have two spraying bottles with the exact same formulation in it, with the same classification and risk management measures but with different label elements (e.g. registration numbers and CE-mark) and different applications areas.

An example of a situation where both types of products are used is a patient's room:

Product used to disinfect the patient room (e.g. bed rails) (MDR applies)

Product used to disinfect the general surfaces (BPR applies)

Depending on what is being cleaned/disinfected, the product/disinfectant would fall either under the Detergent Regulation/BPR or MDR.

In order to avoid unnecessary confusion and possibility of wrong products being used for wrong applications, some of the Member States currently accept **dual use products** where MDR/BPR requirements are captured on the same label. This practice has been accepted by some Notified Bodies and European Competent Authorities. It allows for one product meeting authorisation criteria of both legislations to have the dual use related claims and other obligatory labelling elements properly reflected on the label.

2. A.I.S.E. proposal for labelling of disinfectants in scope of MDR

Where a given product is used for both medical and disinfection applications, A.I.S.E. proposes that combining the "horizontal" legal requirements of the BPR/ MDR on the label is accepted, wherever possible. Where needed, the specific requirements could be clearly separated or optically grouped on the label.

Given the relevancy of the single market for economic operators, a uniform acceptance of such labelling approach is crucial. Moreover, harmonisation of the label elements/requirements across the EU will also help to minimise the number of products being misused.

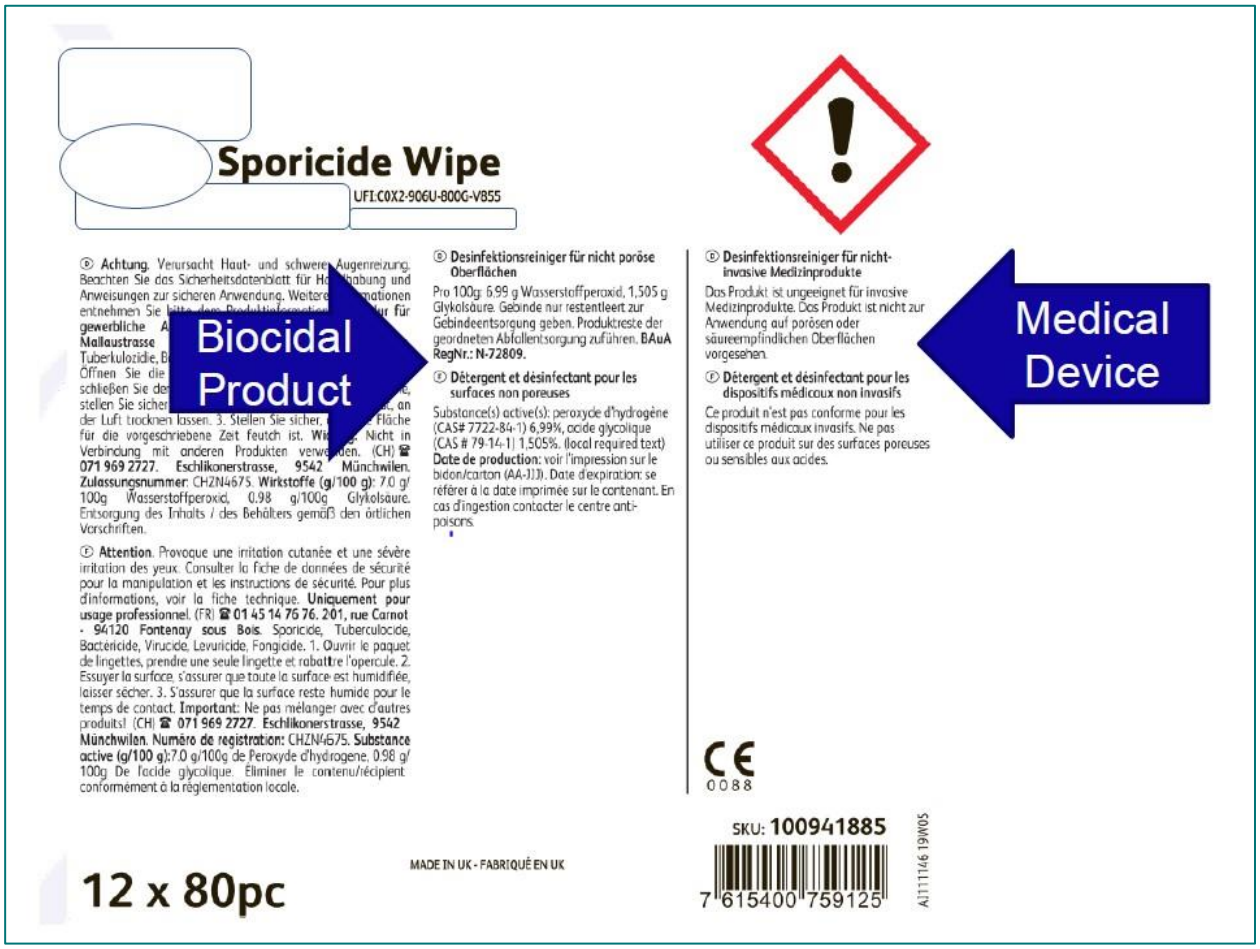
Summary of Key Regulations for labelling of disinfectants in scope of MDR

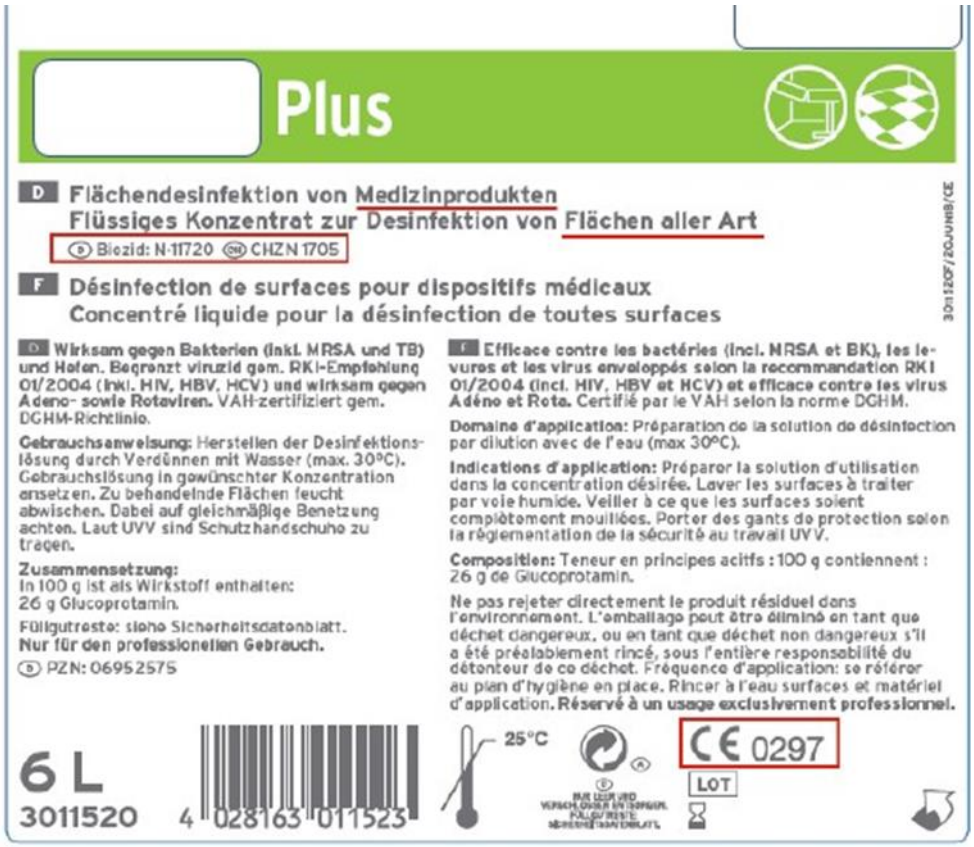
Regulation	CLP (EU) 1272/2008	BPR (EU) 2012/528	MDR (EU) 2017/745
Explanation of legislation	This legislation establishes i) the criteria for classification of substances and mixtures ii) rules on labelling and packaging for hazardous substances and mixtures in the EU/EEA.	Established the general framework for the making available on the market and use of biocidal products, including preservatives used for detergents formulation.	Lays down rules concerning the placing on the market, making available on the market or putting into service of medical devices for human use and accessories for such devices in the Union.
Obligation for labelling	CLP requires that the following elements are provided on the physical on pack label • the name, address and telephone number of the supplier(s) • the nominal quantity • hazard – pictogram(s), signal word and hazard statement(s) • precaution – precautionary statement(s) • disclosure of present ingredients according to CLP requirements (i.e. product identifier) • other mandatory label elements (Unique Formula Identifier (UFI), EUH-statements, etc) • Labelling information must be provided in the official language(s) of the member state where the product is placed on the market (unless otherwise provided). Refer to the CLP Regulation art. 17 for a more detailed understanding of the requirements	BPR requires the following to be reported on the label of biocidal products: • ingredient disclosure (every active substance and its concentration and any nanomaterials) • The authorization number should be reported with authorisation number and details of authorisation holder for the biocidal product • the uses for which the biocidal product is authorized and the directions for use, contact time, frequency of application and dose rate, expressed in metric units, in a manner which is meaningful and comprehensible to the user, for each use provided for under the terms of the authorization should be added • indications of likely adverse effects, warnings for vulnerable groups, and directions for first aid • use restrictions (if any), directions of use and of safe disposal of the product and its packaging (including, any prohibition on the reuse of packaging)	MDR requires the following to be reported on the label of a Medical Device: • the name or trade name of the device; • details necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device; • the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; • if the manufacturer has its registered place of business outside the Union, the name of the authorised representative and address of the registered place of business of the authorised representative; • information labelled in accordance with Section 10.4.5 (CMRs CAT 1A, CAT 1B, Eds under REACH) • the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate

		• formulation batch number and expiry date (under normal conditions of storage) • information on any specific danger to the environment • Where applicable, the categories of users to which the biocidal product is restricted to be added • labelling requirements related to micro-organisms (if applicable) • Labelling information must be provided in the official language(s) of the member state where the product is placed on the market (unless otherwise provided). Refer to BPR Regulation (EC) 528/2012 art 69 for a more detailed understanding of the requirements.[8] Note: Not all the disinfectant product are already under the BPR regime and are still under the remit the of the national BPD implementation act. As a consequence, depending on country specific legislation, other information on biocidal products may need to be provided instead of and/or on top of the information listed above.	• Instruction for use • Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer • Manufacturing date and/or expiry date or/and LOT • In case of invasive device, the list of ingredients shall be listed • CE marking of conformity in accordance with Article 20. • the UDI carrier • where there is no indication of the date until when it may be used safely, the date of manufacture • indication of any special storage and/or handling condition that applies; • warnings and precautions • full list of labelling requirements is included in Annex I, chapter III of MDR

IMAGE: Examples of labels for "dual use products"

[8] For products not yet covered by the BPR authorisation requirement local implementation of Biocidal Product Directive 98/8/WE apply, as a transitional phase. Thus including local requirements for labelling of biocidal products.


Sporicide Wipe
UFI:C0X2-906U-800G-V855
Biocidal Product
Medical Device
Desinfektionsreiniger für nicht poröse Oberflächen
Pro 100g: 6,99 g Wasserstoffperoxid, 1,505 g Glykolsäure. Gebinde nur restentleert zur Gebindeentsorgung geben. Produktreste der geordneten Abfallentsorgung zuführen. BAuA RegNr.: N-72809.
Détergent et désinfectant pour les surfaces non poreuses
Substance(s) active(s): peroxyde d'hydrogène (CAS# 7722-84-1) 6,99%, acide glycolique (CAS # 79-14-1) 1,505%. (local required text)
Date de production: voir l'impression sur le bidon/carton (AA-JJJ). Date d'expiration: se référer à la date imprimée sur le contenant. En cas d'ingestion contacter le centre anti-poisons.
Desinfektionsreiniger für nicht-invasive Medizinprodukte
Das Produkt ist ungeeignet für invasive Medizinprodukte. Das Produkt ist nicht zur Anwendung auf porösen oder säureempfindlichen Oberflächen vorgesehen.
Détergent et désinfectant pour les dispositifs médicaux non invasifs
Ce produit n'est pas conforme pour les dispositifs médicaux invasifs. Ne pas utiliser ce produit sur des surfaces poreuses ou sensibles aux acides.
CE 0088
SKU: 100941885
7 615400 759125
AJ111146 19W05
12 x 80pc
MADE IN UK - FABRIQUÉ EN UK


Plus
D Flächendesinfektion von Medizinprodukten
Flüssiges Konzentrat zur Desinfektion von Flächen aller Art
Biozid: N-11720 CHZN 1705
F Désinfection de surfaces pour dispositifs médicaux
Concentré liquide pour la désinfection de toutes surfaces
D Wirksam gegen Bakterien (inkl. MRSA und TB) und Hefen. Begrenzt viruzid gem. RKI-Empfehlung 01/2004 (inkl. HIV, HBV, HCV) und wirksam gegen Adeno- sowie Rotaviren. VAH-zertifiziert gem. DGHM-Richtlinie.
Gebrauchsanweisung: Herstellen der Desinfektionslösung durch Verdünnen mit Wasser (max. 30°C). Gebrauchslösung in gewünschter Konzentration ansetzen. Zu behandelnde Flächen feucht abwischen. Dabei auf gleichmäßige Benetzung achten. Laut UVV sind Schutzhandschuhe zu tragen.
Zusammensetzung:
In 100 g ist als Wirkstoff enthalten:
26 g Glucoprotamin.
Füllgutreste: siehe Sicherheitsdatenblatt.
Nur für den professionellen Gebrauch.
PZN: 06952575
F Efficace contre les bactéries (incl. MRSA et BK), les levures et les virus enveloppés selon la recommandation RKI 01/2004 (incl. HIV, HBV et HCV) et efficace contre les virus Adéno et Rota. Certifié par le VAH selon la norme DGHM.
Domaine d'application: Préparation de la solution de désinfection par dilution avec de l'eau (max 30°C).
Indications d'application: Préparer la solution d'utilisation dans la concentration désirée. Laver les surfaces à traiter par voie humide. Veiller à ce que les surfaces soient complètement mouillées. Porter des gants de protection selon la réglementation de la sécurité au travail UVV.
Composition: Teneur en principes actifs : 100 g contiennent : 26 g de Glucoprotamin.
Ne pas rejeter directement le produit résiduel dans l'environnement. L'emballage peut être éliminé en tant que déchet dangereux, ou en tant que déchet non dangereux s'il a été préalablement rincé, sous l'entière responsabilité du détenteur de ce déchet. Fréquence d'application: se référer au plan d'hygiène en place. Rincer à l'eau surfaces et matériel d'application. Réservé à un usage exclusivement professionnel.
6 L
3011520
4 028163 011523
25°C
CE 0297
LOT

3. Products specifically intended for cleaning of Medical Devices:

Cleaning is the mechanical or chemical removal of dirt and soil from the human body, an object or an area. Normally, cleaning with soap or detergent is followed by rinsing with water is adequate to remove visible dirt and allergens. Cleaning products are in scope of the Detergent Regulation (EU) 648/2004.

A.I.S.E. proposal for labelling of cleaning products in scope of MDR:

Where a given product is used for both medical and cleaning applications, A.I.S.E. proposes that combining the "horizontal" legal requirements of the Detergent Regulation (EU) 648/2004 and MDR on the label is accepted, wherever possible. Where needed, the specific requirements could be clearly separated or optically grouped on the label.

Given the relevancy of the single market for economic operators, a uniform acceptance of such labelling approach is crucial. Moreover, harmonisation of the label elements/requirements across the EU will also help to minimise the number of products being misused.

Summary of Key Regulations for labelling of cleaning products in scope of MDR

Regulation	CLP (EU) 1272/2008	Det. Reg. (EU) 648/2004	MDR (EU) 2017/745
Explanation of legislation	This legislation establishes i) the criteria for classification of substances and mixtures ii) rules on labelling and packaging for hazardous substances and mixtures in the EU/EEA.	Established EU wide criteria for placing detergents on the market. Primarily targeted environmental concerns: it established criteria for surfactant biodegradability, for limits on phosphates and harmonised labelling criteria especially for consumer products.	Lays down rules concerning the placing on the market, making available on the market or putting into service of medical devices for human use and accessories for such devices in the Union.
Obligation for labelling	CLP requires that the following elements are provided on the physical on pack label • the name, address and telephone number of the supplier(s) • the nominal quantity • hazard – pictogram(s), signal word and hazard statement(s) • precaution – precautionary statement(s) • disclosure of present ingredients according to CLP requirements (i.e. product identifier) • other mandatory label elements	For professional/ Institutional products, information on ingredients is conveyed via the ingredient datasheet as defined in Annex VII C. Any professional/institutional products that can go through wholesales for professionals (e.g. Cash & Carry), should be considered as Institutional/Industrial and this should be reinforced by writing on the label "For professional use only". Refer to the Detergent Regulation Regulation art. 11 for a more detailed understanding of the requirements	MDR requires the following to be reported on the label of a Medical Device: • the name or trade name of the device; • details necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device; • the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; • if the manufacturer has its registered place of business outside the Union, the name of the authorised representative and address of the registered place of business of the authorised representative; • information labelled in accordance with Section 10.4.5

	(Unique Formula Identifier (UFI), EUH-statements, etc) • Labelling information must be provided in the official language(s) of the member state where the product is placed on the market (unless otherwise provided). Refer to the CLP Regulation art. 17 for a more detailed understanding of the requirements		(CMRs CAT 1A, CAT 1B, Eds under REACH) • the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate • Instruction for use • Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer • Manufacturing date and/or expiry date or/and LOT • In case of invasive device, the list of ingredients shall be listed • CE marking of conformity in accordance with Article 20. • the UDI carrier • where there is no indication of the date until when it may be used safely, the date of manufacture • indication of any special storage and/or handling condition that applies; • warnings and precautions • full list of labelling requirements is included in Annex I, chapter III of MDR

To the knowledge of A.I.S.E. there are no evident examples of cleaning products with dual use under the medical device regulation and the Detergent Regulation, however, this guidance is provided to take into account of future developments in technology.

4. Additional considerations

4.1 Multipage labelling

Due to the extensive amount of information that must be provided with a product, through according to different pieces of legislations and in various languages, the use of multipage labelling of products may be considered there are discussions on the need for multipage labelling for products. However, it is highlighted that each legislative text has different requirements when it comes to multipage labels. In the Medical Device Regulation there are no specific provisions for a multipage label, MDR only talks about the label and the Instructions for use.

5. A.I.S.E. POSITION

A.I.S.E. is the International Association for Soaps, Detergents and Maintenance Products. Based in Brussels, A.I.S.E. has been the voice of the industry to EU regulators for over 65 years. Membership consists of 29 national associations across Europe, 18 corporate members and 13 value chain partners. Through this extensive network, A.I.S.E. represents over 900 companies supplying household and professional cleaning products and services across Europe.

The industry is a substantial contributor to the European economy with an annual market value of €38 billion, directly employing 95 000 and 360 000 throughout the value chain. A.I.S.E. has a long history in leading voluntary industry initiatives that focus on sustainable design, manufacturing and consumption, product safety and safe use of products by consumers and professional customers.

When the European Medical Device Regulation (EU) 2017/745 (MDR) comes into force, with a 3-year transition period, it will be directly applicable in all member states. As such, it cannot be overridden in national law. Because of the changes to definitions in the new MDR, cleaning and disinfectant products specifically intended for use with medical devices are now themselves medical devices. Under the previous directive, these products were only included in the definition of accessories.

As such, A.I.S.E. member companies are impacted significantly more than before.

A.I.S.E. supports the introduction of the MDR because it clearly regulates the responsibilities and tasks of economic operators, which will lead to a safer and more harmonious European economic area.

For the sake of appropriate implementation of the MDR, we are working for as consistent an understanding of our industry as is possible. It is important to maintain an environment that encourages innovation, so that our industry can continue to create safe and lifesaving cleaning and disinfectant products that meet ongoing needs. For this to happen, solutions must be found and key questions of interpretation must be clarified. Since most of these questions must be clarified at the European level, A.I.S.E. will do our best to bring the viewpoints of the wider detergents and maintenance products industry to the attention of European authorities.

A.I.S.E. gives the following legal interpretation of the definition of an accessory to a medical device under EU Regulation 2017/745 on medical devices (MDR) in accordance with Article 2 Paragraph 2: All products which are not themselves classified as medical devices, but which are intended specifically to be used with an actual medical device, should be considered accessories. These accessories must support the use of the actual medical device, that is to say allowing it to operate or ensuring its medical function.

Further clarification of the update frequency for clinical evaluation is needed. For our devices, annual updates are not always necessary. A.I.S.E. suggest:

- Class I: 5 years
- Class IIa: 3 years (rationale: primarily employed for user safety; use subject to national or regional regulations)
- Class IIb: 2 years (rationale: high-level disinfectant products are the most critical for patients)

Updates which become necessary as a result of market surveillance are exceptions to the above.

The EU Commission indicated, it should be possible to make a dual use claim in accordance with the Biocidal Products Regulation (BPR) and Medical Device Regulation (MDR) before a device is placed on the market, and it should be possible to complete both approval procedures.

Under the MDR, specific requirements have been set for the qualifications of clinical evaluation authors. For our industry, it would suffice to recommend that an expert employee of the cleaning and disinfectant product manufacturer has specialist knowledge of the products' usage and should be familiar with relevant literature (see also MEDDEV 2.7.1 Rev 4 2016).

In order to ensure improved supervision and traceability of medical devices, legislators intend to introduce a harmonised code system which will enable traceability. The scope of this system extends to all medical devices brought onto the market. It will consist of a unique product number - UDI (Unique Device Identifier). The UDI should be placed on the label of the device and on all higher levels of packaging. Currently, establishment of these systems is a national responsibility. A.I.S.E. member companies see centralisation of this system in the form of a European database as desirable. Likewise, we propose that a certain compatibility between different codes should be facilitated.

APPENDIX 1: EXAMPLE OF A CLINICAL EVALUATION PLAN WITH LITERATURE SEARCH PROTOCOL

1. General

1.1 Scope, Legal Basis, Applicable Standards and Guidelines

1.1.1 Standards and regulations relevant to medical devices

1.1.2 Guidelines and recommendations for the processing of medical devices

1.1.3 relevant standards for assessment of performance and safety; biological evaluation

1.2 Manufacturer of the Device Group

Description of who the manufacturer of the device is and whether the manufacturer is also placing the device on the market

1.3 Changes Made Since the Previous Clinical Evaluation Plan

Overview of updates

2. Definition of Fundamental Safety and Performance Requirements, Classification of the Device Group

Definition of the fundamental safety and performance requirements, which should be supported by clinical and non-clinical data (in accordance with MDR 2017/245, Annex I, Chapter 1 and the Medical Device Directive 93/42/EWG, Annex I).

+ General Requirements.
+ Requirements regarding design and construction.

The main goal of the clinical evaluation is to prove that a product, when used as intended, will at all times perform as it should and will not, in the course of its use, cause harm to patients, users or to the medical device with which it is used. This is based on state-of-the-art laboratory data from both in-house and external investigations.

3. Classification of the Product Group “Cleaner”

Definition of and rationale for the classification.

4. Intended Purpose of the Medical Device; Description of the Device and Components, Intended Performance Characteristics

Here, the names and components of the individual devices or device systems in the group are listed, as well as details of their Product Life Cycle status (e.g. development status, length of time on the market) and whether the device has already been CE-marked. Additionally, the usage of the device is described, as well as its present and historical market position, on which markets the device is available, and how long it has been available on these markets for.

At this point, reference can be made to product contact with users or patients, as illustrated in the following table:

Contact type:	***related to product:*** ☐ *Cleaner* ☐ *Disinfectant* ☐ *Cleaner & Disinfectant* ☐ *Other:* ***related to human body:*** ☐ *directly* ☐ *obliquely* ☐ *non-directly*
Contact place:	***related to product:*** ☐ *Instruments* ☐ *Large Surfaces* ☐ *Surfaces of Medical Devices* ☐ *Other:* ***related to human body:*** ☐ *critical* ☐ *semi-critical* ☐ *non-critical*
Contact time:	☐ *< 60 min* ☐ *60 min – 30 days* ☐ *>30 days* ☐ *Other:*

5. Specification of Intended Target Groups - Indications and Contraindications

Generally not relevant to cleaning and disinfectant products; a description of the use of the medical device group is required.

5.1 Specification of Intended Target Groups

Description of the users and target groups.

6. Intended Clinical Benefits: State of the Art, Clinical Background; Functioning

Here, the current state of the art in the field of cleaning and disinfectant products for the reprocessing of medical devices should be summarised. In addition, applicable standards and guidelines should be cited (as well as information regarding the medical issues and their natural causes which can be treated or diagnosed with the device).

A summary is given of the medical environment in relation to the processing of surgical instruments, endoscopes, or other relevant medical devices, and benchmark solutions as well as previous treatments and alternatives are described. benchmark products currently available on the market are considered with regards to indications of their clinical safety.

This chapter should demonstrate how the cleaning and disinfectant products in question close a gap in the healthcare field, and how they demonstrate an improved balance of risks and benefits in comparison to earlier products.

7. Function of the Device Group

Here, the medical devices in question are comprehensively described, including a short physical and chemical description, technical specifications, mechanical characteristics, their sterility or radioactivity, and how the medical device achieves its intended effect. The operating principle is explained and materials with which the device comes into direct or indirect contact are considered. The extent to which the patient or user could come into contact with the device is also considered, as well as which body parts, tissues or blood components would be involved.

8 Evaluation of Performance

Safety - Methods to be Used for the Assessment of Qualitative and Quantitative Aspects of Performance and Safety

Here, the context and the investigative scope of the clinical evaluation should be described, including which devices/models/sizes are covered in the clinical evaluation report. Likewise, the

technology upon which the medical device is based, the conditions of use, and the intended purpose should be described. Here, all claims that are made about the clinical performance and clinical safety of the medical device are documented.

In the case of cleaners and disinfectant, performance and safety can be assessed on the basis of pre-clinical data from in-house and external laboratory experiments as well as analysis of relevant literature.

8.1 Investigation of Performance in Pre-Clinical Tests

Argumentation for consulting preclinical data instead of clinical studies.

8.1.1 Disinfection management

8.1.2 Cleaning Performance

8.1.3 Material Compatibility

8.1.4 Antimicrobial Activity Test

8.2 Investigation of Device Safety in Pre-Clinical Tests

8.2.1 Preservation Efficacy Testing

8.2.2 Stability Testing

8.2.3 Cytotoxicity, Toxicity (if necessary, biocompatibility tests as per ISO 10993-1 can be used)

8.3 Information from PMS, PMCF, Market Experience and Complaint Management

8.4 Risk Analysis and Risk Management System

Explanation of the implemented risk management system and references to the risk dossier of the device.

9. Parameters for Definition of Acceptability of the Benefit-Risk Ratio

9.1 Fulfilment of General Safety and Performance Requirements (GSPR)

Explanation of which GSPR are documented in the clinical evaluation of the individual device in question.

9.2 Fulfilment of Biocompatibility Requirements

9.3 Fulfilment of Performance Capacity

10. Literature Research Protocol for Systematic Analysis of Scientific Literature in Order to Determine Available Relevant (Clinical and Non-Clinical) Data

As described in 3.1.2, if necessary, provide as a separate document alongside the technical documentation.

10.1 Background

10.2 Goal

10.3 Authors and Sponsors

10.4 Changes

10.5 Inclusion Criteria

10.6 Questions

10.7 Methods

10.7.1 Search Strategy

10.7.2 Data Management

10.7.3 Selection Process

11. Planning of the Post Market Clinical Follow Up (PMCF)

If necessary, provide as a separate document (see Appendix 3)

11.1 General Methods and Procedures

12. Update Plan

13. References

APPENDIX 2: EXAMPLE OF A CLINICAL EVALUATION REPORT (CER)

1. Summary

2. (Objective/Scope): Description, Classification, Intended Purpose

2.1 Device Description - Refer to CEP

2.2 State of the Art, Medical Background: Refer to CEP

3. Changes Since the Previous Version

4. Device and Evaluation/Type of Evaluation

5. Equivalence to Other Devices, References to Earlier or Similar Generations of the Device (Equivalence Estimation)

(Demonstration of equivalence)

The majority of investigations into the device are carried out in-house, as there is little information available regarding comparable devices produced by competitors.

6. Safety

(Professional users, protective equipment). Refer to the safety data sheet. Can also be dealt with in the plan.

7. Risk Management Files

8. Evaluation of the Information from the Performance Evaluation/Device Testing

(Pre-clinical/non-clinical data); evaluation of the information in accordance with the clinical evaluation plan (see CEP point 6).

9. Conclusions

9.1 Compliance with performance and safety requirements

9.2 Benefit-risk Ratio of the Medical Device - State of Related Scientific and Technical Knowledge

9.3 Explanation of the Benefit-risk Ratio

9.4 Suitability of the Information Materials about the Medical Device

9.5 Suitability of the Medical Device for the User

9.6 Declaration of Consistency Between Collected Data, Information Material and Risk Analysis - Declaration of Completeness of the Evaluated Data

9.7 Periodic Review - PMCF - Date of the Next Clinical Evaluation

10. Dates and Signatures

11. Qualifications of the Authors and Person in the Company Responsible for the Clinical Evaluation

12. Accompanying Documents (Appendix/Annex)

13. Document History

14. References and Literature

APPENDIX 3: EXAMPLE OF A POST-MARKET CLINICAL FOLLOW-UP (PMCF) PLAN

1. Purpose

The purpose of this document is to outline Post-Market Clinical Follow-up (PMCF) Plan for <Product or Product Group> as an action to assess the safety and give an input for a Post-Market Surveillance Report (PMSR / PSUR) and thus connect these data to quality and performance of the device during its whole product life cycle.

This document is created in conformity with the current European statutory requirements, the Medical Device Regulation Article 61, Article 84, Annex III and XIV.

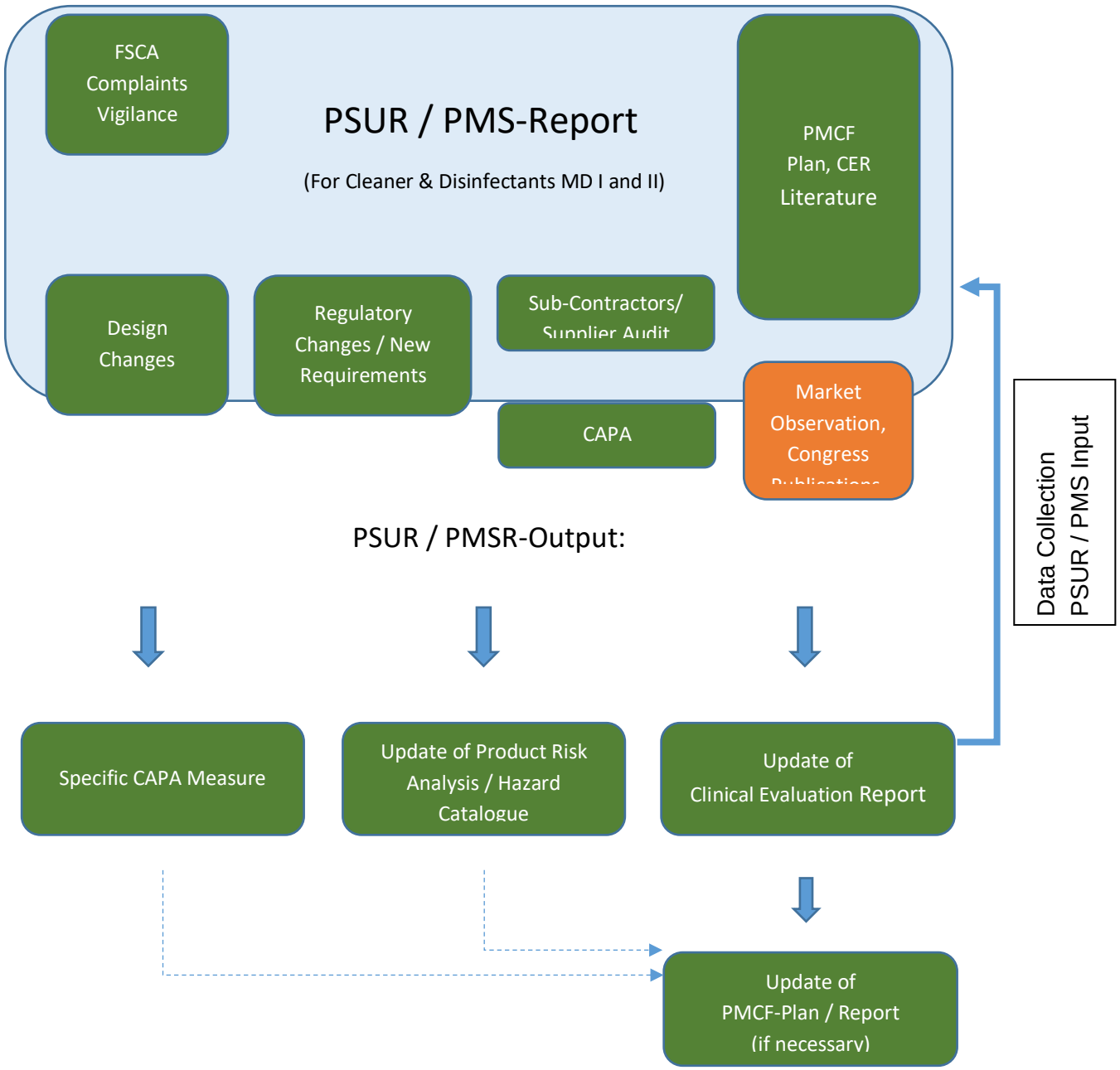
2. Product Group

PRODUCT GROUP NAME	CLASSIFICATION

SAP-BULK NUMBERS	PRODUCT NAMES

3. Interface to other data (PMS)

Within the scope of the CER the following PMCF activities will be conducted and planned to generate post-market data. These PMS and PMCF activities will serve as Inputs for PSUR (MD II) or PMS (MD I) Reports.



4. Evaluation Period

The proactive continuous monitoring of scientific literature, market surveys concerning the product will be performed annually during the whole product life cycle.

5. General PMCF-measures

5.1 Literature review

The results of the continuous literature monitoring will be analyzed and implemented in the PMS. In case of significant observation due to effectiveness, performance and safety of the similar products or its ingredients the CER must be adapted.

The main source of literature research for this type of products is www.pubmed.com.

The search results can be sent to Pubmed in the form of a report and can thus be inserted in the Annex of the CER or PMS.

If other databases are used where no summary search results reports are generated, a manual listing of the search results must be made including search words, date of execution and name of the database.

The sources listed below for literature research are scientifically recognised and can be used, for example:

- www.books.google.de
- www.dimdi.de
- www.pubmed.com
- www.medline.de
- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/
- TextSearch.cfm ("MAUDE" FDA searchable adverse effect database)
- http://www.hc-sc.gc.ca/dhp-mps/medeff/index-eng.php
- (Health Canada "MEDEFFECT" searchable adverse effect database)
- http://ec.europa.eu/idabc/en/document/2256/5637.html
- (European medical device database under construction)
- https://stneasy.fiz-karlsruhe.de/html/english/login1.html
- (Commercial literature database)
- http://www.toxnet.nlm.nih.gov/ (free of charge toxicology databases)
- http://ccinfoweb.ccohs.ca/rtecs/search.html ("RTECS" database)

5.2 Pro-active market observation & surveys

All Market observations, surveys and trainings will be performed within marketing department. The collected data or reports will be submitted annually to quality management for creation of the PMS-Report.

5.3 Post market Clinical Follow-Up Study

According to Article 61, point 10 due to application of this product types no clinical study is necessary.

Rationale:

The Risk assessment for each product was performed and documented. The demonstration of the safety and performance requirements was performed within Clinical Evaluation Report.

Product Name	Link to CER	Link to Risk Analysis

6. Specific PMCF-measures

Summarize newly attained Product Risks and observations from Clinical Evaluation Report

ID	CER-Chapter	Short description	Schedule

7. Conclusion

If no PMCF-Report necessary, the rationale must be given.

APPENDIX 4: CREATION OF A LITERATURE SEARCH PROTOCOL FOR CLEANING AND DISINFECTANT PRODUCTS FOR THE REPROCESSING OF MEDICAL DEVICES

The MEDDEV 2.7.1 already requires a systematic literature search based on a literature search plan which defines the search criteria before the research is carried out.. Changes to or deviations from the plan must be documented and justified. The literature search plan can be part of the clinical evaluation plan or a separate document.

The search protocol is intended to make the literature search replicable, which can also be helpful in updating the clinical evaluation plan. Systematic literature research should illustrate the current state of knowledge about the dangers and effectiveness of the device. Above all, this should look at whether patients are at risk of harm from insufficiently cleaned medical devices and the related inadequate disinfection, infectious protein material (prions) or immune reactions resulting from contamination.

In principle the MEDDEV and the MDR - against the backdrop of medical implants - apply the same standards to the evaluation of clinical studies as they do to the literature search procedure. These are described in e.g. the PRISMA statement (Moher, Liberati et al. 2009) or in the "Cochrane Handbook for Systematic Reviews of Interventions" (http://handbook-5-1.cochrane.org/) (Higgins and Green 2011). **Since there are currently no clinical studies in the field of cleaners and disinfectant products, a sensible middle course should be found to deal with this.**

Defining a Review Question

As specified in the Cochrane Handbook, the definition of a review question can be based on the acronym "PICO". This includes the study population (participants), the procedures/medical measures being considered (types of interventions) and comparisons between them (comparisons) as well as the target criteria/clinical results (outcome measures). However, the literature search does not have to address all 4 of the P-I-C-O components. As such, for the "Cleaner" example these are:

- Participants: no restrictions
- Interventions: cleaning of medical devices such as surgical instruments or endoscopes
- Comparison: not relevant, since medical devices are not used on patients unless the devices have been cleaned
- Outcomes: infections, immune reactions, prion infections (Creutzfeldt-Jacob disease)

Accordingly, the review question can be formulated as:

"Are there randomised controlled trials or other studies of clinical consequences such as infections, immune reactions or prion infections which have been caused by insufficiently cleaned medical instruments such as surgical instruments or endoscopes, but which have not been caused by mistakes in the sterilisation or disinfection process?"

Search Strategy

In the search protocol, the methodology used in the literature search as well as the selected sources of information should be defined and justified. So, for example, English-language literature from the MEDLINE database can be found using the “PubMed” search function. The search terms used should be recorded.

It is possible to link key words using the Boolean operators AND, OR and NOT. A search for the key words ‘reprocessing’ and ‘cleaning’ can be limited to only titles and abstracts by adding the field [Text Word], or can be expanded to include related terms by abbreviating to reprocess* and clean* (this will include e.g. reprocessing, reprocessed...)

Articles which were found outside of the systematic literature search or which researchers were already familiar with can also be integrated into the review.

Data Management

Researchers are also required to document their database search. This can be done by, for example, exporting the search results into an Excel spreadsheet.

Selection Process

The identified literature should be systematically reduced to a manageable (and readable) number of articles through a series of steps.

Once duplicate articles have been removed, articles can be excluded if, for example

- there is no abstract available
- the full text of the article is not available
- the article has not been peer-reviewed (Masters or PhD dissertations)
- the article is only a method description
- the article is written in a language other than English or German

Subsequently, the abstracts can be checked for relevance. Irrelevant articles and duplicates can be excluded. From this selection, articles which are not relevant or which are not the original article can be excluded. So, for example, articles which only describe a method can be viewed as irrelevant, as can publications of the drying of endoscopes.

Evaluation of the Identified Literature

The identified articles should be analysed on the basis of their scientific validity and relevance. In the field of cleaners, most articles are not clinical studies and the identified literature is quite heterogeneous (including reviews, primary research, guidelines etc), so quantitative meta-analysis can be ruled out. Because of the aforementioned lack of clinical literature, including randomised and non-randomised studies, laboratory studies and review articles can also be included in the systematic literature search.

A systematic evaluation of literature identified as relevant can be recorded in a separate document appended to the technical documentation. The selected full-text articles should therefore be checked for possible limitations during the selection process. They should also be evaluated on the basis of potential bias resulting from conflicts of interest or from the study design. The assessment of potential bias should be documented. In order to analyse and evaluate the

literature with regards to its relevance and import, the following aspects (for example) can be investigated:

- aim of the study
- description of the intervention
- study design
- study size (population): the study group being observed must be large enough to assess the statistical significance of the study results.
- groups being compared (comparisons)
- result

Every report should be individually assessed and inspected for limitations and weaknesses.

APPENDIX 5: EXAMPLE OF THE CURRENT STATE OF CND NOMENCLATURE

(Extract from the 2018 CND database)

- **D** *DISINFECTANTS, ANTISEPTICS AND PROTEOLYTICS FOR MEDICAL DEVICES*
- **D01** *DISINFECTANTS, MEDICAL DEVICES, ALDEHYDES*
- **D0101** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE (also associated)*
- **D010101** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE*
- **D01010101** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE, BASIC SOLUTION*
- **D01010102** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE, ACID SOLUTION*
- **D01010103** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE, NEUTRAL SOLUTION*
- **D010102** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE AND POLYPHENOLS*
- **D01010201** *DISINFECTANTS, MEDICAL DEVICES, GLUTARALDEHYDE AND POLYPHENOLS, SOLUTION*
- **D010103** *DISINFECTANTS, MEDICAL DEVICES, ORTHOPHTALALDEHYDE*
- **D010199** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED GLUTARALDEHYDE - OTHERS*
- **D0199** *DISINFECTANTS, MEDICAL DEVICES, ALDEHYDES - OTHERS*
- **D02** *DISINFECTANTS, MEDICAL DEVICES, BIGUANIDES*
- **D0201** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE (also associated)*
- **D020101** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE*
- **D02010101** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE, AQUEOUS SOLUTION*
- **D02010102** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE, HYDROALCOHOLIC SOLUTION*
- **D02010103** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE, GEL*
- **D02010199** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE - OTHERS*
- **D020102** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE AND DETERGENTS*
- **D020103** *DISINFECTANTS, MEDICAL DEVICES, CHLORHEXIDINE AND ANESTHETICS*
- **D020199** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED CHLORHEXIDINE - OTHERS*
- **D0299** DISINFECTANTS, MEDICAL DEVICES, BIGUANIDES - OTHERS
- **D03** CHLORUM DERIVATIVES
- **D0301** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITES (also associated)*
- **D030101** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITE*
- **D03010101** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITE, AQUEOUS SOLUTION*
- **D03010102** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITE, HYDROALCOHOLIC SOLUTION*
- **D03010199** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITE - OTHERS*
- **D030102** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITE AND DETERGENTS*
- **D030103** *DISINFECTANTS, MEDICAL DEVICES, HYPOCHLORITE AND DISINCRUSTANTS*
- **D030199** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED HYPOCHLORITES - OTHERS*
- **D0302** *DICHLORUM-ISOCYANURATES*
- **D0303** *DISINFECTANTS, MEDICAL DEVICES, SODIUM CHLORITES (also associated)*
- **D030301** *DISINFECTANTS, MEDICAL DEVICES, SODIUM CHLORITES AND LACTIC ACID*
- **D030302** *DISINFECTANTS, MEDICAL DEVICES, SODIUM CHLORITE*
- **D030399** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED SODIUM CHLORITES - OTHERS*
- **D0399** *CHLORUM DERIVATIVES - OTHERS*
- **D04** *IODINE DERIVATIVES*
- **D0401** *DISINFECTANTS, MEDICAL DEVICES, IODOPOVIDONE (also assoiated)*
- **D040101** *DISINFECTANTS, MEDICAL DEVICES, IODOPOVIDONE*
- **D04010101** *DISINFECTANTS, MEDICAL DEVICES, IODOPOVIDONE, AQUEOUS SOLUTION*
- **D04010102** *DISINFECTANTS, MEDICAL DEVICES, IODOPOVIDONE, HYDROALCOHOLIC SOLUTION*
- **D04010199** *DISINFECTANTS, MEDICAL DEVICES, IODOPOVIDONE - OTHERS*
- **D040102** *DISINFECTANTS, MEDICAL DEVICES, IODOPOVIDONE AND DETERGENTS*
- **D040199** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED IODOPOVIDONE - OTHERS*
- **D0499** *IODINE DERIVATIVES - OTHERS*
- **D05** *OXYGEN PRODUCERS*
- **D0501** *DISINFECTANTS, MEDICAL DEVICES, PERACETIC ACID (also associated)*
- **D050101** *DISINFECTANTS, MEDICAL DEVICES, PERACETIC ACID AND HYDROGEN PEROXIDE*

- **D050102** *DISINFECTANTS, MEDICAL DEVICES, PERACETIC ACID AND ADAMANTANIC DERIVATIVES*
- **D050103** *DISINFECTANTS, MEDICAL DEVICES, PERACETIC ACID*
- **D050199** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED PERACETIC ACID - OHERS*
- **D0599** *OXYGEN PRODUCERS - OTHERS*
- **D06** *DISINFECTANTS, MEDICAL DEVICES, PHENOLS*
- **D0601** *DISINFECTANTS, MEDICAL DEVICES, POLYPHENOLS (also associated)*
- **D060101** *DISINFECTANTS, MEDICAL DEVICES, POLYPHENOLS*
- **D06010101** DISINFECTANTS, MEDICAL DEVICES, POLYPHENOLS, AQUEOUS SOLUTION
- **D06010199** *DISINFECTANTS, MEDICAL DEVICES, POLYPHENOLS - OTHERS*
- **D060102** *DISINFECTANTS, MEDICAL DEVICES, POLYPHENOLS AND DETERGENTS*
- **D060199** *DISINFECTANTS, MEDICAL DEVICES, ASSOCIATED POLYPHENOLS - OTHERS*
- **D0699** *DISINFECTANTS, MEDICAL DEVICES, PHENOLS - OTHERS*
- **D07** *DISINFECTANTS, MEDICAL DEVICES, ALCOHOLS*
- **D0701** *DISINFECTANTS, MEDICAL DEVICES, ETHANOL*
- **D0702** *DISINFECTANTS, MEDICAL DEVICES, ISOPROPYL ALCOHOL*
- **D0799** *DISINFECTANTS, MEDICAL DEVICES, ALCOHOLS - OTHERS*
- **D08** *DISINFECTANTS, MEDICAL DEVICES, PROTEOLYTIC SUBSTANCES*
- **D0801** *DISINFECTANTS, MEDICAL DEVICES, PROTEOLYTIC ENZYMES*
- **D0899** *DISINFECTANTS, MEDICAL DEVICES, PROTEOLYTIC SUBSTANCES - OTHERS*
- **D99** *DISINFECTANTS AND ANTISEPTICS FOR MEDICAL DEVICES - OTHERS*

APPENDIX 6: GERMAN SPECIFIC REQUIREMENTS

This annex contains some considerations specific to the German case, but it is not an exhaustive list of national requirements.

On 25/08.2019 the Federal Ministry of Health published a draft law, the EU Medical Device Adaptation Act (Medizinprodukte-Anpassungsgesetz-EU – MPAnpG-EU), adapting medical device legislation to EU Regulations 2017/745 and 2017/746.

This is an omnibus bill of which Article 1 introduces the Medical Device Implementation Law (Medizinprodukte-Durchführungsgesetz – MDG) in accordance with EU requirements. Thus, the MDG replaces the Act on Medical Devices (Medizinproduktegesetz, MPG).

As well as explaining the rationale behind the Medical Device Implementation Law, the draft also contains the following key points which supplement EU Regulations 2017/745 and 2017/746:

a. Additional definitions (Chapter 1, § 3)
b. Additional regulations on reporting obligations, the placing on the market and bringing into service of devices, as well as the making available on the market of these devices (Chapter 2, §§ 4-11)
c. Additional provisions on notified bodies, testing laboratories and conformity assessment bodies for third countries (Chapter 3, §§12-13)
d. Additional provisions on clinical trials and performance studies (Chapter 4, §§ 17-37)
e. Additional regulations on vigilance and surveillance (Chapter 5, §§ 38-50)
f. Regulations on competent authorities (Chapter 6, § 52)
g. Regulations on the national information system on medical devices (Chapter 6 § 53)
h. Regulatory powers (Chapter 6, § 55)
i. Special provisions for the Federal Armed Forces (Chapter 7, §§ 57 and 58)
j. Provisions on penalties and fines (Chapter 8, §§ 59-62) and
k. transitional arrangements (Chapter 9, §§ 63-69).

In § 50, the draft of the MDG covers the 'medical device consultant' (Medizinprodukteberater), a role unique to the German national legislature. Consultants' qualifications and responsibilities will resemble those described in the current Act on Medical Devices. As an additional point, specifically related to distributors, there is a pending question on whether distributors should be seen as medical device consultants for their products. The practical result of this would be that they would then have to undergo regular training.

The Medical Device Implementation Law will replace the MPG on the 26 May 2021.

As a specificity for Germany, regarding dual use claim, an agreement was made with the German authorities that such a claim can be stated on a label. The Central Authority of the Länder for Health Protection, ZLG have published a paper on this subject.