Federal Ministry
of Health

“Regulatory Affairs in Medical Technology”

Medical Device Regulation: Implementation on European Level, First Results

Dr. Matthias Neumann
Federal Ministry of Health

Lübeck 2018 Summer Academy
on Medical Technology”
4th July 2018

Federal Ministry of Health

Revision of the European Medical Devices Regulation

- Introduction
- Main Challenges for Manufacturers
- Responsibilities and current structure for EU harmonised implementation
- Road map for implementation
- First results

Federal Ministry
of Health

Main Challenges

Article 10 of the MDR and IVDR is summarising the main new and changed requirements on manufacturers

Beside those requirements also Annex I (General safety and performance requirements) contains a number of new and changed requirements on devices which requires that every device currently on the market require (at least a formal) re-design

Federal Ministry of Health

Challenges (1)

Art. 10 **(2)** Risk-Management-System

Art. 10 **(3)** Clinical Evaluation and PMCF

Art. 10 **(4)** Technical Documentation

Art. 10 **(6)** Performing the right conformity assessment procedure

Art. 10 **(7)** Registration as manufacturer, registration of the devices and UDI-System

Art. 10 **(8)** keep available the technical documentation, declaration of conformity, certificates

Federal Ministry of Health

Challenges (2)

Art. 10 **(9)** Quality Management System (for the first time described in a legislation)

Art. 10 **(10)** Post-Market Surveillance (by the manufacturer)

Art. 10 **(11)** labelling -> language of IfU

Art. 10 **(12)** Obligation to perform corrective action when necessary

Art. 10 **(13)** Obligations in the vigilance system

Art. 10 **(14)** free sampling by CA

Art. 10 **(15)** “new” OEM – OLB business rules

Art. 10 **(16)** Liability for defective devices

Federal Ministry of Health

Article 10(2) Risk-Management-System

Annex I

- Basic principles of a Risk-Management-System are for the first time described in a legal text
- Analysis and assessment of risks (risk management plan, consider also foreseeable misuse etc.)
- Minimise the risks by applying the principle of integrated safety
  - “reduce risks as far as possible” means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.
- Continuous lifecycle process which must make use of the results of the new required post-market surveillance system
- A possible new challenges could be that manufacturers shall provide (if appropriate) training to users.

Federal Ministry of Health

Article 10(3) clinical evaluation

Clinical evaluation always necessary (efforts necessary to justify not performing a clinical evaluation might be higher then providing a simple clinical evaluation make use of clinical data in literature)

Now (and different from all other regulations in the world) a continuous process (as part of the QMS) which must be started (and documented etc.) very early in the device development process and continued during the whole lifetime of the device (also as PMCF)

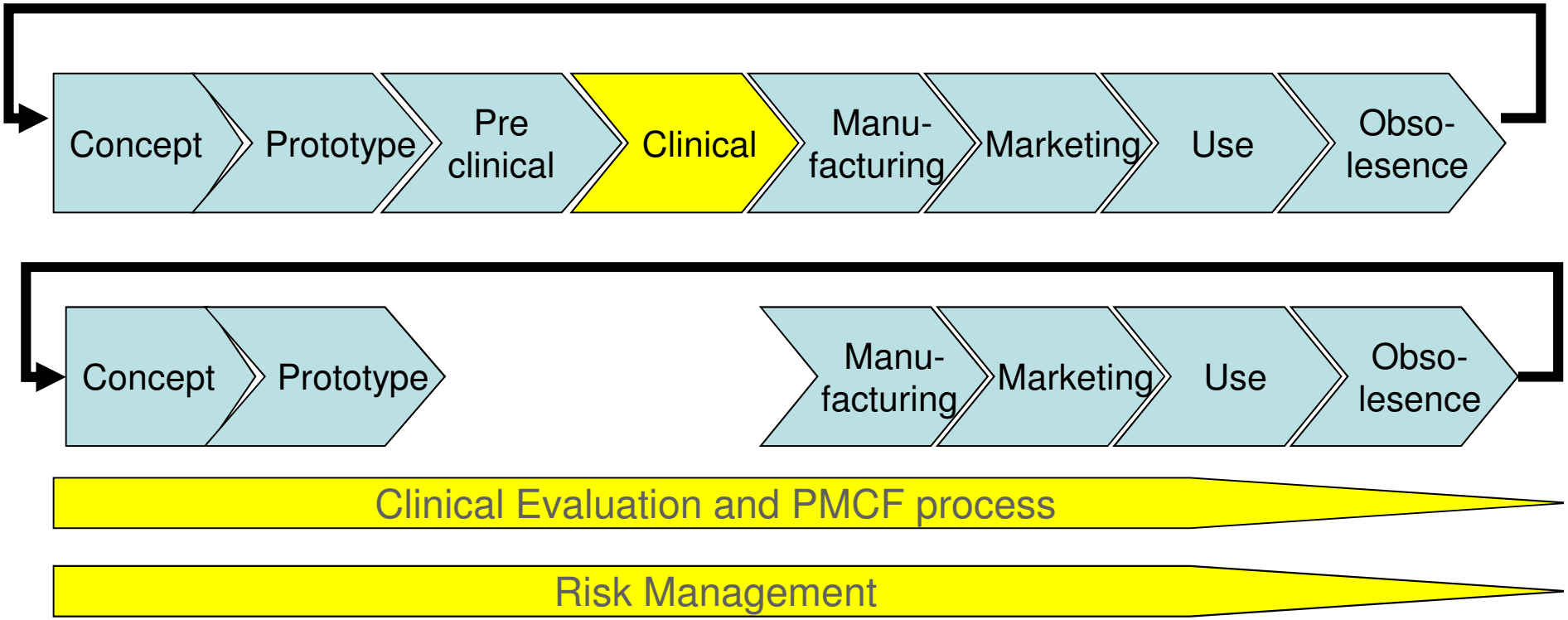
For class III and implantable devices de-facto always a clinical investigation is required. In addition the possibility to refer to clinical data of equivalent devices is now legally more limited

An additional serious new challenge might be the obligation to compare the benefit risk ratio of the device with the benefit risk ration of other medical procedures (alternative device or drug therapies etc.)

Federal Ministry
of Health

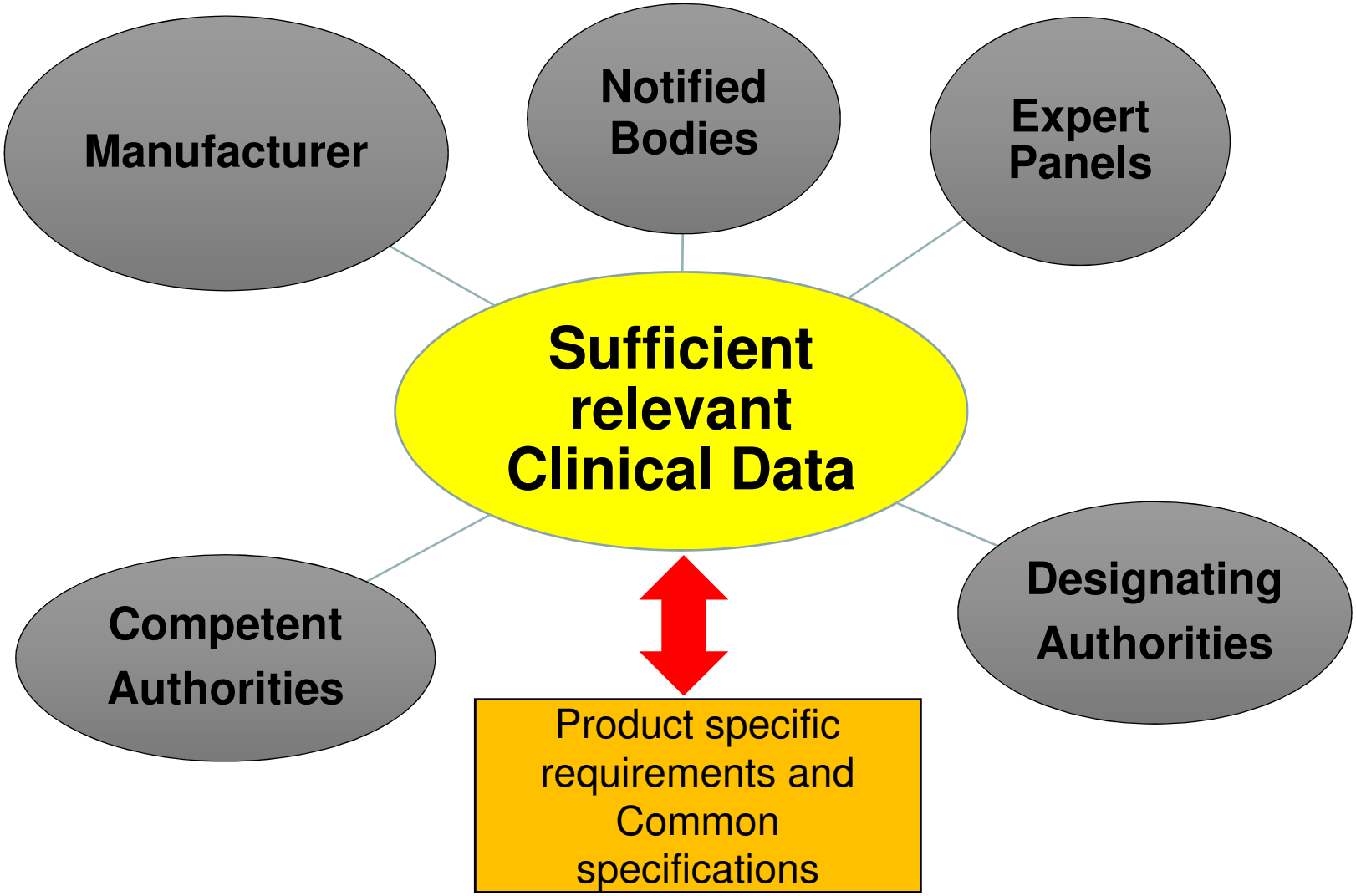
Clinical Evaluation a Lifecycle-Process

chapter VI Annexes XIII und XIV



Federal Ministry of Health

Clinical Evaluation



Federal Ministry of Health

Article 10(4) Technical Documentation

Annex II, Annex III and Annex XIII are describing the content of the technical documentation

Regularly Up-dates necessary in particular with regards to new market surveillance requirements

A number of new and additional “regularly” reports, like

- PMCF
- PMS
- Summary of Safety and Performance
- Periodic Safety Update Reports (jährlich) + in case of class III also assessment by the Notified Body necessary

See also IMDRF Project RPS --- Table of Content ---

Federal Ministry of Health

Article 10(6) Performing the right conformity assessment procedure

No general change of the principle that the conformity assessment procedure is related to the risk class of the device(s)

However

- a number of classification, application rules and definitions are modified or new (rules 13, 19, 21…) and
- some new product specific conformity assessment procedures have been introduced (reusable surgical instruments, substance based devices, expert panel assessment, scrutiny procedure, etc.

Every manufacturer must have again a closer look to find the right conformity assessment route and if relevant **the right Notified Body)**

Federal Ministry of Health

New or changed classification rules, changed definitions

- Braces, Dental fillings or crowns etc. are becoming implantable devices
- Many ingestive (substance based) devices also?

(5) 'implantable device' means any device, including those that are partially or wholly absorbed, which is intended
– to be totally introduced into the human body or
– to replace an epithelial surface or the surface of the eye,
by clinical intervention and which is intended to remain in place after the procedure.
Any device intended to be partially introduced into the human body by clinical intervention and intended to remain in place after the procedure for at least 30 days shall also be considered an implantable device;

Federal Ministry of Health

Substance based devices

Rule 21

Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as:

— class III if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose;

— class III if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body;

— class IIa if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities; and

— class IIb in all other cases.

Federal Ministry of Health

Software – new rule 11

Rule 11

Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause:

- death or an irreversible deterioration of a person's state of health, in which case it is in class III; or
- a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb.

Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb.

All other software is classified as class I. (???)

Federal Ministry
of Health

Software – new rule 11

Due to a change in the definition of a medical device a definition of medical (devices) software is missing

Latest discussion: medical devices software: is every software which is placed on the market with a medical purpose as described in the definition of a medical device, regardless if the software is independent or driving or influencing a hardware medical device

Medical Devices Software can not be an accessory

Medical Devices Software is considered to be an active device (art. 2 para 4), therefore a manufacturer must also analyse the classification rules on active devices

Since nearly all active devices are containing medical devices software, manufacturers must also analyse rule 11.

A first implementing guide for software classification is under development. There will be also references to the IMDRF software risk classification scheme

Federal Ministry of Health

Rule 19 Nanomaterials

Many devices with Nanomaterials will be classified as class III, IIb or IIa. This may also apply to devices with a contemporary powder coating

Rule 19 All devices incorporating or consisting of nanomaterial are:

- in class III if they present a high or medium potential for internal exposure;
- in class IIb if they present a low potential for internal exposure,
- in class IIa if they present a negligible potential for internal exposure,

according to the latest scientific opinion on nanomaterials in medical devices from the relevant Scientific Committee.

Federal Ministry of Health

Rule 19 Nanomaterials

Table 3: An estimation of potential external and internal exposure as starting point for a risk evaluation for medical devices containing nanomaterials

			Type of application of nanomaterials External exposure/internal exposure				
			Free	Fixed (coating)	Fixed (coating)	Embedded	Embedded
Type of device	Type of contact	Duration of contact		Weak (physisorb)	Strong (chemisorb)	In degradable materials*	In non-degradable materials
Surface device	Intact skin	≤ 24 h	H/N	M/N	M/N	L/N	N/N
		>24 h to 30 d	H/N	M/N	M/N	M/N	N/N
		>30 d	H/N	M/N	M/N	H/N	N/N
	Intact mucosal membrane	≤ 24 h	H/L	M/L	M/N	L/L	N/N
		>24 h to 30 d	H/M	M/M	M/L	M/M	N/N
		>30 d	H/M	M/M	M/L	H/M	N/N
	Breached or compromised surface	≤ 24 h	H/H	M/M	M/L	L/M	N/N
		24 h to 30 d	H/H	M/M	M/L	M/M	N/N
		30 d	H/H	M/M	M/L	H/M	N/N
External Communicating device	Blood path, indirect **	≤ 24 h	na	M/M	M/L	L/L	N/N
		>24 h to 30 d	na	M/M	M/L	M/M	N/N
		>30 d	na	M/M	M/L	H/M	N/N
	Tissue/bone/ dentin	≤ 24 h	H/H	M/M	M/L	L/L	N/N
		>24 h to 30 d	H/H	M/M	M/L	M/M	N/N
		>30 d	H/H	M/M	M/L	H/H	N/N
	Circulating blood***	≤ 24 h	na	H/H	H/H	L/L	N/N
		>24 h to 30 d	na	H/H	H/H	M/M	N/N
		>30 d	na	H/H	H/H	H/H	N/N
Implant device	Tissue/bone	≤ 24 h	H/H	H/H	H/L	L/L	N/N
		>24 h to 30 d	H/H	H/H	H/L	M/M	N/N
		>30 d	H/H	H/H	H/L	H/H	N/N
	Blood	≤ 24 h	H/H	H/H	H/L	L/L	N/N
		>24 h to 30 d	H/H	H/H	H/L	M/M	N/N
		>30 d	H/H	H/H	H/L	H/H	N/N

H=high, M=medium, L=low, N=negligible, na= not applicable

H/L means high potential contact and/or external exposure to the nanomaterial / low potential for internal systemic exposure of all organ systems

* the exposure will depend on the degradation time of the medical device

** contacting the blood path at one point. Examples of these types of devices are solution administration sets, transfer sets and blood administration sets (ISO 10993-4:2002)

*** Examples of these types of devices are: intravascular catheters, extracorporeal oxygenating tubing and dialysers (ISO 10993-4:2002).

Federal Ministry
of Health

Rule 13

Rule 13 All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in Article 1 of Directive 2001/83/EC ~~and which is liable to act on the human body~~ with action ancillary to that of the devices, are in Class III.

Possible interpretation:
All devices, which contain in whatever concentration a substance which might be considered as pharmaceutical are in class III and a consultation procedure with the EMA or a national Medicinal Agency is required

Federal Ministry of Health

Article 10 (9) Quality Management System

The quality management system shall address at least the following aspects:

(a) a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system;

(b) identification of applicable general safety and performance requirements and exploration of options to address those requirements;

(c) responsibility of the management;

(d) resource management, including selection and control of suppliers and sub-contractors;

(e) risk management as set out in in Section 3 of Annex I;

(f) clinical evaluation in accordance with Article 61 and Annex XIV, including PMCF;

(g) product realisation, including planning, design, development, production and service provision;

(h) verification of the UDI assignments made in accordance with Article 27(3) to all relevant devices and ensuring consistency and validity of information provided in accordance with Article 29;

(i) setting-up, implementation and maintenance of a post-market surveillance system, in accordance with Article 83;

(j) handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders;

(k) processes for reporting of serious incidents and field safety corrective actions in the context of vigilance;

(l) management of corrective and preventive actions and verification of their effectiveness;

(m) processes for monitoring and measurement of output, data analysis and product improvement.

Federal Ministry of Health

Article 10 (9) Quality Management System

The quality management system shall address at least the following aspects:

(a) a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system;

(b) identification of applicable general safety and performance requirements and exploration of options to address those requirements;

(c) responsibility of the management;

(d) resource management, including selection and control of suppliers and subcontractors;

(e) risk management as set out in in Section 3 of Annex I;

(f) clinical evaluation in accordance with Article 61 and Annex XIV, including PMCF;

(g) product realisation, including planning, design, development, production and service provision;

(h) verification of the UDI assignments made in accordance with Article 27(3) to all relevant devices and ensuring consistency and validity of information provided in accordance with Article 29;

(i) setting-up, implementation and maintenance of a post-market surveillance system, in accordance with Article 83;

(j) handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders;

(k) processes for reporting of serious incidents and field safety corrective actions in the context of vigilance;

(l) management of corrective and preventive actions and verification of their effectiveness;

(m) processes for monitoring and measurement of output, data analysis and product improvement.

ISO 13485 must be revised soon or a European GMP-R will be established

Federal Ministry of Health

Article 10(10) Post-Market Surveillance

(by the manufacturer)

Annex III describes in detail new requirements on the manufacturers post market surveillance system…

As a pro-active systematic lifecycle process by which all available information on the product and on similar products from the field are continuously sampled and assessed

The manufacturer must have suitable and effective methods and procedures in place to investigate and assess the sampled market experience or any complaint. This might include permanent access to special laboratories or test houses etc.

There must be effective processes in place to decide (and document etc.) necessary corrective actions

The traceability of the device must be ensured

Etc.

Federal Ministry of Health

Article 10 (16) Liability

Manufacturers shall, in a manner that is proportionate to the risk class, type of device and the size of the enterprise, have measures in place to provide sufficient financial coverage in respect of their potential liability under Directive 85/374/EEC, without prejudice to more protective measures under national law.

Federal Ministry of Health

Implementation

Who does what?

Every Member State

- **clearance and adoption of the national legislation**
- **Support COM an delegated and implementing acts.**

All Member States together (CAMD)

- **Identification of issues requiring a common understanding or position of CA to achieve a harmonised implementation of the MDR and IVDR**

Commission

- **Establishment of the MDCG, expert panels and EU reference laboratories**
- **Development of EUDAMED and UDI System**
- **Establishment ob delegated or implementing acts**

Federal Ministry of Health

Towards implementation:
delegated/implementing acts

Implementing acts	COM Proposal total	...of which compulsory	Final total	...of which compulsory
MD	26	6	32	8
IVD	24	5	32	6
Delegated acts	**COM Proposal total**	**...of which compulsory**	**Final total**	**...of which compulsory**
MD	17	2	11	0
IVD	15	2	5	0
Total	**82**	**13**	**80**	**14**

- Commission meeting 27-28 October 2016

Federal Ministry of Health

Who does what?

COM (DG GROW) is currently working Implementing acts

- Codes for Notified Bodies already published (now work on a common application template)
- Common Specifications for Reprocessing
- Common Specifications for “cosmetic” devices (Annex XVI)

COM (DG GROW) is developing EUDAMED together with DG DIGIT (Input from MS is only partially accepted)

COM (DG GROW) + some MS + WHO are trying to clarify which nomenclature should become the European MD nomenclature according to article 26 MDR

COM (DG JRC) is dealing with the establishment of expert panels and EU-reference laboratories

COM (DG GROW) has established the MDCG – first meeting 27 November 2017, until end of 2018 the structure of the different MDCG subgroups will be finalised.

Federal Ministry
of Health

Who does what?

Besides the COM activities mainly the MS are working on harmonised implementation of the MDR and IVDR

According to the COM the MS are fully responsible for implementation and the COM is legally bounded to not provide a guidance if the MDR is allowing a delegated ot implementing act .

CAMD founded an Implementation Task Force (ITF) and Transition Subgroup (TSG)

ITF performed a critical analysis of the MDR and IVDR and developed in 2017 a Roadmap which contains measures or guidance which are urgently needed for a harmonised implementation

The identified issues should be resolved by existing expert groups or by new established small Task Forces Subgroups etc.

Federal Ministry of Health

Roadmap

www.camd-europe.eu/news/published-medical-devices-regulationin-vitro-diagnostics-regulation-mdrivdr-roadmap

Home
Aims
Joint Action Projects +
Working Groups +
Media Centre
Glossary
News
Our Locations

Contact Us ›

Published: Medical Devices Regulation/In-vitro Diagnostics Regulation (MDR/IVDR) Roadmap

Home › News › Published: Medical Devices Regulation/In-vitro Diagnostics Regulation (MDR/IVDR) Roadmap

The CAMD network is delighted to be able to publish the high-level Medical Devices Regulation/In-vitro Diagnostics Regulation

Federal Ministry
of Health

Roadmap Clusters

Clinical Evaluation & Clinical investigation (MD) & Performance Evaluation & Performance Studies (IVD)

Scope & Classification

Notified Bodies

Post-Market Surveillance & Vigilance
Eudamed & UDI

Market Surveillance

IVD-specific Issues

Over-arching &Cross-cutting Priorities

Federal Ministry of Health

Clinical Evaluation & Clinical investigation (MD) & Performance Evaluation & Performance Studies (IVD)

	Activity	Recommended responsible parties/ owners	Priority level
1.1	**Clinical evaluation work package** • Guidance on equivalence, well established technologies, clinical evidence • Gap analysis of MEDDEV 2.7/1 • Contribution to relevant Implementing Acts (IA) • Work on interface between various documents/ reports e.g. CER, SSCP, PSUR. • Contribution to guidance on performance evaluation and clinical evidence for IVDs	• CIE WG • IVD WG	High
1.2	**Template document development (see also 4.4)** • Summary of Safety and Clinical Performance (SSCP) [MD] • Summary of Safety and Performance [IVD] • Clinical Evaluation Assessment Report (MD) • Performance evaluation plan and performance evaluation report (IVD) • Clinical Investigation application form (MD) • CI Assessment Report (MD) • Performance study Application Form (IVD) • Performance Study Report (IVD) • SAE/device deficiency reports and timelines (MD and IVD) • PMCF plan and PMCF report (MD) • PMPF plan and PMPF report (IVD)	• CIE WG • IVD WG • NBOG • EUDAMED WG	Medium – High
1.3	**Clinical investigation (MD) and (clinical) performance study (IVD) assessment** • Identification of key principles/ considerations of CI (MD) and PS (IVD) assessment • Development of training materials/methods/ mentoring schemes • Development of coordinated assessment procedure for MD and IVD	• CIE WG • IVD WG	Medium

Federal Ministry of Health

Clinical Evaluation & Clinical investigation (MD) & Performance Evaluation & Performance Studies (IVD)

	Activity	Recommended responsible parties/ owners	Priority level
1.4	**Common specifications** • Template/headers for common specifications – guidance on types of detail required/ expected • Analysis of work undertaken in other regulatory jurisdictions and transferability • Interaction/alignment with harmonised standards • Identification and prioritisation of devices requiring specifications • Transfer of current CTS for IVDs to CS under the IVDR. • Identification of and prioritisation of IVDs requiring CS and for which currently no CTS exist • Applicability to existing products • Interaction with international standards	• CIE WG • IVD WG • NET WG • NB-MED • NBOG / Vigilance WG • COM • JAMS	Medium
1.5	**Companion diagnostics – guidance for their assessment, and use in performance studies** • Development of template for the application dossiers and guidance incorporating MP consultation	• IVD WG • CIE WG • EMA	Low

Federal Ministry of Health

Scope & Classification

	Activity	Recommended responsible parties/ owners	Priority level
2.1	Classification guidance for IVDs around classification rules and scope, giving practical examples	• IVD WG • C&B WG • Software WG	High
2.2	Information and guidance on classification for MDs (changes on classification rules) • Information to highlight changes to classification rules • Guidance on new classification rules/ changes to existing rules e.g. MEDDEV 2.4/1 update/addendum • Software classification guidance (refer to workstream 2.1 IVD Classification)	• C&B WG • Software WG • NET WG • IVDWG	Medium
2.3	Common specifications for annex XVI products for MDs	• COM ad hoc WG • MDCG • NBOG	High
2.4	Implementing act on reprocessing SUDs for MDs	• COM • MDCG	Medium
2.5	Guidance for combination products and companion diagnostics around appropriate level of interaction with relevant authorities (ref: 3.4)	• C&B WG • IVD WG • (HMA-CAMD borderline WG, EMA, medicines CAs, tissues & cells CAs, EDQM) • NBOG	Low

Federal Ministry of Health

Some examples for transition related questions already „clarified“

- What kind of devices may already be placed on the market as MDR conform devices (Art. 120 para 5 -7) before May 2020?
- Which MDR requirements are applicable to those devices and manufacturers considering the fact that the MDR is earliest “fully” applicable after May 2020?
- Which devices (or manufacturers) may make use of article 120 (3) (placing on the market of devices which are still in compliance with MDD/AIMDD and IVDD and have a relevant valid certificate(s)) ?
- Which certificates are necessary?
- Does Article 120 (3) allow stepwise movement from MDD to MDR ?
- What are significant modifications of those devices ?

Federal Ministry of Health

Some examples for transition related questions already „clarified“

www.camd-europe.eu/news/available-now-mdr-and-ivdr-transitional-faqs

CAMD
Competent Authorities for Medical Devices

Log in | Contact Us | Sprache auswählen

Menu | Aims | Joint Action projects | Working Groups | Search

- Home
- Aims
- Joint Action Projects +
- Working Groups +
- Media Centre
- Glossary
- News
- Our Locations

Contact Us ›

Signup to our Newsletter

Email Address

Available now: MDR and IVDR transitional FAQs

Home › News › Available now: MDR and IVDR transitional FAQs

The CAMD network publishes FAQ documents covering the transitional provisions of the MDR and IVDR.

These documents were developed by the CAMD Transition Subgroup (TSG) which was tasked with agreeing and providing greater clarity on the transition-related provisions in the new Regulations.

The TSG has answered around 20 initial questions on the following topics:

- Placing on the market of MDR/IVDR compliant devices until 26 May 2020/2022
- Placing on the market of AIMDD/MDD/IVDD compliant devices after 26 May 2020/2022

Federal Ministry
of Health

“Regulatory Affairs in Medical Technology”

Medical Devices Regulation - Implementation

Thank for your attention

Lübeck 2018 Summer Academy
4. July 2018

Dr. Matthias Neumann
Federal Ministry of Health