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Clinical Evaluation - Equivalence
A guide for manufacturers and notified bodies

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1. Introduction

It is to be noted that whilst this guidance document is not legally binding, it has been put together following contribution from national competent authorities, industry and relevant stakeholders and it should therefore be recognised as best practice. It also tries to support a harmonised approach on establishing and demonstrating equivalence across Europe.

Whilst carrying out a clinical investigation is the most direct way to generate clinical data concerning the safety and performance of medical devices for the purpose of CE marking, data can also be generated by systematic review of

- *clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated,*
- *reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated*[1]

The purpose of this document is to provide additional guidance on establishing and demonstrating equivalence to an existing medical device for the purpose of CE marking under the Medical Device Regulation 2017/745 (hereafter referred to as the MDR). It does not remove the requirement to conduct a clinical evaluation in accordance with Article 61 and Annex XIV of the MDR.

This guidance should be read in conjunction with the MDR and MEDDEV 2.7/1 revision 4, the current European guidance on clinical evaluation; it does **not** introduce any new requirements. Only the text of the MDR is authentic in law, in cases of divergence between the MEDDEV and the MDR, the MDR takes precedence.

2. Background

It has been recognised that some of the requirements set out in MEDDEV 2.7/1 rev 4 are not quite aligned with the MDR and that further guidance to address the differences would be of benefit to industry and other stakeholders. This guidance attempts to highlight the differences between the two documents specifically with regards to equivalence.

The regulation text, being legally binding, takes precedence over the text in MEDDEV 2.7/1 rev 4 where differences are identified.

3. Scope

This guidance covers the demonstration of equivalence based on clinical data pertaining to one existing device for which equivalence to the device in question is claimed. Such data represents only one of the sources of clinical data with respect to Article 61(3)(a) of the MDR. Non-exhaustive guidance and references have been provided with respect to device considerations for medical devices incorporating an ancillary medicinal product.

This guidance does not cover devices without an intended medical purpose listed in Annex XVI of the MDR.

4. Equivalence definition

Section 3 of Annex XIV of the MDR requires that technical, biological and clinical safety and performance characteristics are considered when establishing equivalence to another medical device. Whilst these general characteristics are aligned with the MDR definition, there are differences in the criteria that are set out for each of the three characteristics. Differences in criteria are highlighted below and this is accompanied by some explanatory text.

4.1 Technical characteristics

Regulation 2017/745	MEDDEV 2.7/1 rev 4
The device is of similar design; is **used under similar conditions of use**; has similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms; uses similar deployment methods, where relevant; has similar principles of operation and critical performance requirements.	- be of similar design, and - **used under the same conditions of use**, and - have similar specifications and properties (e.g. physicochemical properties such as type and intensity of energy, tensile strength, viscosity, surface characteristics, wavelength, surface texture, porosity, particle size, nanotechnology, specific mass, atomic inclusions such as nitrocarburising, oxidability), and - use similar deployment methods (if relevant), and - have similar principles of operation and critical performance requirements

(a) Regulation 2017/745 stipulates use under **similar conditions** whereas the MEDDEV states use under **same** conditions with regard to technical characteristics. It is important to note that, the MDR applies limits to the interpretation of 'similar' with respect to the conclusions which are required (see Section 5).

(b) Different examples are given for specifications and properties of the materials/substances when considering technical characteristics across the two definitions. These are examples only and are to be considered as such. They must not be interpreted as an exhaustive list of specifications and properties of technical characteristics when considering equivalence to another device.

4.2 Biological characteristics

Regulation 2017/745	MEDDEV 2.7/1 rev 4
The device uses the same materials or substances in contact with the same human tissues or body fluids **for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables**	Use the same materials or substances in contact with the same human tissues or body fluids.

(a) Manufacturers must consider the additional text in the MDR.

(b) The principles outlined in ISO 10993-18:2005 which covers chemical characterisation of materials can be adopted to establish and demonstrate the identity of materials and the type and quantity of degradation products and leachables.

4.3 Clinical characteristics

Regulation 2017/745	MEDDEV 2.7/1 rev 4
The device is used for the same clinical condition or purpose, including similar severity and stage of disease, at the same site in the body, in a similar population, including as regards age, anatomy and physiology; **has the same kind of user**; has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.	- used for the same clinical condition (including when applicable similar severity and stage of disease, **same medical indication**), and - used for the same intended purpose, and - used at the same site in the body, and - used in a similar population (this may relate to age, **gender**, anatomy, physiology, possibly other aspects), and - not foreseen to deliver significantly different performances (in the relevant critical performances such as the expected clinical effect, the specific intended purpose, the duration of use, etc.)

(a) The MDR additionally requires that, for manufacturers to compare clinical characteristics, the device must have the **same kind of user**. Manufacturers must therefore ensure that consideration is given to the **intended** user of both devices. For example, a device intended for professional use and a device intended for home use, intended for the same indication and to achieve the same purpose, may have a different safety and performance profile due to the environment in which they are intended to be used.

(b) The MDR does not explicitly state that the medical device needs to be used for the **same medical indication** as the equivalent device; it is understood that in general, this is covered by the requirement that both devices should be used for the same clinical condition or purpose which is set out in both definitions.

4.4 Medical devices with an ancillary medicinal substance

For medical devices with an ancillary medicinal substance such as wound dressings incorporating silver or drug-eluting stents, the demonstration of equivalence requires special considerations. Manufacturers intending to use equivalence to obtain data concerning the clinical safety and performance of a medical device with an ancillary medicinal substance should consider biopharmaceutic and pharmacokinetic[1] and other bioequivalence aspects.[2]

A manufacturer should consider the need for a medicinal product consultation.[3] Manufacturers cannot claim equivalence of a device with an ancillary medicinal substance to a device without an ancillary medicinal

[1] European Medicines Agency, Committee for Medicinal Products for Human Use, Guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms, EMA/CPMP/EWP/280/96 Corr1, February 2013.
[2] European Medicines Agency, Committee for Medicinal Products for Human Use, Guideline on the investigation of bioequivalence, Doc. Ref. CPMP/EWP/QWP/1401/98 Rev. 1, July 2008.
[3] MDR, Annex IX, Chapter II, section 5.2(b)

substance and vice versa. For example, the manufacturer of a heparin coated catheter should not claim equivalence to a drug-free catheter even if both catheters are otherwise identical. See section 6.

Similarly, manufacturers must not claim equivalence of the ancillary medicinal substance to a standalone medicinal substance.

5. 'Similar' versus 'same' components of characteristics

Regulation 2017/745	MEDDEV 2.7/1 rev 4
The characteristics listed in the first paragraph shall be similar to the extent that there would be no clinically significant difference in the safety and clinical performance of the device. Considerations of equivalence shall be based on proper scientific justification.	For assuming equivalence, - similar means that no clinically significant difference in the performance and safety of the device would be triggered by the differences between the device under evaluation and the device presumed to be equivalent.

With regards to the technical characteristics, the MDR definition requires 'similar' conditions of use, whereas MEDDEV 2.7/1 rev 4 requires 'same' conditions of use. It is important to note that, as shown in the table above, the MDR applies limits to the interpretation of 'similar' with respect to the conclusions which are required. The corresponding wording from MEDDEV 2.7/1 rev 4 is presented for information above.

6. Similar versus Equivalent Devices

For claiming equivalence, the device under evaluation should:

- meet each of the criteria concerning clinical, technical and biological characteristics as defined in Annex XIV, section 3 of the MDR;
- be similar to the device to which equivalence is claimed, to the extent that there would be no clinically significant difference in the safety and clinical performance of the device. In such cases, the manufacturer is expected to fully identify, disclose and justify the differences between the two devices, based on proper scientific justification.

It is important to note that some similar devices are equivalent, some are not. Consideration must be given to the characteristics mentioned above and a gap analysis should be conducted by the manufacturer to assess any clinically significant difference of any variations. If equivalence can be demonstrated based on the assessment of the relevant aspects of technical, biological and clinical characteristics then the data can be used to support the conformity assessment.

In cases where equivalence cannot be demonstrated under the MDR, the data may be useful for a variety of other purposes, such as:

1. Ensuring that the risk management system is comprehensive by identifying relevant hazards and clinical risk.
2. Understanding the state of the art, the natural course of disease and alternative available treatment options.
3. Helping to define the scope of the clinical evaluation, by identifying any design features in similar devices that pose special performance or safety concerns.

4. Helping to inform clinical investigation design or post-market clinical follow-up design, and the post-market surveillance system.

Where gaps in clinical evidence have been identified as a result of the demonstration of equivalence, the plan to address these gaps should be addressed as an outcome of clinical evaluation.

7. Considerations when demonstrating equivalence

The clinical data of an equivalent device can be used to demonstrate compliance to the general safety and performance requirements as per Annex I of the MDR.

For identifying, appraising and analysing available data from the scientific literature to establish equivalence, manufacturers will find facilitative guidance in sections 8-10 of MEDDEV 2.7/1 rev 4. Data sources may include clinical data of the equivalent device.[4]

Data Identification

The data relating to the claimed equivalent device must meet the definition of clinical data as defined in the MDR (Article 2(48)). This data may then progress to data appraisal and analysis in order to evaluate the clinical data for the purpose of confirmation of conformity with the relevant GSPR.

In the event that the data does not meet the definition of clinical data as defined in the MDR, this is not clinical data and cannot be subject to data appraisal, analysis and evaluation for the purpose of confirmation of conformity with the relevant GSPR.

With respect to other studies reported in the scientific literature (Article 2(48) second indent), which may include animal or other pre-clinical data; this data can be used towards establishing equivalence between two devices, however such data alone cannot by definition be used for the demonstration of compliance to clinical aspects of GSPR.

Data Analysis

The following should be considered when analysing data to establish and demonstrate equivalence:

MEDDEV 2.7/1 rev 4 states that equivalence should only be claimed to a single device. This means that manufacturers should not use different parts of different devices to claim equivalence to the device under evaluation.

Manufacturers may identify more than one equivalent device to the device under evaluation, but each device should in its entirety be equivalent to the device under evaluation. Equivalence to each device should be fully investigated, demonstrated and described in the clinical evaluation report. This should include an analysis as to why some of the equivalent devices might have shown significant differences in their safety and performance profile in the literature.

Data Access Considerations and Specific requirements

The MDR notes specific requirements in addition to the demonstration of equivalence in order not to perform a clinical investigation which must be taken into account.

[4] As defined in Article 2(48), MDR.

For **implantable devices and class III devices,** there must be a contract in place that allows full access to the technical documentation on an ongoing basis.[5]

For implantable devices and class III devices, article 61(5) also requires that the clinical evaluation of the equivalent device has been performed in compliance with the requirements of the MDR. As such, it will not be possible to claim equivalence to a device certified with respect to the Directives.

For **all other devices**, it is necessary for a manufacturer to demonstrate they have sufficient levels of access to the data.[6] If a manufacturer is not able to demonstrate sufficient levels of access to the data, equivalence claims cannot be made for the purpose of conformity assessment. This data may be sourced from devices which are certified with respect to the Directives, however it must still meet the definition of clinical data in accordance with Article 2(48) of the MDR.

With respect to **modifications of a device already marketed by the same manufacturer**, the manufacturer is required to demonstrate that the modified device is equivalent to the marketed device (Article 61(4) second indent). In this context, a marketed device is considered to be a device already placed on the market and CE marked with respect to both the MDR and MDD/AIMDD.

[5] Article 61(5), MDR.
[6] Annex XIV, section 3, MDR.

Annex I – Equivalence Table

This table should be used to clearly demonstrate equivalence and to qualify the data on a device by device basis. The items in column 2 of the Table are examples only and are to be considered as such. They must not be interpreted as an exhaustive list of specifications, properties, parameters and/or aspects for demonstrating equivalence to another device.

It is recommended that to carry out an appropriate demonstration of equivalence, the manufacturer should identify differences and place at least as much emphasis on the differences between the two devices rather than the similarities and establish whether these differences lead to a significant difference in the safety and performance of the device from the device that equivalence is claimed. Full explanations should be provided for the differences deemed not likely to significantly affect the clinical performance and safety of the device.

Where more than one product is deemed to be equivalent to the device, the below table can be used to identify the most relevant device, where manufacturers are able to acquire the required data. Equivalence of every single device to the device under evaluation should be fully investigated, demonstrated, and described in the clinical evaluation report.

		Device 1	**Device 2 (marketed device)**	**Differences**		
				List of differences	**Impact on safety and performance of the differences identified. Yes / No**	**If 'no' - Rationale for claiming no clinically significant difference in the safety and clinical performance of the device**
Technical characteristics	Device is of similar design					
	Used under similar conditions of use					
	Similar specifications & properties including physiochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength & software algorithms					
	Uses similar deployment methods where relevant					
	Where relevant, has similar principles of operation & critical					

	performance requirements					
Biological characteristics	Uses the same materials or substances in contact with the same human tissues or body fluids			**Not applicable**	**Not applicable**	
	Similar kind and duration of contact with the same human tissues or body fluids					
	Similar release characteristics of substances including degradation products and leachables					
Clinical characteristics	Same clinical condition or purpose, including same severity.			**Not applicable ***	**Not applicable ***	
	Same site in the body			**Not applicable***	**Not applicable ***	
	Similar population (including age, anatomy & physiology)					
	Same kind of user					
	Similar relevant critical performance in view of the expected clinical effect for a specific intended purpose					

*Differences are not possible as the criteria must be the same. The device under consideration can not have additional uses compared to the equivalent device.