MDCG 2023-7

Guidance on exemptions from the requirement to perform clinical investigations pursuant to Article 61(4)-(6) MDR

and on

'sufficient levels of access' to data needed to justify claims of equivalence

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1. Abbreviations

CER:	Clinical evaluation report
CI:	Clinical investigation
CS:	Common Specification
DUE:	Device Under Evaluation
ED:	Equivalent Device
MDR:	Regulation (EU) 2017/745 on medical devices
PMCF:	Post Market Clinical Follow Up
WET:	Well Established Technology (specifically the WET devices listed in Article 61(6)(b) of the MDR)

2. Introduction

For ease of reference, the text of Article 61 paragraphs (4)-(6) is included below:

Article 61
Clinical evaluation

4. *In the case of implantable devices and class III devices, clinical investigations shall be performed, except if:*
   - *the device has been designed by modifications of a device already marketed by the same manufacturer,*
   - *the modified device has been demonstrated by the manufacturer to be equivalent to the marketed device, in accordance with Section 3 of Annex XIV and this demonstration has been endorsed by the notified body, and*
   - *the clinical evaluation of the marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements.*

   In this case, the notified body shall check that the PMCF plan is appropriate and includes post market studies to demonstrate the safety and performance of the device. In addition, clinical investigations need not be performed in the cases referred to in paragraph 6.

5. *A manufacturer of a device demonstrated to be equivalent to an already marketed device not manufactured by him, may also rely on paragraph 4 in order not to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in that paragraph:*
   - *the two manufacturers have a contract in place that explicitly allows the manufacturer of the second device full access to the technical documentation on an ongoing basis, and*
   - *the original clinical evaluation has been performed in compliance with the requirements of this Regulation, and the manufacturer of the second device provides clear evidence thereof to the notified body.*

6. *The requirement to perform clinical investigations pursuant to paragraph 4 shall not apply to implantable devices and class III devices:*
   (a) *which have been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation:*
      - *is based on sufficient clinical data, and*

— *is in compliance with the relevant product-specific CS for the clinical evaluation of that kind of device, where such a CS is available; or*

(b) that are sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips or connectors for which the clinical evaluation is based on sufficient clinical data and is in compliance with the relevant product-specific CS, where such a CS is available.

Article 61(4) of Regulation (EU) 2017/745 on medical devices (MDR) requires clinical investigations to be performed for implantable and class III devices, except in four specific cases as outlined in:

CASE 1) indents 1-3 of Article 61(4);
CASE 2) Article 61(6)(a);
CASE 3) Article 61(6)(b);
CASE 4) Article 61(5).

These four cases which are exempted from the requirement to perform clinical investigations are independent of each other; i.e. the criteria outlined in one paragraph do not apply to the other paragraphs unless directly referenced.

One important consequence of this independence of cases is that the requirement for a contract, pursuant to Article 61(5), does not apply to the cases outlined in indents 1-3 of Article 61(4), Article 61(6)(a) and Article 61(6)(b). For these cases, it is only necessary to demonstrate equivalence in accordance with the criteria listed in Annex XIV Section 3 MDR to be able to use the associated clinical data in the clinical evaluation.

In addition to outlining the technical, biological and clinical characteristics to be taken into consideration for the demonstration of equivalence, Annex XIV Section 3 mandates that “It shall be clearly demonstrated that manufacturers have sufficient levels of access to the data relating to devices with which they are claiming equivalence in order to justify their claims of equivalence”. The requirement to have sufficient levels of access to the data required to establish equivalence does not in itself require a contract between the two manufacturers (see Section 5 of this guidance for further detail).

3. Scope

This guidance is intended to clarify the exemptions from the requirement to perform clinical investigations, and associated conditions related to the demonstration of equivalence, for implantable and class III medical devices to be placed on the European market. It also provides examples and considerations relevant to the demonstration of “sufficient levels of access to the data” per Annex XIV Section 3.

4. When are clinical investigations not mandatory according to Article 61(4)-(6) of the MDR?

Article 61(4) states that clinical investigations shall be performed for implantable and class III devices. Indents 1-3 of Article 61(4) outline the first case which can be

exempted from this requirement. Articles 61(5) and 61(6) outline additional exemption cases, as illustrated in Appendix I. Appendix I shows the parallel nature, and thus independence, of these cases. The conditions that apply to each case are summarised in Table 1 in this section.

N.B.: Devices which are neither class III nor implantable are outside the scope of this document. The need for a clinical investigation(s) for such devices is determined by the objectives of the clinical evaluation and the sufficiency of existing clinical evidence to meet those objectives. Please refer to MDCG 2020-5 and MDCG 2020-6 for further guidance.

The beginning of the first sentence of Article 61(4) provides the general obligation, namely "in the case of implantable devices and class III devices, clinical investigations shall be performed". The remainder of Article 61(4), as well as Article 61(5) and 61(6) describe circumstances under which these devices are exempted from the requirement to conduct clinical investigations; they do not describe conditions for demonstrating equivalence, nor do they describe when data from EDs may be used in a clinical evaluation.

As summarised in the Introduction to this guidance, the cases in which implantable and class III devices are exempted from mandatory clinical investigations are independent of each other, except where a dependence is explicitly indicated[1, 2]. In other words, the criteria outlined in one paragraph do not apply to the other paragraphs unless directly referenced. Specifically, the requirement for a contract as described in Article 61(5) does not apply to the exemption cases outlined in Articles 61(4) and 61(6).

A manufacturer may use clinical data generated from another manufacturer's ED in the clinical evaluation of the DUE, without a contract, in any of the cases 1 to 3[3]. The only requirement in this respect is that the equivalence criteria described in Annex XIV Section 3 are met.

Use of ED data may enable a manufacturer to demonstrate that their clinical evaluation is based on "sufficient clinical data". However the manufacturer is only exempted from the requirement to perform clinical investigations if the conditions outlined in the relevant exemption case are met, as summarised in Table 1 below.

[1] Article 61(4) states "In addition, clinical investigations need not be performed in the cases referred to in paragraph 6". The words "in addition" indicates additional exemption cases which do not rely on the exemption criteria of Article 61(4) being met. i.e., CASE 2 and CASE 3, as described in Article 61(6)(a) and Article 61(6)(b), do not need to satisfy the additional requirements listed in Article 61(4).
Article 61(5) states "a manufacturer […] may also rely on paragraph 4 in order not to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in that paragraph". This indicates that the exemption case outlined in Article 61(5) is dependent on criteria described in Article 61(4) being met. In legal terms, the phrasing "may also rely upon" indicates a dependence on the referenced paragraph; Article 61(5) has a dependency on Article 61(4), but Articles 61(4) and 61(6) are not dependent on Article 61(5).

[2] It can be inferred from this independence of paragraphs that the devices described in CASE 1 and CASE 4 are neither legacy devices as outlined in CASE 2 nor "sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips or connectors" as outlined in CASE 3. i.e., the DUE described in Article 61(5) and indents 1-3 of Article 61(4) are new devices which have not previously been marketed under either the Directives or the MDR.

[3] N.B., in CASE 4, a contract with at least one manufacturer will be required along with the other conditions described in Table 1. However, data from other manufacturers' devices (with which equivalence is demonstrated) can be used without a contract to supplement the data in the clinical evaluation, for those indications covered by the contract. See also footnote 11.

Table 1: Criteria for exemption from the Article 61(4) requirement for clinical investigations for implantable and class III devices	
CASE 1: Indents 1-3 of Article 61(4)	• DUE has been designed by modifications of a device already marketed by the same manufacturer. • Equivalence is demonstrated between the DUE and the manufacturer's ED in accordance with Section 3 of Annex XIV; demonstration of equivalence has been endorsed by the notified body. For further guidance on the demonstration of equivalence, please refer to MDCG 2020-5. • The clinical evaluation of the marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements[4, 5]. • PMCF plan is appropriate and includes post market studies to demonstrate the safety and performance of the DUE[6].
CASE 2: Article 61(6)(a)	• DUE has been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC. • The clinical evaluation is based on sufficient clinical data[7]. • The clinical evaluation is in compliance with the relevant product-specific CS for the clinical evaluation of that kind of device, where such a CS is available.
CASE 3: Article 61(6)(b)	• DUE is one of the listed types of devices: "sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips or connectors". • The clinical evaluation is based on sufficient clinical data[7]. • The clinical evaluation is in compliance with the relevant product-specific CS for the clinical evaluation of that kind of device, where such a CS is available.
CASE 4: Article 61(5)[8]	• Equivalence is demonstrated between the DUE and the other manufacturer's ED in accordance with Section 3 of Annex XIV;

[4] The MDR does not prohibit the use of data from another manufacturer's ED in the clinical evaluation of the manufacturer's already marketed device. This does not imply that a manufacturer will rely on equivalence in perpetuity: the additional requirement for PMCF studies to demonstrate the safety and performance of the DUE ensures that clinical data on the DUE itself will be collected post market; this data will be included in future revisions of the clinical evaluation report per Article 61(11). There may however be circumstances in which it is appropriate to continue to include data from EDs in the clinical evaluation, even when clinical data has been generated on the DUE.
[5] The clinical evaluation for the manufacturer's ED does not supersede the clinical evaluation for the DUE; the DUE clinical evaluation and its documentation are still required, in accordance with Article 61(1).
[6] See also MDCG 2020-8: Post-market clinical follow-up (PMCF) Evaluation Report Template - A guide for manufacturers and notified bodies (April 2020)
[7] "Clinical data" includes data from any of the sources listed in the Article 2(48) definition. This includes data from "a device for which equivalence to the device in question can be demonstrated". The definition does not include a requirement for a contract between the manufacturers.
Additional note: MedDev 2.12/2 indicated that PMCF studies should be undertaken for devices when the clinical evaluation was based on equivalence. In some cases, execution of such studies may have been a condition of certification under the Directives. The acceptance of clinical evidence from EDs as part of the clinical evidence package to support MDR certification does not invalidate any such conditions of certification.
[8] Article 61(5) states: "A manufacturer of a device demonstrated to be equivalent to an already marketed device not manufactured by him, may also rely on paragraph 4 in order not to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in that paragraph"; i.e., the exemption requirements of Article 61(4) must also be met in addition to the exemption requirements laid out in Article 61(5). This does not include the requirement for the device to be a design modification of the manufacturer's own already marketed device.

	demonstration of equivalence has been endorsed by the notified body (via Article 61(4)). • The clinical data from the clinical evaluation of the ED is sufficient to support the intended purposes of the DUE (via Article 61(4))[9]. • The two manufacturers have a contract in place that explicitly allows the manufacturer of the ED full access to the technical documentation on an ongoing basis. • The clinical evaluation of the other manufacturer's ED has been performed in compliance with the requirements of the MDR[10, 11]. • PMCF plan is appropriate and includes post market studies to demonstrate the safety and performance of the DUE[6] (via Article 61(4)).

In the case where a clinical investigation(s) is determined to be mandatory[12] in order to obtain the needed clinical data to support the clinical evidence for a claimed indication for use, the MDR does not specify the number or extent of the clinical investigation(s) required. However, as a minimum, mandatory clinical investigation(s) should be understood to mean a pivotal clinical investigation(s) generating pivotal data.

5. Demonstration of "sufficient levels of access to the data" required to justify claims of equivalence

In addition to outlining the technical, biological and clinical characteristics to be taken into consideration for the demonstration of equivalence, Annex XIV Section 3 MDR requires manufacturers to have "[…] sufficient levels of access to the data relating to devices with which they are claiming equivalence in order to justify their claims of equivalence". As clarified above, demonstration of "sufficient levels of access" does not require a contract in all circumstances. A contract is only required for the exemption case described in Article 61(5). It should also be noted that Annex XIV Section 3 refers specifically to the data required to *justify claims of equivalence*: i.e., the requirement is for sufficient access to establish the clinical, technical and biological characteristics against which equivalence is evaluated, not access to the complete technical documentation.

A contract as described in Article 61(5) is presumed to provide full access to the data needed for the demonstration of equivalence. However, in the cases where a contract is not required, other means of access to data can prove to be adequate to support demonstrations of equivalence. This includes CASEs 1, 2, and 3; it also includes a specific subset of CASE 4, in which equivalence is fully demonstrated with more than one device from more than one manufacturer, and there is a contract in place with at

[9] The MDR does not prohibit the use of equivalence, demonstrated in compliance with the MDR, in the clinical evaluation of ED.
[10] The clinical evaluation for the other manufacturer's ED does not supersede the clinical evaluation for the DUE; the DUE clinical evaluation and its documentation are still required, in accordance with Article 61(1).
[11] The MDR does not prohibit the use of clinical data from more than one manufacturer's ED in the clinical evaluation of the DUE. In this case, only one contract with one manufacturer is required for the exemption from the requirement for clinical investigations to apply for the specific indications for use covered by the existing contract.
[12] Article 61(4) MDR

least one of the manufacturers, see footnotes 3 and 11. The manufacturer of the DUE must document their justification within the CER as to why the level of access they have obtained is sufficient, and this has to be accepted by the notified body[13].

Table 2 in Appendix II provides some examples of means of access to the data relevant for the demonstration of equivalence and suggests a hierarchy in relation to the level of access to this data. It also indicates potential limitations of these methods and means by which these limitations might be addressed. Table 2 is for illustrative purposes only, and is not intended to be exhaustive or prescriptive.

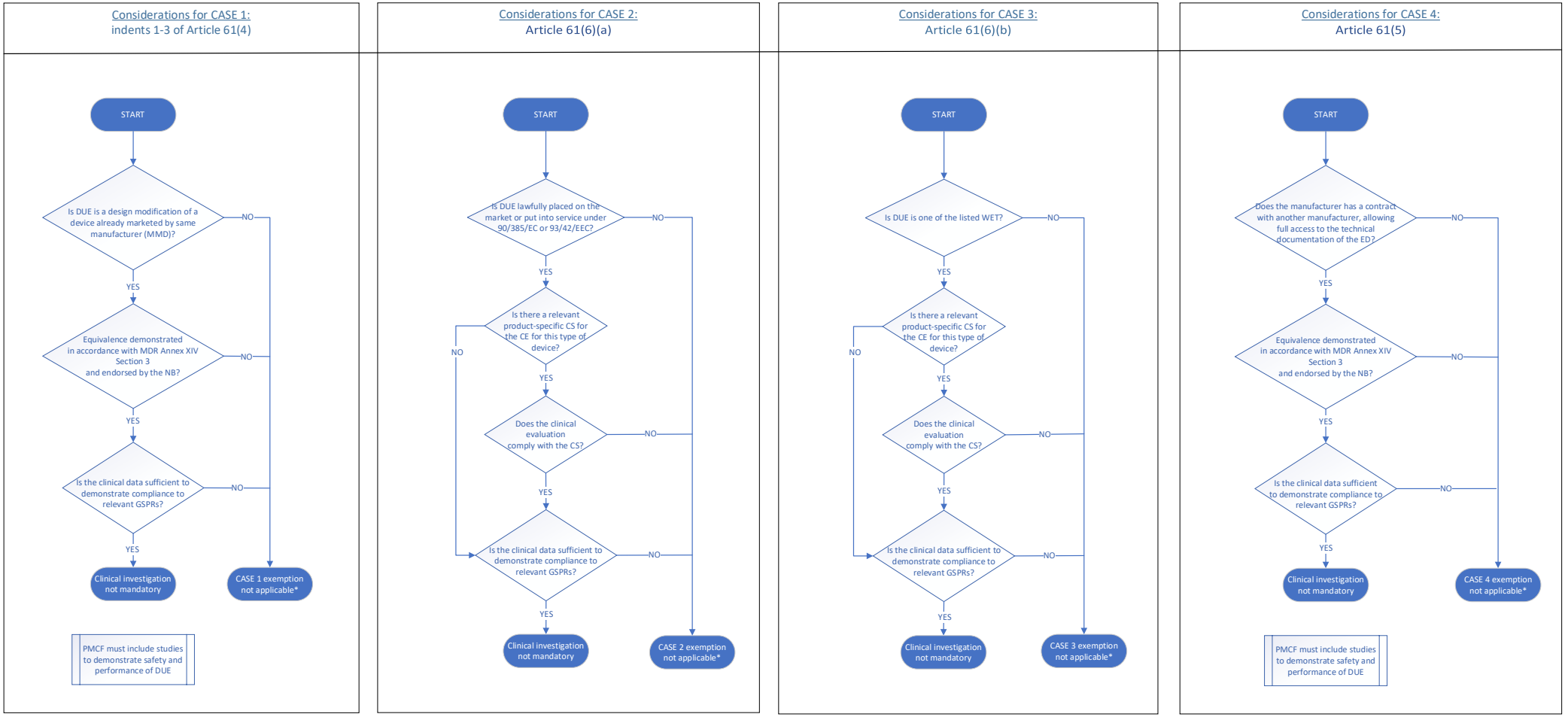
N.B.: A higher level of access is indicated where limitations are considered unacceptable and cannot be adequately addressed. In this context, an unacceptable limitation is one which compromises the completeness or accuracy of the demonstration of equivalence such that it cannot be presumed that the DUE has similar safety and performance characteristics to the device with which equivalence is claimed.

It should also be noted that a higher level of access to data does not directly correlate to a stronger demonstration of equivalence. For example, in example 1a of Table 2, the manufacturer of the DUE has complete access to the data required to demonstrate equivalence, but the devices could still have differences in one or more of the clinical, technical or biological equivalence criteria described in Annex XIV Section 3 of the MDR. By contrast, in the case described in example 1d of Table 2, it may be presumed that the DUE is identical to its claimed equivalent.

If a manufacturer is not able to demonstrate sufficient levels of access to the data needed for the demonstration of equivalence, equivalence claims cannot be made for the purpose of conformity assessment[13].

[13] For further guidance on the demonstration of equivalence, please refer to MDCG 2020-5

Appendix I: Summary of the cases when implantable and class III devices may be exempted from mandatory clinical investigations



*****if none of the cases is applicable, clinical investigation(s) is mandatory for implantable and class III devices. In all cases above, Article 61(11) MDR applies.

Appendix II: Hierarchy of levels of access to the data regarding the clinical, technical and biological characteristics to be considered for the demonstration of equivalence

Table 2: Hierarchy of levels of access to device equivalence data			
Examples of means of demonstrating "sufficient access to data"		Level of access and potential limitations	Means of addressing limitations[14]
1a.	Contract with the manufacturer of the ED allowing full access to the technical documentation on an ongoing basis	• Level of access: Full.	• N/A
1b.	DUE is a design modification of a device already marketed by the same manufacturer	• Level of access: Full.	• N/A
1c.	Rights to DUE acquired with transfer of all relevant design and clinical data at the time of acquisition	• Level of access: Full.	• N/A
1d.	Device with the same design specification and intended purpose is supplied to several manufacturers by the same production sub-contractor, and manufacturer has access to the technical specifications necessary to demonstrate technical and biological equivalence	• Level of access: High. However, information on clinical safety and performance of the EDs may be limited to data available in the public domain; this could introduce additional biases, such as publication bias, to the literature evaluation.	• Clinical data on the DUE (including data from pre- or post-market clinical sources)[15] • Literature data appraisal in accordance with relevant standards and guidance, to identify and evaluate potential sources of bias

[14] These examples are not intended to be exhaustive or prescriptive. Limitations associated with access to data may be addressed without using every means listed in this column.
[15] Clinical data on the DUE can corroborate conclusions on safety, performance and clinical benefit based on data from EDs. The higher the quality and quantity of clinical data available on the DUE, the less likely it is that limitations with respect to access to data would be considered unacceptable as defined in Section 5 of this guidance.

			• PMCF to supplement the available data and continually update the clinical evaluation as per Annex XIV Part B[16]
2.	Comparative analysis and/or testing of devices based on samples of both devices (DUE and ED), coupled with information available in the public domain (e.g. IFU, surgical technique brochures, SSCP, etc.)	• Level of access: Medium. • Information regarding device history and design changes may be limited, particularly in cases where the state of the art for the category of devices has had significant evolution over its history. • There may be inaccurate correlation of design variants to studies published in literature, due to above limitations of information regarding device history and design changes. • Information on clinical safety and performance of the other manufacturer's EDs may be limited to data available in the public domain; this could introduce additional biases, such as publication bias, to the literature evaluation.	• Evaluation of the design history of the ED and potential impact of knowledge gaps with respect to ability to correlate a specific design variant with studies published in the literature • Clinical data on the DUE (including data from pre- or post- market clinical investigations)[15] • Literature data appraisal in accordance with relevant standards and guidance, to identify potential sources of bias • PMCF to supplement the available data and continually update the clinical evaluation as per Annex XIV Part B[16]
3a.	Device with the same design specification and intended purpose is supplied to several manufacturers by the same production sub-contractor, but access to data needed to establish equivalence	• Level of access: Medium to low, depending on the availability and quality of publicly available information; this could introduce additional biases, such as publication bias, to the literature evaluation.	• Clinical data on the DUE (including data from pre- or post-market clinical sources) [15] • Literature data appraisal in accordance with relevant standards and guidance, to

[16] Clinical data on the DUE generated through PMCF activities can corroborate conclusions on safety, performance and clinical benefit based on data from EDs, and can be considered a means of addressing residual risk associated with limitations related to the level of access to device data which have been evaluated and determined to be acceptable.

	only available through publicly available information		identify and evaluate potential sources of bias • PMCF to supplement the available data and continually update the clinical evaluation as per Annex XIV Part B[16]
3b.	Product specification determined solely through publicly available information	• Level of access: Low, depending on the availability and quality of publicly available information. • There may be additional limitations with respect to accuracies in publicly available information / inability to verify publicly available information	• Evaluation of the design history of the ED and potential impact of knowledge gaps with respect to ability to correlate a specific design variant with studies published in the literature • Clinical data on the DUE (including data from pre- or post-market clinical investigations)[15] • Literature data appraisal in accordance with relevant standards and guidance, to identify potential sources of bias • PMCF to supplement the available data and continually update the clinical evaluation as per Annex XIV Part B[16]