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~~Questions & Answers on Implementation~~ Questions & Answers for applicants, marketing authorisation holders of medicinal products and notified bodies with respect to the implementation of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations ((EU) 2017/745 and (EU) 2017/746)

This Question and Answer (Q&A) document provides practical considerations concerning the implementation of the medical devices and the *in vitro* diagnostic medical devices regulations.

This document has been produced to provide guidance to Applicants, Marketing Authorisations Holders (MAH) and notified bodies (NB) as regards aspects falling within the scope of the Agency's activities and should be read in conjunction with the new medical devices Regulation (EU) 2017/745, and the new *in vitro* diagnostic medical devices Regulation (EU) 2017/746. The medical devices regulation (MDR) and *in-vitro* ~~diagnostics~~diagnostic medical devices regulation (IVDR) replace the three existing Directives (90/385/EEC, 93/42/EEC, and 98/79/EC and 90/385/EEC) for medical devices. The ~~Regulations entered into force on 25 May 2017; however, they will have a transition period to allow manufacturers, notified bodies and authorities to comply with the changes and will come into~~ MDR has come into full application on 26 May ~~2020~~2021 but provides for ~~medical~~a transitional period for certain devices and until 26 May 2024. The IVDR will come into application on 26 May 2022 for *in vitro* ~~diagnostics~~diagnostic medical devices but also provides for a transitional period for certain devices until 26 May 2024. These regulations ~~lay down roles and include provisions concerning the~~ responsibilities ~~for~~of EMA ~~and~~ National Competent Authorities (NCA) for medicinal products, and medical devices and notified bodies as regards combinations of medicinal products with medical devices as follows:

- For medical devices that form an integral product with a medicinal product (Regulation (EU) 2017/745, second subparagraph of Article 1(8) and 1(9)), new requirements to provide an EU certificate or an opinion from a notified body designated under Regulation (EU) 2017/745¹ for the type of device in question is applicable in certain circumstances (Art. 117).

¹ Regulation 2017/745 Article 117

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- For medical devices incorporating a medicinal substance ~~(with action ancillary to the device)~~², [Regulation \(EU\) 2017/745 Article 1 \(8\)](#), the notified body shall seek a scientific opinion from either ~~the NCAs~~³ [an NCA](#) or EMA³. The notified body shall seek the opinion of EMA for medicinal products falling exclusively within the scope of ~~centralized~~⁴ [centralised](#) procedure⁴, or that incorporate human blood or plasma derivatives.
- For [medical](#) devices that are composed of substances, or of combinations of substances, that are systemically absorbed by the body in order to achieve their intended purpose, ~~the notified body shall seek a scientific opinion from either the NCAs~~⁵ [an NCA](#) or ~~the~~ EMA⁵ [\(Regulation \(EU\) 2017/745 Article 52\(11\)\)](#)⁶.
- For companion diagnostics, the notified body shall seek a scientific opinion from either ~~the NCAs~~⁷ [an NCA](#) or ~~the~~ EMA⁷ [\(Regulation \(EU\) 2017/746, Article 48\(3\) and \(4\)\)](#)⁸.
- ~~This~~ [The European Commission may consult EMA when deliberating on the regulatory status of products in borderline cases involving medicinal products](#)⁹.

~~For medicinal products with~~ [document covers:](#)

- [Medical devices that form an integral product with a medicinal product,](#)
- ~~Medicinal products that include a~~ [medical device](#)¹⁰, ~~there are new requirements to provide an opinion from a notified body~~
[in the secondary packaging](#)
- ~~This update of the questions and answers focuses on aspects relating to the implementation and applicability of the requirements of Regulation (EU) 2017/745 to~~ [marketed medicinal product \(co-packaged\),](#)
- [Consultation procedure for ancillary medicinal](#) ~~products with an~~ [substances that are](#) integral ~~or co-packaged part of~~ [medical device](#) ~~devices.~~

This ["questions and answers" document](#) is ~~a living document and the questions and answers are~~ being updated continuously⁷, and will be marked by "~~NEW~~⁷New" or "Rev." with the relevant date upon publication.

² ~~Regulation 2017/745 Annex IX 5.2~~

³ [Regulation 2017/745 Annex IX 5.2](#)

⁴ Annex I, Regulation (EC) No 726/2004

⁵ ~~Regulation 2017/745 Annex IX 5.4~~

⁶ [Regulation 2017/745 Annex IX 5.4](#)

⁷ ~~Regulation 2017/746 Annex IX 5.2, Annex X 3(k)~~

⁸ [Regulation 2017/746 Annex IX 5.2, Annex X 3\(k\)](#)

⁹ ~~Regulation 2017/745 Article 4, Regulation 2017/746 Article 3~~

¹⁰ ~~Regulation 2017/745 Article 117~~

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~~1. Medicinal product medical device combinations ('combination products')~~

1. Combinations of medicinal products and medical devices

1.1. What regulatory framework does a product incorporating both medicinal product and medical device fall under? ~~New Oct 2019~~ Rev. June 2021

~~Medicinal products and medical devices that are placed on the market together are generally known as "combination products".~~

Products which combine a medicinal product (or substance) and a medical device are regulated either by Regulation (EU) 2017/745 or Directive 2001/83/EC, depending on their principal mode of action. Certain combinations of medicinal products and medical devices are governed by or require consultation of a medicine competent authority, as laid down in Articles 1(8) and 1(9) of the MDR.

The regulatory framework for devices incorporating medicinal substances as an ~~integral part~~ part is laid down in Article 1(8) of MDR:

- Where the action of the medicinal substance is **ancillary to the action of the medical device**, the product is regulated as a medical device and must be CE marked. ~~As the action~~ For these combinations of the medicinal product is considered ancillary products and medical devices, a scientific opinion on the quality and safety of the ancillary substance must be provided from ~~a~~ one of the national competent authorities or from the EMA (referred to as medicines authority) before a notified body can issue ~~an EU~~ certificate for the combined product. For more information and for a list of products previously reviewed by EMA, please see EMA webpage on Ancillary medicinal substances in medical devices
- Where the action of the medicinal substance is **principal**, ~~the combination product is regulated under~~ and not ancillary to the action of the medical device, the DDC is governed by the medicinal products framework. In that case, the relevant general safety and performance requirements of the Annex I of the MDR apply to the device part.

The regulatory framework for ~~administration~~ medical devices intended to administer medicinal products is laid down in Article 1(9) MDR:

- If the medicinal product and administration device ~~is~~ are marketed as a **single integral product** intended **exclusively for use in the given combination** and is **not reusable**, the ~~combination product~~ DDC is ~~regulated under~~ governed by the medicinal products framework. ~~In that case, the relevant general safety and performance requirements of Annex I of the MDR apply to the device part.~~
- In all other cases, ~~the administration device is regulated under~~ (e.g. where the medical device framework. When the medical device is not physically combined is co-packaged with the medicinal product the device or when the product information of the medicinal product refers to a specific device to be used and the device is obtained separately), the administration device is governed by the medical device framework. These administration devices must meet the requirements of the MDR and will need to be CE marked. ~~See section 2. of the Q&A's for additional information concerning co-packaged medical devices.~~

~~Throughout~~ For the purpose of this document, integral products ~~that, in accordance with falling within~~ MDR Article 1(8) second subparagraph and 1(9) second subparagraph, and for which the principal mode of action is pharmacologic, metabolic or immunologic, are regulated under the medicinal products framework, and are referred to as integral Drug-Device Combinations (integral-DDCs). ~~Additional~~ in the Q&A hereafter.

There are cases where a medicinal product and a medical device are placed on the market in the same secondary packaging but do not form an integral product, for example, a vial containing a medicinal product solution, with an (empty) CE marked sterile syringe. This product is not considered a drug-device combination as the medical device falls under the first subparagraph of Article 1(9) of the MDR. Furthermore, devices referenced in the medicinal product information-and-examples-of-, or medicinal products referenced in the information supplied with the device, are not considered drug device combinations. Requirements for these products are providedcovered in section 2-3 of thethis Q&A's-A.

1.2. How do I choose a notified body for my ~~co-packaged/integral~~ drug-device? New Oct 2019 combination? Rev. June 2021

A notified body (NB) within the European Union (EU) is ~~an entity~~ a conformity assessment body designated ~~by an EU competent authority~~ in accordance with the MDR and/or IVDR to assess the conformity of medical devices before being placed on the Union market. Companies are free to choose ~~the~~ which notified body they engage with; the only criterion is that the notified body must be designated to carry out the conformity assessment procedure for the particular medical device ~~type(s)~~ for which a certification or notified body opinion is sought. Applicants can check the NANDO (New Approach Notified and Designated Organisations) website, by clicking on 'Legislation' and select the relevant Directive/Regulation to search for a designated notified body ~~designated for~~ according to the ~~product types and technical competences~~ codes/scope needed.

2. Medicinal product with an integral Drug-Device Combinations

2.1. When is my medical device (integral DDC)

2.1.1. When is my medicinal product considered to form an integral product with the administration device? a medicinal product? Rev. June 2021

There are two types of DDCs according to MDR Articles 1(8) and 1(9) (see also Question 1.1).

~~2.1.1.~~ 1. A medical device that incorporates, as an integral part, a substance which, if used separately, would be considered a medicinal product and where the action of that substance is principal, the integral product will be regulated as a medicinal product (second subparagraph of Article 1(8)). Examples include an ingestible sensor that is incorporated into a medicinal product.

If a medical device used to administer a medicinal product is placed on the market in such a way that the two constituents parts (the medical device and medicinal product) form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single integral product shall be governed by Directive 2001/83/EC or Regulation (EC) No 726/2004, as applicable.

2. The second paragraph of Article 1(9) of the MDR sets out three cumulative conditions that need to be satisfied at the moment of ~~the~~ placing on the market:

- i. the device and the medicinal product form a single integral product;
- ii. the single integral product is intended exclusively for use in the given combination;
- iii. which the single integral product is not reusable.

For medicinal products meeting either one or both the above ~~conditions~~ definitions, the ~~single~~ integral product shall be governed by Directive 2001/83/EC or Regulation (EC) No 726/2004, as applicable, ~~however.~~ However, the relevant general safety and performance requirements set out in Annex I to Regulation (EU) 2017/745 shall apply as far as the safety and performance of the device part of the ~~single~~ integral product ~~are~~ is concerned.

Examples of integral products which are not reusable are pre-filled syringes, pre-filled pens, nebulizers pre-charged with a specific medicinal product, patches for transdermal drug delivery and pre-filled inhalers.

~~An example of combinations which are not integral products is a vial containing a drug solution with an (empty) co-packaged syringe.~~

Some devices are not considered to form an integral product with the medicinal product and are treated as a container closure system e.g. nozzle on the top of the container for eye drops, syringe for reconstitution (without purpose for administration of the medicinal product) or can be treated as an excipient e.g. transdermal patches (using passive diffusion), in which case, they do not fall under the second subparagraphs of Article 1(8) or (9) MDR and hence, do not need to comply with Section 3.2., point 12, of Annex I of Directive 2001/83/EC, as amended by Article 117 MDR.

Note: the above examples are provided as a guide, however some devices could be classified differently due to additional features and functionality. If in doubt over the classification of your product as a

[medicinal product, device or drug-device combination, it is recommended that you consult a National Competent Authority \(NCA\).](#)

2.2. What is Article 117 and what does it mean for medicinal products? Rev. ~~Oct-2019~~[June 2021](#)

Article 117 of Regulation (EU) 2017/745 (~~amending~~[amends](#) Annex I to Directive 2001/83/EC, point 12 of section 3.2), [which now](#) requires that the [DDC](#) marketing authorisation ~~application for a integral-DDC should~~[dossier must](#) include, where available, the results of the assessment of conformity for the device [part](#) (i.e. the declaration of conformity ~~or~~ the relevant [EU](#) certificate issued by a notified body).

If the dossier does not include the results of the assessment of conformity, and ~~a~~[an](#) EU certificate from a notified body would be required if the device was used separately, then the applicant will be required to provide an opinion from a notified body on the conformity of the device part with relevant requirements of Annex I to Regulation (EU) 2017/745 as part of the ~~marketing authorisation application.~~[Marketing Authorisation Application.](#)

Article 117 applies to ~~medicinal products that form an integral product with a medical device, (also known as integral-DDC).~~[DDCs referred to under the second subparagraphs of MDR Articles 1\(8\) and 1\(9\).](#)

Article 117 does not apply in the case of combined advanced therapy medicinal products as defined under Article 2(1)(d) of Regulation (EC) No 1394/2007.

2.3. How will the ~~medical devices Regulation~~[MDR](#) and in particular Article 117 impact ~~new~~ marketing authorisation applications? Rev. ~~Oct-2019~~[June 2021](#)

Marketing authorisation applications for ~~an integral~~[a](#) DDC submitted as of 26 May ~~2020~~[2021](#), must demonstrate that the device part meets the relevant requirements of Annex I of Regulation (EU) 2017/745 as follows:

- If the device ~~component~~[part](#) has [a](#) CE marking, then the applicant ~~is expected~~[has](#) to provide, ~~where available,~~ a **Declaration of Conformity** or ~~the~~, ~~where applicable,~~ [an EU certificate issued by a notified body](#) ~~certificate designated for the type of device part in question,~~ allowing the manufacturer to affix CE marking to the device.
- If the ~~device part does not hold a CE marking and the~~ dossier does not include a declaration of ~~Conformity and~~[conformity or where applicable, an](#) EU [certificate issued by a](#) notified body ~~certificate and~~[designated for the type of](#) device ~~component is~~[part which has](#) a risk classification of sterile class I, measuring class I, class IIa, class IIb or class III medical device, then the applicant must provide an **opinion from a notified body** on the conformity of the device part with the relevant general safety and performance requirements set out in Annex I to Regulation (EU) 2017/745.

[Additional information may be requested during the review of the benefit/risk assessment of the medicinal product in order to ensure a safe and effective use of the DDC.](#)

Table 1. Summary of changes for **Marketing Authorisations Applications involving integral DDCs**

TypeRisk class of New submissions as of 26 th May 2020-2021 integral medical device included in the MAA	
Class I (sterile, measuring or reusable surgical instrument*), Class IIa, Class IIb Class III	The marketing authorisation dossier should must include a Declaration of Conformity or an EU certificate issued by a notified body certificatedesignated for the medical type of device, where available part in question. If the above-mentioned abovementioned documentation is not available then an opinion** from a notified body must be provided for the medical device.
Class I (non-sterile, non-measuring, or non-reusable surgical instrument)	The marketing authorisation dossier should must include a Declaration of Conformity for the medical device, where available.
* the reader should note that integral DDC as referred to in second subparagraph of Regulation 2017/745 Article 1(9) are not reusable	
**opinion on the conformity of the device part with the relevant general safety and performance requirements set out in Annex I to Regulation 2017/745	

2.4. When is it required to provide the ~~notified body opinion/ EU certificate~~ **declaration of conformity/ EU certificate issued by a designated notified body / notified body opinion with my Marketing Authorisation Application (MAA)? ~~Rev. Oct 2019~~ **June 2021****

Applications for a marketing authorisation of ~~an integral~~ a DDC submitted as of 26 May 2020-2021 must comply with the requirements of [Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by Article 117 of Regulation \(EU\) 2017/745.](#)

-The submission of evidence of compliance with the general safety and performance requirements of the MDR in the ~~MAA marketing authorisation dossiers~~ of integral DDCs as required under ~~Article 117 will the amended Directive 2001/83 do~~ not apply to ~~marketing authorisation applications~~ **MAAs** submitted before 26 May 2020, ~~2021, i.e. the date of application of the MDR.~~

2.5. At what stage of the MAA do I need to submit the notified body opinion? ~~Rev. June 2021~~

EMA/NCAs strongly recommend submitting the ~~EU certificate /~~ **EU certificate / notified body opinion** already ~~as part of in~~ the dossier of the initial marketing authorisation application for the medicinal product to facilitate a smooth running of the procedure. In case the applicant cannot provide the required documentation at the time of MAA submission, the ~~applicant relevant documents must be provided before an opinion on the medicinal product application can be issued. Applicants~~ should discuss ~~at the EMA/NCA pre-submission meeting~~ their plans to provide the required documentation ~~during the EMA/NCA pre-submission meeting.~~ The absence of the required documentation may result in additional clock stops during the procedure, ~~as the documentation is necessary for the adoption of a favourable CHMP opinion.~~

Questions & Answers on Implementation of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations ((EU) 2017/745 and (EU) 2017/746) Questions & Answers on Implementation Questions & Answers for applicants, marketing authorisation holders of medicinal products and notified bodies with respect to the implementation of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations EMA/321925/2021 [Rev.2](#)

2.6. How does Article 117 of the ~~medical devices regulation~~ MDR impact currently authorised ~~integral~~ DDCs? ~~Rev. Oct 2019~~ June 2021

Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by Article 117 of MDR, is not intended to apply retrospectively to ~~integral~~ DDCs already authorised or to those MAAs that have been ~~already~~ submitted prior to 26 May ~~2020~~ 2021.

However, if after the granting of the marketing authorisation there is a ~~substantial~~ change to the design or intended purpose of the device ~~component, (part)~~, or a new device is introduced, any required ~~certificate/~~ declaration of conformity ~~/NB / EU certificate / notified body~~ opinion should be submitted as part of the ~~variation/extension application, as~~ appropriate regulatory procedure to EMA/NCA (see also ~~Q0~~ Q2.7).

As for any other changes, the MAH should determine whether there is a potential impact on quality, safety and/or efficacy of the DDC. If the MAH determines that the change impacts the registered information, a variation application according to the variation guideline will be required. If the change does not impact the registered information but the MAH concludes that there is an impact on the quality, safety and/or efficacy of the DDC, a variation application must also be submitted. In cases where the need for a variation and/or the category of the change is unclear, it is recommended that the medicines competent authority that issued the marketing authorisation be consulted.

In line with the advice provided in the EMA Q&A for Post-authorisation procedural advice for users of the centralised procedure, given the relatively short timelines for variations procedures, the (new/updated) EU declaration of conformity / EU certificate issued by a designated notified body / notified body opinion for medical devices should be provided at the time of submission of the application to avoid any delays of the procedure.

2.7. Will I need to provide a (new or updated) EU ~~certificate~~ / declaration of conformity / EU certificate issued by a notified body / notified body opinion if there are changes to the device ~~submitted through a variation~~ / extension? (or device part) after the initial marketing authorisation of the Drug Device Combination? Rev. June 2021

~~There are two cases where a new or updated EU certificate / declaration of conformity / notified body opinion is needed.~~

Article 117 requirement applies post-authorisation to all marketing authorisations, irrespective whether ~~already compliant with Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by Article 117 MDR~~ at the time of the initial MAA, in case of changes that may affect the safety and performance of the device part or the intended use of the device. Contractual agreements between the MAH and the medical device manufacturer should ensure appropriate level of communication and action as regards changes to the device part. There are two situations where a (new or updated) EU declaration of conformity / EU certificate issued by a notified body / notified body opinion must be submitted in a post-authorisation setting of the medicinal product.

a) Addition or full replacement of the device ~~component~~ or device part

~~In cases where~~ Where a device ~~component of a an DDC will be~~ (or device part) is replaced or a new device ~~will be~~ is added ~~for applications submitted as of 26 May 2020~~, a new EU ~~certificate~~ / declaration of conformity / EU certificate issued by a notified body / notified body opinion ~~will need to~~ must be provided ~~as part of the variation/extension application, as appropriate.~~

~~This requirement applies to all marketing authorisations, including those already compliant with Article 117 MDR at the time of the initial MAA.~~

~~b) Substantial design changes to the device component~~

~~In cases where the MAH introduces substantial changes to the medical device component, a new (updated) EU certificate / declaration of conformity / opinion from a notified body will need to be provided as part of the variation/extension application, as appropriate.~~

~~Changes to the device component are considered substantial if the changes affect the performance and safety characteristics of the device.~~

~~It is the responsibility of the marketing authorisation holder to determine if the changes are substantial and EMA/NCAs expect that the MAHs liaise with the notified body and submit to EMA/NCA the necessary documentation as part of a variation/ or extension application.~~

~~This requirement applies to all marketing authorisations, even those that had complied with Article 117 MDR with their initial MAA.~~

~~If the variation does not affect~~ **b) Changes to the device or to a device part**

Where the medical device ~~then a new/~~manufacturer plans to introduce changes that may affect the safety and performance of the device part or the conditions prescribed for the intended use of the device part, there are three possible situations:

- **For devices covered under a manufacturer's EU declaration of conformity only (no involvement of a notified body):** the device part manufacturer is responsible to ensure compliance with the MDR, including changes to the device part. The EU declaration of conformity should be updated accordingly, if necessary.
- **For devices covered under an MDR EU certificate issued by a notified body:** if the assessment of changes leads to the issuance of a new/supplemented EU certificate according to the requirements established in the relevant annexes (Annexes IX, X, XI) of the MDR, the EU certificate must be provided as part of an appropriate post-authorisation regulatory procedure.
- **For devices holding a notified body opinion/ ~~certificate is:~~** if the assessment of changes lead to the issuance of a new notified body opinion, the new notified body opinion must be provided as part of an appropriate post-authorisation regulatory procedure.

Contractual arrangements between the notified body and the device manufacturer will address the information obligations and the assessment of changes to the device.

As for any other changes, the MAH should determine whether there is a potential impact on quality, safety and/or efficacy of the DDC. If the MAH determines that the change impacts the registered information, a variation application according to the variation guideline will be required. If the change ~~does not required~~ impact the registered information but the MAH concludes that there is an impact on the quality, safety and/or efficacy of the DDC, a variation application must also be submitted. In cases where the need for a variation and/or the category of the change is unclear, it is recommended that the medicines competent authority that issued the MA be consulted.

In line with the advice provided in the EMA Q&A for Post-authorisation procedural advice for users of the centralised procedure, given the relatively short timelines for ~~variation/extension~~ variations procedures, ~~for medical devices the documentation to support the CE mark or the~~ (new/updated) EU declaration of conformity / EU certificate issued by a designated notified body / notified body opinion for medical

devices should be ~~submitted as part of the documentation provided~~ at the time of submission of the variation/extension application to avoid any delays of the procedure.

2.8. Is it possible to submit a notified body certificate issued under the Directives (90/385/EEC or 93/42/EEC) to comply with Article 117? New June 2021

A medical device with a certificate that was issued in accordance with the Medical Device Directives 90/385/EEC or 93/42/EEC and which remains valid under the transitional provisions of Article 120(2) of the MDR, can still be submitted to support requirements of Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by Article 117 of the MDR.

Article 120(3) of the MDR provides for a transition period also for class I devices having a declaration of conformity that was drawn up prior to 26 May 2021 under the Directive 93/42/EEC and for which the conformity assessment procedure under the Regulation (EU) 2017/745 requires involvement of a notified body for the first time, the declaration of conformity can be accepted until 26 May 2024 to satisfy requirements of Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by Article 117.

2.9. How will the notified body opinion be reflected in the European Public Assessment Report (EPAR)? New June 2021

An EPAR provides public information on a medicinal product, including how it was assessed, and reflects the scientific conclusions of the EMA / NCA.

The EPAR will summarise information on the medical device part, relevant to the use with/of the medicinal product, whether a declaration of conformity or, where applicable, an EU certificate or a notified body opinion was submitted as part of the marketing authorisation application for the medicinal product. The applicant/MAH will be requested to identify information in the EPAR that is considered to be commercially confidential and to make a proposal including justifications for deletions/alternative wording. The notified body opinion itself will not be published separately.

2.8-2.10. What is the impact of the MDR ~~on medicinal products including an integral medical device for~~ and Article 117 on marketing authorisation applications of a DDC on a Mutual Recognition Procedure submitted on or after the 26 May ~~2020? New Oct-2019~~ 2021? Rev. June 2021

As the Mutual Recognition Procedure (MRP)/Repeat Use Procedure (RUP) is a new application for a marketing authorisation in the concerned ~~member states~~ Member States, the dossier must comply with the regulatory requirements applicable at the time of the MRP/RUP application. If the requirements have changed since the ~~national original National~~, Decentralised or Mutual Recognition procedure, then the dossier will need to be updated. Therefore, if ~~the an~~ application for ~~the MRP/RUP a DDC~~ is submitted in the MRP/RUP on or after 26 May ~~2020 and the authorisation includes an integral medical device 2021~~ then the General Safety and Performance Requirements (GSPR) of the MDR and Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by Article 117 of the MDR will need to be met apply and the applicable supporting documentation such as the ~~Declaration~~ declaration of ~~Conformity~~ conformity, certificate of conformity or notified body opinion ~~should~~ must be included in the dossier. **A**

Prior to the commencement of the MRP/RUP, a variation application is required to add a ~~new Notified Body Opinion,~~ declaration of conformity ~~or,~~ certificate of conformity or notified body opinion, to formally

update the [original](#) dossier ~~will be required~~ in the reference ~~member state~~ [Member State](#) and, where applicable, existing concerned ~~member states before the commencement of the Mutual Recognition/Repeat~~ [Member States](#).

2.11. Do the requirements of MDR Article 117 also apply to an application for medicinal products to be used outside of the European Union (Article 58 or EU-M4all)? Rev. June 2021

[EMA's Committee for Medicinal Products for Human Use](#) ~~procedure~~ [\(CHMP\)](#) assesses medicines and vaccines under Article 58 of [Regulation \(EC\) No 726/2004](#) to the same rigorous standards as medicines intended for use in the European Union. Therefore, the requirements of Annex I to Directive 2001/83/EC, point 12 of section 3.2, as amended by MDR Article 117 also apply by analogy to Article 58 applications (called EU-M4all).

Are the requirements for UDI (unique device identifier) applicable to integral DDCs? New Oct 2019

2.12. ~~No, if the~~ a medicinal product that incorporates, as an integral part, a medical device ~~is governed by?~~ Rev. June 2021

[A DDC falling under](#) the medicinal products legislation, ~~then does not have to meet~~ MDR obligations related to UDI ~~are not required and~~. [A device part related UDI](#) should [therefore](#) not be applied to the package of ~~the combination product. This is reflected~~ such a DDC. Additional information is provided in the [MDCG 2019-2 guidance on application of UDI rules to device-part of products referred to in Article 1\(8\), 1\(9\) and 1\(10\) of Regulation 2017/745](#).

~~Even if~~ [In cases where](#) the ~~integral~~ device [part of a DDC](#) is CE marked, ~~it is expected that the~~ [product](#) labelling for the integral DDC should follow the labelling requirements for medicinal products [as](#) outlined in the QRD (working group on Quality Review of Documents) templates. ~~For integral devices with a CE mark, the~~ [Where an](#) UDI ~~may be assigned to~~ [is already directly marked on](#) the device ~~itself, however the~~ [part, it does not need to be removed](#). [The](#) UDI should not appear on the labelling or outer package of the medicinal product.

3. Medicinal ~~product with~~ products that include a medical device in the secondary packaging of the marketed medicinal product (co-packaged-device)

3.1. How will the ~~implementation of the Medical Device Regulation~~ MDR affect the co-packaged medical device? ~~New Oct 2019~~ Rev. June 2021

~~Applicants~~ Applicants for marketing authorisations of medicinal products where a medical device (e.g. spoons, measuring cups, inhalers, spacers) is provided within the secondary packaging of the marketed medicinal product (i.e. co-packaged) and does not form an integral product with the medicinal product will need to ensure that their co-packaged medical device is CE marked in accordance with the relevant legislation on medical devices to continue placing the product on the market. ~~This also applies if a specific medical device is referenced in the SmPC.~~

- ~~Devices~~ Medical devices certified by a notified body can benefit from a ~~transition~~ transitional period provided for in MDR Article 120 ~~(2)(3)~~, which allows devices with a valid certificate under the ~~Medical Device Directive~~ Directives 93/42/EEC (~~MDD~~) and ~~Active Implantable Medical device Directive~~ or 90/385/EEC (~~AIMDD~~) to be placed on the market up to the latest ~~2726~~ **May 2024**, although ~~they~~ the medical device manufacturer will need to comply with certain requirements of the MDR from 26 May ~~2020~~ 2021 (see FAQ's published by the CAMD MDR/IVDR transition subgroup: [FAQs – MDR Transitional provisions](#)).
- ~~Self-declared~~ CE marked Class I devices must be in compliance with the MDR by ~~26 May 2020~~ **2021**. If your self-CE marked Class I device is up-classified by the MDR then the transition period provided for in MDR Article 120(3) is applicable.

3.2. What requirements for medical device labelling are applicable to medical devices "co-packaged" with medicinal products? New June 2021

Co-packaged products need to be distinguished from drug-device combinations that form a single integral product governed either by Directive 2001/83/EC or Regulation (EC) No 726/2004 or by Regulation (EU) No 2017/745 (see also Q2.1).

In the case of co-packaged products, the medical device must be in conformity with the MDR¹¹. This includes requirements regarding the information to be supplied with the device, which are part of the general safety and performance requirements laid down in Annex I of the MDR.

In accordance with Annex I, Chapter III, 23.1 (b) of Regulation (EU) 2017/745, the information required on the label of the medical device (e.g. CE marking, identification of the device, identification of the manufacturer (and, if applicable of the authorised representative), lot/serial number, UDI carrier etc.) should be provided on the device itself or on its own packaging.

The product information annexes (SmPC, labelling and package leaflet) of the medicinal product which is co-packaged with a medical device, should follow the requirements of Directive 2001/83/EC (see QRD (Quality Review of Documents) templates) and should not include any administrative information such

¹¹ In accordance with Article 120(3) and (4) of the MDR, certain devices that are covered by a valid declaration of conformity or certificate issued in accordance with Directive 90/385/EEC or Directive 93/42/EEC may be placed on the market during a transitional period ending on 26 May 2024 and be further made available on the market until 26 May 2025.

[as device manufacturer/ authorised representative, CE mark \(incl. NB number\), device symbols, UDI or references to device vigilance reporting that is provided on or with the medical device.](#)

[In accordance with Annex I, Chapter III, Section 23.1 \(d\) of Regulation \(EU\) 2017/745, instructions for use \(IFU\) for class I and class IIa are not required if such devices can be used safely without any such instructions and unless IFU are required by another provision in Section 23. If IFU are required, they should be provided together with the device.](#)

[Relevant information for the use of the co-packaged device, especially if necessary for the intended use of the medicinal product with the device should be included in the appropriate sections of the medicinal product package leaflet and SmPC, as applicable \(for details please refer to the SmPC guideline & the QRD \(Quality Review of Documents\) template\).](#)

[The MAH may itself be the manufacturer of the co-packaged medical device or assume the responsibility of the device manufacturer in accordance with Article 16\(1\)\(a\) of the MDR. In this case, the MAH is responsible for compliance with the MDR during the lifecycle of the device and only the contact details of the MAH needs to be provided.](#)

[Where the MAH is not the manufacturer of the co-packaged medical device, the medical device manufacturer remains responsible for compliance with the MDR during the lifecycle of the device and needs to be identified on the device label and/or IFU.](#)

[3.3. Do I need to submit a declaration of conformity / EU certificate as part of the dossier for a co-packaged medical device? New June 2021](#)

[It is the responsibility of the applicant/MAH to ensure that the medical devices co-packaged with the medicinal product meet the applicable general safety and performance requirements set out in MDR Annex I and are in compliance with the entirety of the MDR before the combined product is placed on the market.](#)

[For marketing authorisations of medicinal products co-packaged with a medical device submitted or approved prior to 26 May 2021, and where the dossier contains a CE certificate or declaration of conformity, it is not necessary to submit a variation to the marketing authorisation to replace the previous evidence of conformity with a new EU certificate or declaration of conformity in compliance with the MDR.](#)

[3.4. What actions, if any, do I need to take if my co-packaged device is up-classified and requires to be certified by a notified body for the first time? New June 2021](#)

[If the marketing authorisation includes a co-packaged medical device that did not require a notified body assessment under the Medical Device Directive \(MDD\) but will now require a notified body assessment under the MDR, there is a transition phase up until 26 May 2024 where the device may continue to be placed on the market if it continues to comply with the MDD, provided there are no significant changes in the design and intended purpose of the medical device. However, the requirements of the MDR with respect to post-market surveillance, market surveillance, vigilance and registration of economic operators of devices will apply.](#)

4. Consultation procedure for ancillary medicinal substances in medical devices (Art 1(8))

4.1. What type of consultation procedure needs to be submitted for an ancillary medicinal substance that has already been consulted under the medical device Directive 93/42/EEC? New June 2021

According to Article 52(9) MDR, as clarified by MDCG Guidance 2020-12 notified bodies are required to request a consultation with a medicine competent authority as part of the conformity assessment under the MDR for ancillary medicinal substances already consulted under the medical device Directive 93/42/EEC.

It is possible to take the opportunity of an upcoming variation to request an opinion in accordance with the MDR. Please consult the table below to determine whether a full initial consultation or a follow-up (variation) consultation should be submitted.

This guidance is only applicable to the EMA consultation. For nationally competent authorities (NCA) consultation, please refer to their national guidance or liaise with the NCA.

Table 1. EMA consultation for ancillary medicinal substances under MDR where a consultation already took place under the Directive 93/42/EEC

<u>Procedure type</u>	<u>Timetable</u>	<u>Conditions</u>	<u>Documentation</u>
<u>Type IA variation</u>	30 days	<u>Previous opinion issued by EMA</u> No change to device No change to ancillary No change to NB assessment or only 'administrative' changes	<ul style="list-style-type: none"> Full package including description of the manufacturing process and the data relating to the usefulness of incorporation of the substance into the device (according to section 5.2 Annex IX of the MDR)
<u>Type IB variation</u>	First phase 30 days (with possibility to RSI and assessment of responses up to 60 days)	<u>Previous opinion issued by EMA</u> Minor variation (as classified by analogy to Commission Regulation (EC) No 1234/2008) or / and change to NB's assessment of conformity (this includes where the NB is different to MDD consultation)	<ul style="list-style-type: none"> Declaration from manufacturer and NB detailing which elements are changed, if applicable
<u>Type II variation</u>	First phase 60 or 90 days (with possibility to RSI and assessment of responses up to 210 days)	<u>Previous opinion issued by EMA</u> Major variation (as classified by analogy to Commission Regulation (EC) No 1234/2008)	
<u>Full initial consultation</u>	up to 210 days	<u>A different CA has issued the previous opinion</u>	In addition to above: <ul style="list-style-type: none"> NCA opinion from previous consultation

