8 December 2025
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Combination Products Operational Group (COMBO)

Terms of reference

1. Background

The Regulation (EU) 2017/745 on medical devices (MDR), Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR) as well as the Directive 2001/83/EC on medicinal products for human use, and Regulation (EC) No 726/2004 for medicinal products for human use through the centralised procedure, establish specific requirements and consultation processes for products that combine medicinal product and medical device components (including in-vitro diagnostics) or are subject to certain requirements from both regimens.

In view of clarifying and streamlining practical aspects related to the application of the requirements and processes for combination products and medical devices consultation procedures, the EMA has established an operational group with representatives from national authorities and notified bodies i.e. the Combination Products Operational Group (COMBO).

Of note, throughout this document where the term 'device(s)' is used in a generic manner it should be understood as also including in vitro diagnostics.

2. Scope

Topics falling within the scope of this group should be related to products where a significant interplay exists between the legislation on medicinal products (Directive 2001/83/EC and Regulation (EC) No 726/2004 – (excluding combined advanced therapy medicinal products according to Regulation (EC) No 1394/2007) - and the legislation on medical devices (MDR or IVDR – (including medical devices referred in MDR annex XVI and accessories for medical devices[1]). Those products, referred hereafter as 'combination products', may be:

- medicinal products that form an integral product with a medical device (referred to in Article 1(8), 2nd subparagraph, or Article 1(9), 2nd subparagraph MDR that are subject to the

[1] See MDR Art. 1(4) and IVDR Art. 1(2)

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requirement laid down in Annex I section 3.2 point 12 of Directive 2001/83/EC as amended by Art 117 MDR - ('medicine with an integral device');

- medicinal products that include a medical device, including an in vitro diagnostic, in their secondary packaging - ('medicine with a co-packaged device');
- medicinal products in exclusive use with a medical device supplied separately, including in vitro diagnostics - ('devices referenced in the medicinal product information').
- medical devices incorporating with an ancillary medicinal substance (referred to in Article 1(8), 1st subparagraph, MDR that are subject to a consultation procedure with a medicines authority in accordance with Article 52(9) and Annex IX section 5.2 or Annex X section 6 MDR) – ('medical devices with an ancillary medicinal substance');
- companion diagnostics within the meaning of Article 2(7) IVDR that are subject to a consultation procedure with a medicines authority (in accordance with Article 48(3) or (4) and Annex IX section 5.4 or Annex X section 3, point (k) IVDR) – ('companion diagnostics');
- Medical devices composed of (a combination of) substances absorbed by or locally dispersed in the human body which devices, or their products of metabolism, are systemically absorbed by the human body in order to achieve their intended purpose, are subject to a consultation procedure with a medicines authority (in accordance with Article 52(11) and Annex IX section 5.4 or Annex X section 6 MDR) – ('substance based devices systematically absorbed').

3. Objectives

The COMBO aims to provide a regular forum for dialogue, sharing experiences, achieving mutual understanding, and reflecting on potential solutions on technical and procedural issues related to combination products and consultation procedures within the current EU legal framework. The COMBO group aims to complement, rather than duplicate, the work of other relevant bodies or groups, including the MDCG sub-groups. If the implementation of a solution to an issue discussed within COMBO falls within the mandate of another body or group, COMBO will transmit a summary of its discussion and conclusions to that body or group for its consideration and potential further action, when relevant.

The objectives of the COMBO are as follows:

1. Serve as a forum that brings notified bodies and regulators from both pharmaceutical and medical devices frameworks together to facilitate dialogue on technical and procedural aspects by providing direct, efficient and targeted channels of interactions regarding the combination products falling within the scope of the group.
2. Enhance mutual understanding and alignment of the respective regulatory frameworks, the roles, remit and assessments by regulators and notified bodies for the products and procedures in scope of this group, to help map issues;
3. Foster and explore potential solutions on identified issues, in the context of the current framework, in particular with the view to clarify and streamline processes and scope of activities;
4. Contribute to the development and/or update of guidance documents, templates and forms, as a result of potential solutions discussed by the group.

4. Composition

The COMBO aims to be a relatively small group to facilitate dialogue and solution-orientated exchange and consists of:

- 2 streams dedicated to combination products and consultation procedures respectively related to the implementation of the MDR and of the IVDR.
- representatives of the medical devices competent authorities (from relevant MDCG working groups), the medicinal products competent authorities (from EMA Working Groups and CMDh), and the Notified Body Coordination Group (NBCG-Med), nominated with expertise respectively for combination products and consultation procedures in the area of MDR and IVDR.
- relevant EMA staff including the chairperson, topic lead of the streams and participants *as per* agenda topics in relation to their involvement of respective combination products and consultation procedures in the area of MDR, IVDR and Directive 2001/83/EC.
- representatives of the European Commission from Directorate-General for Health and Food Safety, Unit in charge of Medical Devices.

To this end, the core members of the COMBO are appointed from the following organisational entities as follows:

Organisational entities	MD	IVD
EMA	4 representatives	3 representatives
Notified Body Coordination Group – NBCG-Med	4 representatives from different notified bodies	3 representatives from different notified bodies
Medicines Competent Authorities	4 representatives	3 representatives
Devices Competent Authorities - MDCG	4 representatives from MDCG	3 representatives from MDCG
European Commission	2-3 representatives from the European Commission (DG SANTE)	2-3 representatives from the European Commission (DG SANTE)

Nominations from authorities and notified bodies should ensure an adequate representation of different Member States.

The individuals nominated by the Notified Body Coordination Group (NBCG-Med) act as representatives of the NBCG-Med and are responsible for liaising with NBCG-Med to make sure to represent the views of notified bodies in general and to keep other notified bodies appropriately informed.

Notified bodies and Competent Authorities representatives can nominate an alternate that can act as proxy in case of needs. *Ad hoc* participation of other representatives of the core group stakeholders or representatives of other stakeholders is possible depending on the agenda topics.

Engagement with Industry stakeholders is foreseen through the Industry platforms meetings or, as appropriate, interested parties meetings.

5. Organisational matters

- **Roles and Responsibilities**

COMBO Chairperson: is responsible for the efficient conduct of the meetings, internal reporting and external reporting on the activities of the COMBO to the relevant fora (e.g. Scientific Committees, MDCG) where applicable. The COMBO Chairperson is a representative of EMA secretariat.

COMBO topic lead: there are 2 representatives of EMA secretariat nominated respectively for the MD and IVD streams. They are responsible for the meeting's agenda and minutes of the respective stream (MD and IVD) and can act as back-up chair for their assigned stream.

Core members: contribute to the achievement of the COMBO purpose and objectives and lead or contribute to specific activities identified in the workplan.

Alternates: receive both the agendas and minutes of each meeting and will be invited to participate in specific agenda items on an ad hoc basis, according to their field of expertise.

- **Other organisational aspects**

- The COMBO meets in principle quarterly. The annual frequency will be adapted depending on specific needs and priorities ranging from 2-4 meetings/yr.
- Topics of interest are captured in the COMBO workplan.
- Meeting draft agenda are circulated approximately 1 to 2 weeks in advance to all participants
- The highlight report will be prepared within 2 weeks of the meeting and will be endorsed by written procedure.
- Agendas and highlights of the meetings are published on the EMA website.
- Specific topic-driven focus groups could be organised to advance on certain priorities. Any topic-driven focus groups would report back to COMBO.
- The operation and composition of the COMBO is reviewed annually to take into account progress and need for the implementation of requirements and activities related to combination products and consultation procedures.
- The meeting secretariat and organisational support is provided by EMA.

6. Document history

The COMBO Terms of Reference will be reviewed at any time as required, particularly following changes in scope and role as well as evaluation parameters.

Document version	Month/Year	Changes
1.0	Dec / 2025	Initial version