Human Medicines Division
EMA/289031/2024

Business process description

Title: Referral procedures		
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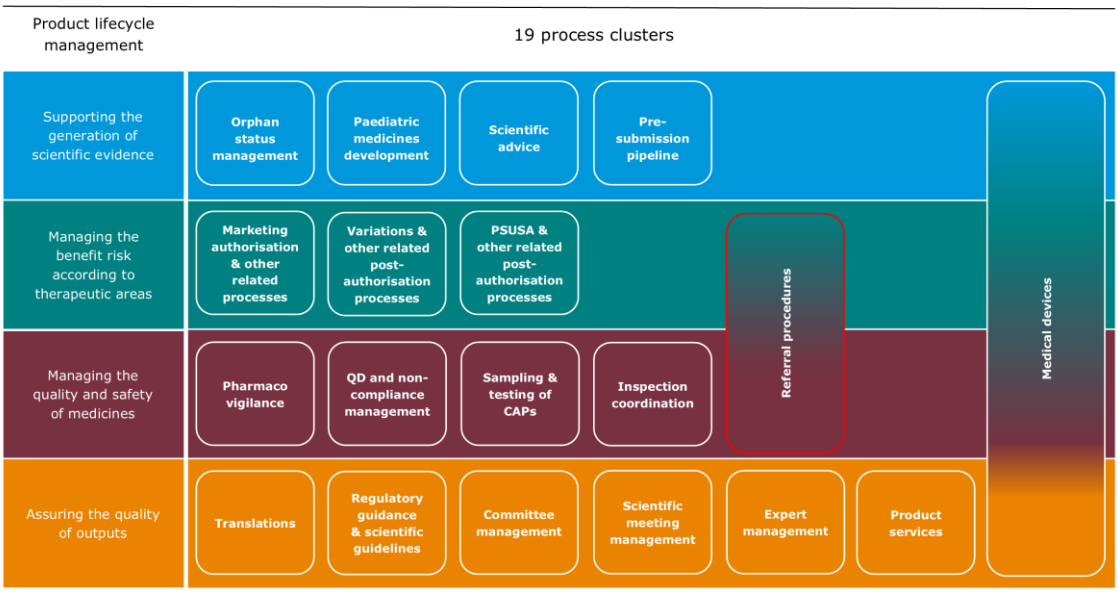
1. Introduction

The purpose of this document is to describe the high-level & end-to-end process for referral procedures on human medicines (Articles 29(4), 30, 31, 107i of Directive 2001/83/EC, Articles 5(3) and 20 of Regulation (EC) 726/2004, Article 13 of Commission Regulation 1234/2008, Article 29 of Regulation (EC) 1901/2006), which are used to resolve issues such as concerns over the safety, efficacy, quality, benefit-risk balance of a medicine or a class of medicines.

This process is part of the Human Medicines Division's process map (image below) which provides a high-level overview of the 19 process clusters within the operating model of the Human Medicines Division.

Human Medicines Division process map
Managing the product lifecycle and medical devices



Referral procedures:

Referral procedures on human medicines encompass both nationally authorised products and centrally authorised products as well as marketing authorisation applications. These procedures require the EMA to carry out a scientific assessment of the issue 'referred' to it, in relation to a particular medicine or class of medicines, or scientific matter, so that it can make a recommendation for a harmonised position across the EU.

2. Changes since last revision

New business process description

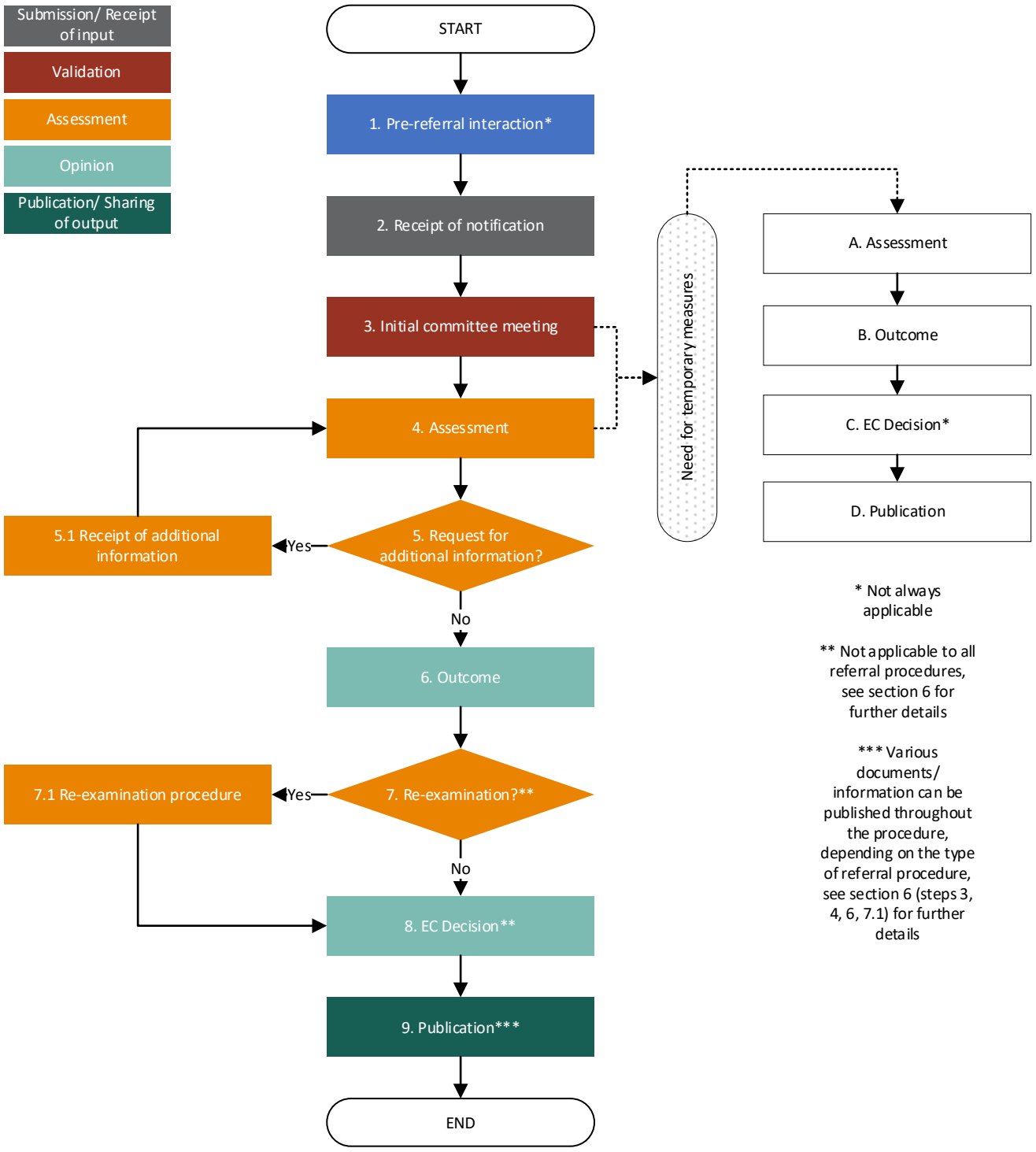
3. Related documents

- Referral procedures: human medicines
- Procedural advice on the re-examination of CHMP opinions

4. Abbreviations/Definitions

CAPs	Centrally authorised products
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - human
EC	European Commission
EEA	European Economic Area
EMA	European Medicines Agency
EPAR	European public assessment report
EU	European Union
MAH	Marketing authorisation holder
NAPs	Nationally authorised products
NCA	National competent authority
PRAC	Pharmacovigilance Risk Assessment Committee
PSUSA	Periodic safety update report single assessment
QD	Quality defect

5. Process map(s)



Note: Blue colour represents other steps of a process that are not covered by the above legend

6. Procedure

Step	Description
1.	**Pre-referral interaction** *Note: This step is not always applicable.*
2.	**Receipt of notification** • A notification or letter is received from the EC, any NCA in EU/EEA Member State, EMA, or the MAH/applicant to trigger a referral procedure.
3.	**Initial committee meeting** • The committee (PRAC or CHMP) adopts the relevant documents as applicable (e.g. list of questions to MAH(s), timetable) and the procedure starts. *Note:* *- If applicable, EMA publishes information at the start of the procedure on the EMA procedure webpage. This is not applicable to Article 29(4) of Directive 2001/83/EC, Article 13 of Commission Regulation 1234/2008, Article 29 of Regulation (EC) 1901/2006.* *- In exceptional cases, where urgent action is necessary to protect public health, temporary measures can be assessed (A) and adopted (B) by the committee in this step while the scientific assessment is ongoing and until a final scientific position is reached. The measures can be adopted in the context of referral procedures under Article 31, Article 107i of Directive 2001/83/EC and Article 20 of Regulation (EC) 726/2004, followed by an EC decision (C) if applicable. EMA publishes (D) information on the adopted temporary measures.*
4.	**Assessment** • Referral procedures resulting from the evaluation of data from pharmacovigilance activities are assessed by PRAC, which formulates a recommendation that is then transferred either to CHMP (if CAPs are concerned) or to CMDh (if only NAPs are concerned). • All other referral procedures are assessed by CHMP only. *Note:* *- If applicable, EMA publishes information during the assessment of the procedure on the EMA procedure webpage. This is not applicable to Article 29(4) of Directive 2001/83/EC, Article 13 of Commission Regulation 1234/2008, Article 29 of Regulation (EC) 1901/2006.* *- In exceptional cases, where urgent action is necessary to protect public health, temporary measures can be assessed (A) and adopted (B) by the committee in this step while the scientific assessment is ongoing and until a final scientific position is reached. The measures can be adopted in the context of referral procedures under Article 31, Article 107i of Directive 2001/83/EC and Article 20 of Regulation (EC) 726/2004, followed by an EC decision (C) if applicable. EMA publishes (D) information on the adopted temporary measures.*

Step	Description
5.	**Request for additional information?** Is there a request from the committee (PRAC or CHMP) for additional information? • If yes, go to step 5.1 • If no, go to step 6 *Note: The outcome must be reached within the legal timeframe, as applicable.* *In the context of referral procedures, the request for additional information is formally named list of questions or list of outstanding issues.*
5.1	**Receipt of additional information** • Once required information is received, go to step 4
6.	**Outcome** • For referral procedures resulting from the evaluation of data from pharmacovigilance activities, PRAC adopts a recommendation. This recommendation is transferred either to CHMP for adoption of an opinion (if CAPs are concerned) or to CMDh for adoption of a position (if only NAPs are concerned). • For all other referral procedures, CHMP adopts an opinion. *Note: EMA publishes the information on the recommendation/opinion on the EMA procedure webpage.*
7.	**Re-examination?** • If yes, go to step 7.1 • If no, go to step 8 *Note:* *- Referral procedures under Article 107i of Directive 2001/83/EC, Articles 5(3) and 20 of Regulation (EC) 726/2004, and Article 29 of Regulation (EC) 1901/2006 are not subject to a re-examination.* *- For referral procedures assessed by PRAC, re-examination procedure may occur after the PRAC recommendation. For other procedures, it may occur after CHMP opinion.*
7.1	**Re-examination procedure** At the end of the re-examination: • For referral procedures resulting from the evaluation of data from pharmacovigilance activities, PRAC adopts a final recommendation. This recommendation is followed by either a CHMP opinion (if CAPs are concerned) or a CMDh position (if only NAPs are concerned). • For all other referral procedures, CHMP adopts a final opinion. Go to step 8 *Note: EMA publishes the information on the recommendation/opinion after re-examination on the EMA procedure webpage.*

Step	Description
8.	**EC decision** • The EC decision is issued *Note: This step is not applicable to Article 5(3) procedures or referral procedures for which the CMDh position is adopted by consensus.*
9.	**Publication** • The final publication of documents relating to the outcome, and the EPAR revision if CAPs are concerned, are published on the EMA procedure webpage.