EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Procedure for liaising between the EMA, the CHMP and the CTFG on the potential CHMP negative opinion, pre-opinion or post-authorisation withdrawal, suspension or revocation of a Marketing Authorisation with impact on EU clinical trials		
Status: **PUBLIC**		Document no.: SOP/INSP/2033
Lead author	Approver	Effective date: 29-FEB-12
Name: Ana Rodriguez Sanchez Beato	Name: Fergus Sweeney	Review date: 28-FEB-15
Signature: On file	Signature: On file	Supersedes: n/a
Date: 24-FEB-12	Date: 24-FEB-12	TrackWise record no.: 3209

1. Purpose

Early dialogue between the Agency/CHMP (Co)-Rapporteurs/ Clinical Trials Facilitation Group (CTFG)/National Competent Authorities (NCA) is essential in case CHMP/(Co)-Rapporteurs identify safety issues or lack of efficacy that could lead to a regulatory action with potential impact on any ongoing/completed/future clinical trials.

These safety or lack of efficacy issues may be identified during the initial evaluation and could lead to a negative opinion or a withdrawal of a Marketing Authorization Application (MAA) or can be identified in the post-authorisation phase and lead to referral opinion, a suspension, revocation or withdrawal of a Marketing Authorization (MA), urgent safety restrictions or a negative opinion or a withdrawal for a variation or line extension

This dialogue should be maintained throughout the scientific review process through the Agency and its scientific committees up to the finalisation of the CHMP opinion and beyond (e.g. to address the complete removal of the medicinal product from the market or the lifting of the suspension of the marketing authorisation).

A procedure is therefore needed on the way to communicate between the Agency, the CHMP/Pharmacovigilance Working Party (PhVWP) and the CTFG/NCA and to clarify the scope, the roles and responsibilities of the people involved, the means to communicate, the nature of the information to be communicated and the steps to be taken to facilitate this communication.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

2. Scope

This procedure covers the communication between the Agency, the CHMP/PhVWP and the CTFG in the context of the centralised procedure or a referral during the following situations and when an impact on EU clinical trials is envisaged due to safety issues or lack of efficacy:

- Negative opinion or pre-opinion withdrawal of a MAA
- Negative opinion or pre-opinion withdrawal for a variation or line extension of a MA
- Suspension of a MA or lifting of a suspension of a MA
- Revocation of a MA
- Withdrawal of a MA
- Urgent Safety Restrictions

As consequence of these types of outcomes or regulatory actions, the CTFG/NCAs involved in the authorisation of clinical trials with the medicinal product/active substance concerned, may decide on the suspension, premature ending, modification of ongoing clinical trials, or preclude any new clinical trials from commencing.

Issues related to the quality of the Investigational Medicinal Product falls under the Quality Defects Procedure and therefore outside of the scope of this procedure.

3. Responsibilities

The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of section 9. The main key players to ensure that this procedure is adhered to are the PTMs in the P-CI-CNC section, the PTLs handling the procedure (H-SE and H-QM for centralised procedures and P-R-CP for referrals and Article 20 procedures) and the P-MI-PIN SH in the medical information sector.

4. Changes since last revision

New SOP.

5. Documents needed for this SOP

N/A

6. Related documents

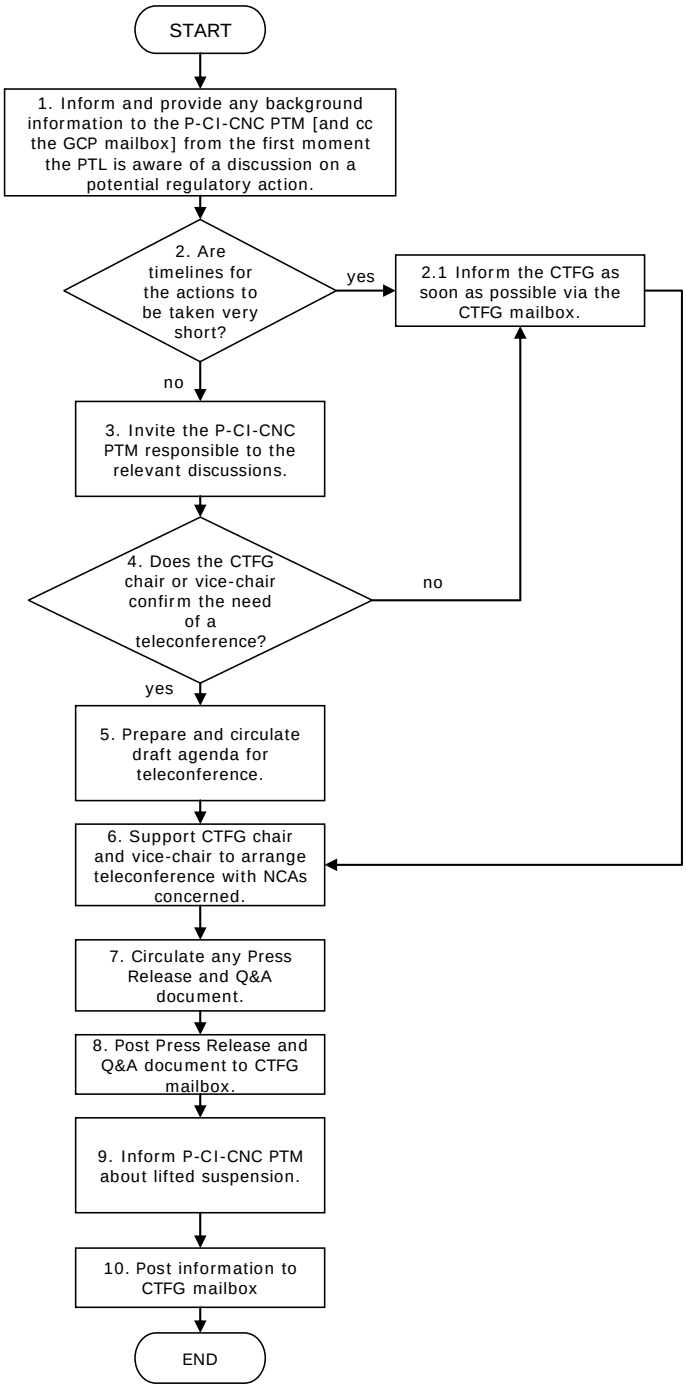
- SOP/H/3193 Master Files for referrals
- SOP/PDM/1004 Core master files of medicinal products for human and veterinary use following the centralised procedure
- SOP/H/3052 Urgent Safety Restrictions

7. Definitions

- CHMP Committee for Medicinal Products of Human Use
- CT Clinical trials

- CTFG Clinical Trials Facilitation Group
- EudraCT EU database on clinical trials
- H-QM Quality of Medicines Sector in the Human Medicines Development and Evaluation Unit
- H-SE Safety and Efficacy of Medicines Sector in the Human Medicines Development and Evaluation Unit
- MA Marketing authorisation
- MAA Marketing authorisation application
- NCA National Competent Authority
- P-CI-CNC Clinical and Non-clinical Compliance Section in the Patient Health Protection Unit
- PhVWP Pharmacovigilance Working Party
- P-MI-PIN Public Information and Stakeholders Networking Section in the Medical InformationSector
- PTL Product team leader handling the procedure (which leads to negative opinion, pre-opinion or post-authorisation withdrawal, suspension or revocation of a MA)
- PTM Product team member
- P-R-CP Community Procedures Section in the Patient Health Protection Unit
- SH Section Head

8. Process map(s)/ flow chart(s)



9. Procedure

Step	Action	Responsibility
1	Inform and provide any background information to the P-CI-CNC PTM [and cc the GCP mailbox (GCP@ema.europa.eu)] from the first moment the PTL is aware of a discussion on a potential regulatory action, as indicated below, due to safety issues or lack of efficacy: • Negative opinion or pre-opinion withdrawal of a MAA • Negative opinion or pre-opinion withdrawal for a variation or line extension of a MA • Suspension of a MA or lifting of a suspension of a MA • Revocation of a marketing authorisation • Withdrawal of a marketing authorisation • Urgent Safety Restrictions	PTL
2	Discuss the issue with the PTL /PTM-S/E for centralised procedures or P-R-CP PTL for referrals in order to have better understanding of the potential impact on EU clinical trials, the information to be requested to the MAH/applicant (e.g. list of their clinical trials ongoing, actions taken with respect to clinical trials and the communication to the NCAs concerned) and on the timelines for the actions to be taken in order to decide on the communication strategy to be followed: If the timelines the actions to be taken are expected to be very short (e.g. few days) or there is an urgency for immediate notification for serious safety reasons, proceed with step 2.1 If longer timelines are expected, because more discussion within the CHMP and/or with experts groups is recommended, proceed with step 3	P-CI-CNC PTM
2.1	Inform the CTFG as soon as possible via the CTFG mailbox (AllHumanCTFG@ema.europa.eu) and copy the PTL, P-MI-PIN SH Rapporteurs and GCP mailbox (GCP@ema.europa.eu). Include in that communication a report from EudraCT with the information on the clinical trials (commercial and non-commercial) ongoing with the product used as a test or comparator in order to estimate the impact that the regulatory action decided might have on the clinical trials running in the EU in conjunction with any additional background information provided by the PTL. Then continue from step 6 or 7, as applicable.	P-CI-CNC PTM
3	Invite the P-CI-CNC PTM responsible for that product to the relevant discussions held before the CHMP decides on the actions to be taken for its further communication to the CTFG.	PTL

Step	Action	Responsibility
4	Inform the CTFG chair and vice-chair about the matter of concern (including the EudraCT report mentioned in step 2.1) and discuss with them the need or not to set up a teleconference involving the Rapporteurs, the PTL, the P-CI-CNC PTM and other relevant people, as appropriate. If T-con is required, go to step 5 If T-con is not required, communicate to the CTFG as indicated in step 2.1.	P-CI-CNC PTM
5	Prepare and circulate to all parties involved in the teleconference a draft agenda which shall cover, among others topics, the following: • Update on the case and CHMP/PhVWP discussions • Impact on ongoing clinical trials • Communication to Member States & sponsors • Advice to investigators on patient discontinuation and treatment follow-up • Need for additional clinical data • Agreement on further communications (i.e. T-con as step 5 or via CTFG mailbox as step 2.1, as needed)	P-CI-CNC PTM
6	Support the CTFG in arranging further teleconference(s), for the chairman and vice-chairman to discuss the case directly with the NCAs concerned, for their decision making process on the actions to be taken with respect to the clinical trials ongoing at Member State level.	P-CI CNC secretary
7	Provide to the P-CI-CNC PTM any Press Release and Questions & Answers (Q&A) document about the case of concern.	P-MI-PIN SH
8	Post the information provided in step 7 in the CTFG mailbox (AllHumanCTFG@ema.europa.eu) for information and cc GCP mailbox (GCP@ema.europa.eu).	P-CI-CNC PTM
9	Inform the P-CI-CNC PTM when a suspension of a MAA is lifted.	PTL
10	Post that information in the CTFG mailbox (AllHumanCTFG@ema.europa.eu) and cc GCP mailbox (GCP@ema.europa.eu).	PC-I-CNC PTM

10. Records

The product mailbox will be copied in all correspondence reflecting this communication to ensure that records of these exchanges are maintained. Product related information will be saved in the respective product folder/referral folder in DREAM as normal practice.