



**PROCEDURE FOR REVIEW OF INFORMATION ON MEDICINAL PRODUCTS
BY PATIENTS' AND CONSUMERS' ORGANISATIONS**

1. Introduction

The European Medicines Agency (EMA) is responsible for providing information about medicines authorised via the centralised procedure. This includes information directed to the patient or the public, such as the Package Leaflet (PL) and the EPAR (European public assessment report) summary.

- The PL is supplied to the patient in the package in which the medicinal product is contained, and provides information related to the use of the medicine.
- The EPAR summary is a lay-language document, available on the EMA website, which contains general information about the medicine. It also provides a summary of the grounds on which the EMA based its recommendation for the medicine to receive a marketing authorisation.

Both documents are prepared during the course of the procedure for evaluating the marketing-authorisation application for a medicine. This procedure follows specific deadlines and must take into account some confidentiality matters.

As expressed in the 'Framework on the Interaction between the EMA and Patients' and Consumers' Organisations' ([EMA/354515/2005](#)), to ensure that the Agency provides information in a way that fulfils patients' and the general public's expectations, the EMA needs to set up adequate consultation with patients' and consumers' organisations (PCOs).

This document describes the procedures for involving PCOs during the EMA review of the PLs and EPAR summaries.

The EMA Medical Information Sector (MIS) will organise procedures for the quality-review of product information, including the PL, and for the preparation of EPAR summaries as part of its responsibilities for interacting with PCOs.

2. Background

Articles 78(1) and 78(2) of Council Regulation (EC) No 726/2004 provide a mandate for the EMA to develop interaction with PCOs:

1. *"The Management Board shall, in agreement with the Commission, develop appropriate contacts between the Agency and the representatives of the industry, consumers and patients and the health professions. These contacts may include the participation of observers in certain aspects of the Agency's work, under conditions determined beforehand by the Management Board, in agreement with the Commission."*

2. “The committees referred to in Article 56(1) and any working parties and scientific advisory groups established in accordance with that Article, shall in general matters establish contacts, on an advisory basis, with parties concerned with the use of medicinal products, in particular patient organisations and health-care professionals’ associations. Rapporteurs appointed by these committees may, on an advisory basis, establish contacts with representatives of patient organisations and health-care professionals’ associations relevant to the indication of the medicinal product concerned.”

The EMEA/CHMP Working Group with Patients Organisations (forerunner of the Patients’ and Consumers’ Working Party) recommended that feedback be sought from patients on the readability of information contained in package leaflets, public statements and similar materials intended for the public.

3. Proposed scope of interaction

The procedure to consult PCOs during the preparation of PLs and EPAR summaries follows a stepwise approach.

For the time being, it is proposed to focus on the clarity and understandability of the English versions of PLs and EPAR summaries. At a later stage, and based on the experience gained, consideration will be given to involving patients in the review of translated versions of these documents, as well as to the review of other documents addressed to the public, such as the question-and-answer documents published at the time of withdrawal or refusal of a marketing-authorisation application.

For over a year, a procedure has been in place for PCOs to review the PLs of those medicines for which a renewal application has been submitted (i.e. five years after the initial authorisation was granted). Further to the positive experience acquired with this procedure, it is now proposed to extend the scope to include the review of PLs for *new* medicines, i.e. those for which an initial marketing authorisation is being sought¹.

As for EPAR summaries, PCOs will continue to be involved in the review of those for newly authorised medicinal products, as has been the case since the procedure was initiated over a year ago.

Retrospective feedback on published EPAR summaries – in all linguistic versions – is encouraged from PCOs on a voluntary basis.

The purpose of the consultation and interaction between the EMEA and PCOs is not to rewrite the documents, but to ensure that the information is clear and understandable by the target audience, and that it fulfils their needs in terms of information content.

4. Procedural principles for the interaction

Organisations and experts to be involved

- Any organisation that is consulted must fulfil the ‘Criteria to be fulfilled by Patients’ and Consumers’ Organisations’ ([EMEA/14610/04/Final](#)) and be listed in the EMEA’s approved list of eligible organisations (See: <http://www.emea.europa.eu/Patients/organisations.htm>).
- The ‘Rules of involvement of member(s) of Patients’ and/or Consumers’ Organisations in Committees related activities’ ([EMEA/161660/2005](#)) will apply. Since patients will act as experts in these procedures, they will have to adhere to the same rules as all other experts

¹ It should be specified that only complete/stand-alone applications and fixed-combination applications as per Article 8(3) and Article 10(b) of Consolidated Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use, as amended by Directive 2002/98/EC, Directive 2004/24/EC and Directive 2004/27/EC, will be subject to review.

participating in EMEA activities, especially with regard to confidentiality undertaking, and they will have to adhere to the EMEA Code of Conduct.

- Since the documents to be reviewed are in English, experts should be fluent in English. In addition, they should have access to appropriate information-technology equipment and to the Internet.

Identification of a list of experts

- Every organisation fulfilling the criteria for involvement in EMEA activities will be invited to designate experts for review of documents. After consideration, the EMEA will nominate them as EMEA experts and they will be included in the Agency's database of European experts. As far as possible, for consistency and efficiency reasons, each organisation should nominate one of their members as a coordinator.
- The coordinator will be responsible for collecting comments from the expert (or experts) within their own organisation. The coordinator will also have the responsibility of ensuring that experts from their organisation adhere to the above-mentioned rules, in particular with regard to confidentiality undertakings and declarations of interests.
- The EMEA will prepare a list of nominated PCO experts, identifying the coordinator for each organisation, as well as the area of expertise of each expert, if relevant.
- This list will be updated according to organisations' proposals, as necessary.

Consultation process

- For each document to be produced, the EMEA will consult an organisation that specialises in the therapeutic area of the product, if one is available from the previously identified list. If there is no specialised organisation available, a general organisation will be consulted. If there is more than one organisation having expertise in the field, the EMEA will select which organisation to consult on a rota basis. Experts who have participated in specific training organised by the EMEA will be preferred.
- The EMEA will send the request for review to the coordinator.
- When providing comments to the EMEA, the coordinator will have to identify the expert(s) having participated to the review.
- The EMEA will organise only one round of consultation and will ensure processing of the comments as part of EMEA marketing-authorisation procedures. The final version will be circulated for information to the organisation having participated.
- The EMEA will monitor the PCOs' input in these reviews and will provide regular feedback to the Patients' and Consumers' Organisations Working Party (PCWP).
- The EMEA will organise training sessions on a regular basis in order to introduce the procedure to the nominated experts. Preference for attending the training sessions will be given to those recently added to the list of experts.

5. Implementation

For each type of document, the specific procedure is annexed.

The procedure for review of EPAR summaries and PLs at the time of renewal was initially implemented in May 2007, following the constitution of the PCWP, identification of the list of experts for review of product information, and the organisation of initial training on reviewing procedures.

Implementation of the extended procedure to include review of the English-language (EN) versions of the PLs of new medicines at the time of initial evaluation for marketing authorisation is expected to begin in the third or fourth quarter of 2008.

Annex I
Procedure for review of PL

1. Package Leaflet

The Package Leaflet (PL) is part of the product information that is approved at the time of marketing authorisation by the regulatory authority. It is initially prepared by the applicant (pharmaceutical company), when requesting a marketing authorisation. The PL is prepared in accordance with legal requirements, as well as with EMEA templates and guidance.

For centrally authorised medicines, the EMEA reviews the PL proposed by the company at the time of initial evaluation for marketing authorisation and after the commercialisation of the product. During EMEA reviews, scientific and linguistic amendments are proposed by assessors, and the quality and content of the PL are deeply scrutinised prior to finalisation of the product information by the EMEA's relevant scientific committee, the Committee for Medicinal Products for Human Use (CHMP).

2. Initial marketing-authorisation procedure

The EMEA is responsible for the centralised procedure. This procedure results in a single marketing authorisation that is valid across the European Union, as well as in Iceland, Liechtenstein and Norway. The marketing-authorisation applicant (pharmaceutical company) shall submit a consolidated dossier on the medicine to be authorised, including a proposal for the English version of the PL. This dossier is evaluated by the Agency's relevant scientific committee (CHMP) within 210 days, at the end of which the committee adopts an opinion on whether the medicine should be marketed or not. This opinion is then transmitted to the European Commission, which issues a formal decision on the authorisation of the product.

In parallel to the scientific assessment, the EMEA and its Quality Review of Documents (QRD) group perform a linguistic review of the English version of the PL between Days 121-165 of the assessment procedure (before the CHMP gives a final opinion).

Upon receipt from the company of an EN PL at Day 121, the EMEA forwards it to all QRD members for comments (via written procedure) within 15 days. The consolidated comments are sent to the company by Day 157 for implementation.

In order to make the EMEA/QRD review more transparent, and to allow for direct dialogue with the applicant, the procedure foresees the possibility of a meeting at the EMEA around Day 165 (EMEA QRD sub-group meeting). At such meeting, the EN product information (summary of product characteristics, PL and labelling) will be reviewed by 2-3 EMEA representatives and 2 QRD representatives, with the (optional) participation of 1-2 company representatives. Such review should focus on linguistic, stylistic and template-related issues, and will also verify whether the proposed EN text is suitable for translation.

3. Renewal procedure

A Community marketing authorisation is initially valid for five years, and may be renewed after this period on the basis of a re-evaluation of the risk-benefit balance by the CHMP. To this end, the marketing-authorisation holder (pharmaceutical company) shall submit a consolidated dossier on the medicine, including a revised proposal for PL. This dossier must be assessed within 90 to 120 days by the CHMP before the marketing authorisation expires. This procedure is called the 'renewal procedure'.

In parallel to the scientific assessment, the EMEA and its QRD group perform a linguistic review of the English version of the product information. Linguistic comments are consolidated and sent to the pharmaceutical company by Day 75 of the procedure.

4. Patients' and consumers' organisations

The purpose of the consultation and interaction between the EMEA and PCOs is not to rewrite the document, but to confirm that the information is clear and understandable by the target audience, and that it fulfils the public's needs in terms of information content. It is acknowledged that the PL of every medicine undergoes a readability testing by target patient groups by Day 120 of the evaluation procedure (Articles 59(3) and 61(1) of Council Directive 2001/83/EC, as amended by Directive 2004/27/EC). The current procedure does not intend to be a repetition of it. In addition, it allows for review later in the evaluation procedure, and after various changes have been made in the text.

a. Review of PLs at the time of initial evaluation for marketing authorisation

It is proposed that PCOs experts perform the review in parallel to QRD members, i.e. within 15 calendar days after receipt of the proposed English version of the PL at Day 125 of the procedure. The compilation of comments will be performed for both groups (QRD members and PCO experts) at the same time. A compiled version will be sent to the company by Day 157.

At the request of the EMEA, and depending on the comments received and the issues to be discussed, PCO experts may be invited to participate in the EMEA QRD sub-group meeting to be held at Day 165.

The documentation will be exchanged by e-mail (via a secure system called Eudralink), and comments should be made clear by using track changes mode (without modifying the original text).

The procedure would be as follows:

- Start of the evaluation procedure (Day 1).
- EMEA Medical Information Sector (MIS) will provide the PL to be reviewed to the coordinator of the selected organisation at Day 125 of the procedure.
- The coordinator will organise the review and send back comments to MIS within 15 days after receipt of the document.
- QRD will validate comments and transmit them to the applicant, without naming the organisation, upon receipt, by Day 157.
- PCO experts will be informed by then if an EMEA QRD sub-group meeting is to be held, and if their participation is requested.
- The CHMP will adopt the PL as part of its opinion by Day 210.
- The final PL will be sent to the coordinator of the reviewing organisation for information.

b. Review of PLs at the time of the renewal of a marketing authorisation

It is proposed that PCO experts perform the review in parallel to QRD members, i.e. within 15 calendar days. The compilation of comments will be performed for both groups (QRD members and PCO experts) at the same time, i.e. by Day 75.

The documentation will be exchanged by e-mail, and comments should be made clear by using track changes mode.

The procedure would be as follows:

- Start of the renewal procedure.
- EMEA Medical Information Sector (MIS) will provide the PL to be reviewed to the coordinator of the selected organisation.
- The coordinator will organise the review and send back comments to MIS within 15 days after receipt of the document.
- QRD will validate comments and transmit them to the applicant, without naming the organisation, upon receipt, by Day 75.
- The CHMP will adopt the PL as part of its opinion.

- The final PL will be sent to the coordinator of the reviewing organisation for information.

Annex II

Procedure for review of EPAR summary

1. EPAR summary

When a marketing authorisation is granted for a medicine, the EMEA publishes a European public assessment report (EPAR). The EPAR provides a comprehensive summary of available data on the quality, safety and efficacy of the product, justifying its marketing authorisation. The EPAR also includes a summary written in a manner that is understandable to the public.

The EPAR and the EPAR summary have to be prepared within 70 days of a CHMP positive opinion being adopted, to be available at the time of the marketing authorisation.

The first draft of the EPAR summary is prepared by the EMEA, within the Medical Information Sector, immediately after the CHMP opinion. According to the internal procedure for the preparation of EPAR summaries, the first draft prepared by the Medical Information Sector is sent for consultation first to CHMP and EMEA project managers (10 days), and then to the applicant (5 days). The EPAR summary is finalised within about one month, and has to be adopted by the CHMP as part of the full EPAR. Finally, the EPAR summary has to be translated into all official EU languages before publication.

2. PCO experts review

The purpose of the consultation and interaction between EMEA and PCOs is not to rewrite the document, but to ensure that the information is clear and understandable by the target audience, and that it fulfils their needs in terms of information content.

It is proposed to consult PCOs at the same time as the CHMP Rapporteur/Co-Rapporteur and EMEA project managers, i.e. the 10-day consultation that takes place approximately between Day 10/15 and Day 20/25 following the CHMP opinion.

Given the short timeframe, the documentation will be exchanged by e-mail, and comments should be made as clear as possible.

The procedure would be as follows:

- CHMP opinion (Day 0).
- The EMEA Medical Information Sector (MIS) will provide the document to be reviewed to the coordinator of the selected organisation (Day 10/15).
- The coordinator will organise the review and send back comments within 10 days after receipt of the document (Day 20/25).
- The Medical Information Sector will implement the comments together with those received from other parties.
- The revised EPAR summary will be proposed for adoption to the CHMP (around Day 30).
- The final EPAR summary will be sent to the coordinator of the reviewing organisation for information.