EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Stakeholders and Communication Division

Training Manual

Review of EMA documents addressed to the general public, by patients and consumers

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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1. Introduction

The initiative proposing the involvement of patients and consumers in the review of package leaflets (PL) and summaries of the European Public Assessment Report (EPAR) originates from the Recommendations and Proposals for Action (EMA/149479/2004-Final) of the European Medicines Agency/CHMP Working Group with Patients' Organisations. This recommended that feedback be obtained from patients and consumers on the readability of information that is specifically addressed to patients and the general public. This exercise was extended to also include the review of the Agency's safety communications from 2010.

This training manual contains all the relevant information you might need as a patient expert to review PLs, EPAR summaries and safety communications. It also includes an introduction to the activities of the European Medicines Agency (EMA).

Detailed information about the EMA, the involvement of patients and consumers in its activities, including the Working Party with Patients' and Consumers' Organisations (PCWP), is also available on our website: http://www.ema.europa.eu.

2. The European Medicines Agency (EMA)

Marketing authorisations and renewals

The European Medicines Agency is an agency of the European Union (EU), located in London. The Agency is responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the EU (the "centralised procedure"). Under the centralised procedure, companies submit a single marketing authorisation application to the Agency and, once granted by the European Commission (EC), the authorisation is valid in all EU Member States.

All medicines derived from biotechnology and other high technology processes must be approved via the centralised procedure. The same applies to all medicines intended for the treatment of AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions, and other viral diseases, as well as all designated orphan medicines intended for the treatment of rare diseases.

The Agency's Committee for Medicinal Products for Human Use (CHMP) reviews the marketing authorisation applications. For each application two members of the Committee (the "Rapporteur" and "Co-rapporteur") lead the work. The Committee assesses whether the benefits of the medicine outweighs its risks and based on this evaluation, the CHMP will recommend or not, the authorisation of the medicine. The CHMP recommendation is transmitted to the EC, which may then grant a marketing authorisation based on the Committee's opinion.

At the time of marketing authorisation, the Agency publishes a European Public Assessment Report (EPAR) for the medicine. The EPAR reflects the scientific conclusions reached by the CHMP at the end of the evaluation process. It contains an **EPAR summary** written in a manner that is understandable to the public, and the product information.

The product information includes three key documents:

- **Summary of product characteristics (SmPC)** which summarises the characteristics of the medicine and provides information on the product. The SmPC is addressed to prescribers and pharmacists. The SmPC forms the basis of:
- **Package leaflet**, which contains information addressed to the patient;
- **Labelling**, the information appearing on the labels and containers.

EU law regulates the way in which these documents are written and presented. The information is initially proposed by the pharmaceutical company, written according to official templates, and then assessed and revised as part of the marketing authorisation application by the CHMP and the QRD[1].

A marketing authorisation is usually valid for five years, and may be renewed on request of the company on the basis of a re-evaluation of its benefits and risks. A renewal dossier, submitted with an update of the product information, is evaluated by the CHMP who will issue an opinion recommending or not, the renewal.

If renewed, the marketing authorisation is usually valid for an unlimited period. However, the CHMP may decide to grant a renewal for a further five years, requesting that a further renewal procedure is carried out after this time period.

EMA Glossary (terms and abbreviations)

[1] The Working Group on the Quality Review of Documents (QRD) is composed of representatives from Member States' national authorities, the European Commission and the European Medicines Agency.

3. Review of EMA documents by patients and consumers

3.1 Introduction

The EMA is responsible for providing information about medicines authorised via the centralised procedure which includes information directed to patients and the public. During the preparation of this information the Agency interacts with patients and consumers to ensure that it is adequately formulated and comprehensible to the target audience.

The package leaflet (PL) is supplied to the patient in the package in which the medicine is contained, and provides information related to the use of the medicine.

The EPAR summary is a lay-language document, which provides a summary of the grounds on which the EMA/CHMP based its recommendation for the medicine to receive a marketing authorisation.

Safety communications refer to documents which are specifically addressed to the public once a medicinal product has been authorised and which convey an important (emerging) message relating to the product (e.g. a product is withdrawn or suspended for safety reasons, has a new contraindication or warning, or there is a product defect).

This document describes the procedures for involving patients/consumers in the review of PLs and EPAR summaries and in the preparation and dissemination of Agency safety communications.

3.2 Proposed scope of interaction

The purpose of the consultation between the EMA and patients/consumers on these documents is not to rewrite them but to ensure that the information is clear and understandable by the target audience.

3.3 Procedural principles for the interaction

Organisations and experts to be involved

Any organisation that proposes patient experts to review the above mentioned documents must fulfil the Criteria to be fulfilled by patients' and consumers' organisations (EMA/MB/24913/2005 rev. 1) and be listed in the EMA's list of "eligible organisations" on our Patients and consumers' webpage.

The Rules of involvement of member(s) of patients' and/or consumers' organisations in committees related activities' (EMEA/483439/2008 rev. 1) will apply. Patient experts should adhere to the same rules as all other experts participating in EMA activities, especially with regard to confidentiality.

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

Identification of a list of experts

All of the EMA eligible patient/consumer organisations are invited to propose experts for participation. Once they have completed the relevant paperwork, they can be included in the Agency's European expert database. Additional experts may be proposed whenever necessary.

Where appropriate, each organisation should nominate a coordinator who will be the initial reference contact point between the EMA and the organisation and will have the responsibility of ensuring that experts from their organisation adhere to the above-mentioned rules.

Consultation process

For each document produced, the EMA will consult experts within one of the eligible organisations that specialises in the therapeutic area of the medicine. If there is no specialised organisation available, general organisations will be consulted. If there is more than one organisation having expertise in the field, the EMA will select which organisation(s) to consult. Experts who have participated in specific training organised by the EMA will have preference.

The EMA will send the request for review to the coordinator. When providing comments to the EMA, the coordinator should identify the expert(s) having participated to the review.

The selected patient expert(s) may discuss the document with other experts within their organisation, however all experts consulted must have signed the confidentiality undertaking in advance.

The EMA will organise only one round of consultation and will ensure processing of the comments as part of EMA procedures. The final version will be circulated for information to the organisation having participated.

The EMA will monitor the patients/consumers input in these reviews and will provide regular feedback to the PCWP.

Training

All nominated experts will be invited to attend training sessions at the EMA; preference for attending these sessions will be given to those recently added to the list of experts. Outside of the training sessions, all training material will be provided to new experts.

Confidentiality

All documents subject for review and covered in this procedure are confidential (i.e. PLs, EPAR summaries and safety communication material) until they are made public. All experts must have signed a confidentiality undertaking at the time of being involved in the review.

4. Procedure for review of 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, in accordance with legal requirements, as well as with EMA/EC templates and guidance.

For centrally authorised medicines, the EMA reviews the PL proposed by the company at the time of initial evaluation and after the commercialisation of the medicine. During EMA 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 medicine's information by the EMA's scientific committee - the Committee for Medicinal Products for Human Use (CHMP).

Patient experts review

The purpose of the consultation between the EMA and patient experts is not to rewrite the document, but to ensure that the information is clear and understandable by the target audience, and that it fulfils the public's needs in terms of information content.

Patient experts perform the review in parallel to QRD members; thereafter the comments are compiled and sent to the company.

The documentation will be exchanged by e-mail (via a secure system called Eudralink) with any comments made preferably using track changes mode or comment boxes.

The procedure for reviewing new PLs is as follows:

- Depending on the therapeutic area of the product, the EMA will either :

  a) send the PL for review to the coordinator of an organisation specialised in this area with a deadline of approximately 10-15 calendar days, or

  b) if there is no specialised organisation, an email will be sent to all organisations requesting availability for the review of the PL. Once an organisation has responded, EMA will provide the PL for review with a deadline of approximately 10 days.
- The Patient expert will perform the review and send any comments to EMA within the deadline.
- EMA/QRD will validate comments and transmit them to the applicant, without naming the organisation.
- The CHMP will adopt the PL as part of its opinion.
- The final PL will be included within the 'human medicines highlights' which is published on the EMA website each month.

The procedure for evaluating renewal PLs is the same as for new applications (above), apart from the overall application timeline (days) which are shorter, but which does not affect the review time for the PL.

5. Procedure for review of an EPAR summary

When a marketing authorisation is granted for a medicine, the EMA 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 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 EMA immediately after the CHMP opinion and is sent for review to the EMA project managers, then to CHMP (Co)-Rapporteurs and the patient experts, and finally to the applicant. The EPAR summary is finalised within about one month, and has to be adopted by the CHMP as part of the full EPAR. Finally, it is translated into all official EU languages before publication.

Patient experts review

The purpose of the consultation between EMA and patient experts is not to rewrite the document, but to ensure that the information is clear and understandable by the target audience.

Patient experts will be consulted at the same time as the CHMP Rapporteur/Co-Rapporteurs and the documentation will be exchanged by secure e-mail (Eudralink system).

The procedure is as follows:

- Following an adopted opinion on a medicine, the EMA will prepare a draft EPAR summary.
- Depending on the therapeutic area of the product, the EMA will either:

  a) send the draft EPAR summary for review to the coordinator of the selected organisation with a deadline of approximately 10 calendar days, or

  b) if there is no specialised organisation, an email will be sent to all organisations requesting availability to review the draft EPAR summary. Once an organisation has responded, they will receive the PL for review with the remaining deadline.
- The Patient expert will perform the review and send any comments (preferably using track changes mode or comment boxes) to the EMA within the deadline.
- The EMA will implement the comments where possible, together with those received from other parties.
- The final EPAR summary, together with feedback on any comments, will be sent to the reviewer for information.

6. Procedure for review of safety communications

Safety communications concern authorised medicines and tend to relate to major safety issues: withdrawal or suspension of a medicine from the market, new contraindications or warnings, restriction of use or product defects leading to safety concerns.

Safety communications often relate to 'referral' procedures. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of the safety concern for the EU. The EMA communicates on safety referrals at different stages of the procedure and patient experts will be involved in the review of all related communications.

Preparation of safety communications implies short timelines with limited predictability but at the same time needs to take into account views of many stakeholders. The procedure involves multiple stages of review and input from internal and external experts. Once finalised safety communication are published on the Agency website. The final version may differ substantially from the initial draft reviewed.

It is not initially proposed to include the review of documents on withdrawals or refusals of applications unless patients or consumers have been involved in the medicine's benefit/risk evaluation (during evaluation).

Patient experts review

The purpose of the consultation and interaction between EMA and PCOs on safety communications is to ensure that the message to be conveyed is clear and comprehensible to its targeted audience.

Patient experts will be consulted at the same time as or after the CHMP Rapporteur/Co-Rapporteurs and the documentation will be exchanged by secure e-mail (Eudralink system).

The procedure is as follows:

- When the EMA is aware of an upcoming safety concern, it will contact the selected organisation(s) requesting availability to review the related communication, indicating the expected timelines.
- As soon as a draft document is available it will be forwarded to the selected expert(s), usually giving 12-24 hours to provide comments on the text, however in some urgent cases only 3-4 hours may be available for consultation.
- The expert(s) are welcome to contact the EMA for further discussion or clarification on the specific issues and in some cases; particularly when timelines are tight, comments may be given via telephone.
- The reviewer will receive a link to the final document at the time of publication for dissemination within the organisation and to any other interested parties - no confidentiality applies at this stage, as the document is published on the EMA website.

7. Technical requirements

The documents sent for review by the Agency are in Word format. The expert is asked to insert his/her comments using the track changes option or a new comment box from the 'review' menu, which allows the document to be modified while all changes are marked. Once the document has been reviewed, it will need to be saved and sent back to the Agency.

During the review procedure experts may need to exchange confidential documents with each other and with the Agency by e-mail. When this is necessary, a secure (encrypted) system must be used.

Eudralink is a secure e-mailing system for the exchange of confidential documents, and enables files to be sent securely over the internet via a user-friendly web-interface. This system creates packages containing one or more file, up to a maximum size to 40 megabytes per file. The recipient receives via ordinary email a message with a link that allows him/her to access the package.

Upon request from the expert, the Agency will set up a Eudralink account for them. To obtain this account, experts need an e-mail address provided by the organisation they are representing (name.surname@organisation.org). Other personal accounts (@hotmail.com, @yahoo.com etc.) are not recommended.

Further help related to Eudralink can be requested from the EMA Eudra Service Desk:

E-mail: eudralink@ema.europa.eu

Telephone: (+44-20) 7523 7523

8. Frequently asked questions (FAQs)

1. **How many documents will I get to review per year?**
   In general, it is unlikely for an organisation to receive more than one or two documents of each type per month. An expert may expect to be involved in the review of 5-6 documents per year.

2. **How long it will take to review the document?**
   Depending on the length and the complexity of the document, it should not take more than 30 minutes to 1 hour at the most to review an EPAR summary. In general, PLs are longer and more detailed than EPAR summaries; however, their review should not take more than 1-2 hours.

3. **Will you notify me beforehand when a document for review is going to be sent out? If so, how long before?**
   For PLs and EPAR summaries, there is no advanced notification; however, the expert will usually have 10-15 days to complete the review. For safety communications, the co-ordinator will be asked for the availability of experts as soon as the Agency is aware that there will be such a communication, which would be approximately 4 days beforehand.

4. **What happens if I cannot meet the deadline?**
   Please inform the EMA as soon as possible if you are unable to meet the deadline, as we may still be able to re-send the document to another reviewer.

5. **Can the experts send their comments directly, or do they have to go through the co-ordinator?**
   According to the procedure, one of the tasks of the co-ordinator is to collate the comments and send them back to the Agency. If for any reason the co-ordinator is unable to send the reviewed document back to the Agency, then the expert who performed the review can send it to the Agency using Eudralink.

6. **Who should I contact if I have a question on a topic about the document under review?**
   Please contact the PCWP secretariat (PCWPSecretariat@ema.europa.eu), who will be able to either answer your question or refer you to another person at the Agency.

7. **Can I discuss the document with other colleagues from my organisation?**
   Yes you can, as long as they are registered as experts with the Agency and they have an up to date (electronic) declaration of interests (DOI) and confidentiality undertaking. When sending the comments back collated in one document, please identify all the experts who have participated in the review by name.

8. **Can I also review documents in other therapeutic areas?**
   Yes, you can. We will always try to target the document to be reviewed by a patient/consumer organisation with expertise within the relevant therapeutic area, but in the case that no specific organisation can be identified we will send the document to be reviewed to another organisations.

9. **How do I implement my comments/changes on the document?**
   The documents sent for review are in 'Word' format. When you start your review, please be sure that the option 'Track changes' from the 'Tools' menu is on. Then work on the document as usual, your comments/changes will be highlighted in the final version.

10. Will I receive any feedback on my comments? If so, when?

For the review of EPAR summaries, you will receive feedback on your comments after the summary has been published on the Agency website, about one month after you have completed the review. For the review of PLs you will be sent the version which is sent to the marketing authorisation holder and wherein you would see if your comments have been included. The final PL, once published, will be listed within the 'human medicines highlights' sent out each month.

11. Can I give my password to someone else to send the document back through Eudralink?

Your Eudralink password is strictly personal and confidential, and it should not be given to anyone else. If for some reason you are not able to send the reviewed document through EudraLink, please contact the PCWP secretariat (PCWPSecretariat@ema.europa.eu).

12. What can I do if I forget my Eudralink password?

If you need assistance with any Eudralink-related issue, please contact the Eudra Service Desk: E-mail: eudralink@ema.europa.eu Telephone: (+44-20) 7523 7523.

13. How should I fill in the declaration of interests form?

A guidance document has been prepared to facilitate completion of this form. Any declared interests will be evaluated in the same way as all experts involved in the Agency's activities. Please refer to the Guidance to complete declaration of interests – confidentiality undertaking and expert nomination form for patients and consumers involved in committees' activities.

14. Do I need to send a CV when sending the declaration of interests form?

Yes, before validating your DOI you will be required to have an eCV, however for patient representatives, you may tick the box "patient representative" and you do not have to fill in anything else, unless you wish you.

15. How often do I renew my declaration of interests?

Each expert has to renew his/her declaration of interests annually. Also, they should be updated and re-submitted to the Agency any time there is a change in the information provided. The Agency will contact you and will inform you when your declaration of interests is due for renewal.