



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Stakeholders and Communication

Incorporating patients' views during evaluation of benefit-risk by the EMA Scientific Committees

The purpose of this document is to establish terms of reference which streamline the involvement of patients in benefit-risk discussion and evaluation within the Agency's scientific committees, its working parties and scientific advisory groups in a consistent, efficient way whenever it is appropriate. In particular it aims at:

- Identifying in which situations it may be helpful to seek input from patients
- Defining what is expected from patient involvement in benefit/risk evaluation (patient values and utilities) when they are consulted
- Establishing an appropriate process to select and support patients

1. Introduction

The added value of input received from patients to the benefit/risk evaluation has been demonstrated through existing EMA experience, and it is generally agreed that their contribution enriches the quality of opinions given by the Agency's scientific committees. Patients have already been involved during benefit-risk evaluations in specific cases, usually with very positive results. Building upon this experience, there is a will and a need to evolve towards a more structured approach to this process.

The 'Reflection paper on the further involvement of patients and consumers in the Agency's activities', (EMA/MB/753771/2009) as adopted by the Management Board already proposed, among other actions, the development of clear criteria on when patients should be involved in benefit/risk considerations, and which should be the format of such interaction/consultations.

More recently and as part of the 2013 EMA reorganisation, the need to better meet the needs of stakeholders has been highlighted as one of the three key elements reflecting the Agency's renewed focus. In this respect, it is proposed to consolidate the Agency's interactions with patients and healthcare professionals, which includes progressing and further involving them in the evaluation of benefit-risk. In order for the scientific outcomes to be complete and comprehensible, they should take into account patient experience, ultimately contributing to the safe and rational use of medicines.



The CHMP work programme for 2011-2013 (EMA/CHMP/65166/2011) gives high priority to this initiative and foresees the development of adequate methodology to incorporate patient's views and values in the scientific discussion in a consistent, structured manner.

http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2011/01/WC500101505.pdf

Finally the pharmacovigilance legislation has brought additional basis for the inclusion of patients in benefit-risk discussions and has placed patients and civil society in the centre of medicines regulation and evaluation. Specific considerations refer to the incorporation of patients as full members of the 'Pharmacovigilance and Risk Assessment Committee' (PRAC), direct patient reporting as well as requests for providing further information about the risk and the benefits of the medicines authorised in the EU.

More recently a workshop on "[patients' voice in medicines evaluation](#)" held at the EMA in September 2013 concluded that there is a need to progress further in this area and to implement this paper.

2. Legal basis

Article 78 of Regulation (EC) N° 726/2004 allows the EMA scientific committees and their Rapporteurs to establish contacts on an advisory basis with patient representatives relevant to the indication of a medicinal product. In accordance with this, a procedure is proposed to enable benefit-risk assessments performed by the scientific committees, its working parties and its scientific advisory groups to take into account the view of patients whenever appropriate.

Article 61a(d) of Regulation (EU) N° 1235/2010 amending Regulation (EC) N° 726/2004 foresees that one member and one alternate member is a patient representative at the PRAC.

3. Scope

Evaluation of benefit-risk at the EMA is performed primarily by the CHMP and the PRAC, therefore this document refers specifically to the activities within these two committees. This covers meetings of scientific advisory groups (SAGs) as well as other ad-hoc experts groups which may discuss issues related to benefit-risk. It also covers activities aimed at providing pharmaceutical companies with scientific advice and protocol assistance during drug development (Scientific Advice Working Party (SAWP)).

Patient representatives are also involved in the work of other EMA scientific committees and working parties. Although the activities of these committees and working parties may often not be directly related to benefit-risk, the principles laid down here may apply (e.g. involvement of young patients in the evaluation of Paediatric Investigation Plans by the Paediatric Committee).

Patients should be consulted in all cases where their involvement can bring added value to the benefit/risk discussion, and this document aims at defining clear criteria on 'when' (a priori) it would be beneficial to involve patients and at describing the procedure by which this consultation can be implemented.

Patients who are consulted during benefit-risk evaluation will give their views and may participate actively in the discussions. However, legislation so far only allows them to take part in decision-making as member of the PRAC.

This document does not cover participation of patient representatives and lay persons in public hearings. Although discussions in public hearings are expected to often relate to benefit-risk, this participation will be dealt in a separate document.

For the purpose of this document, patient (or patient representative) means an individual, patient, carer or parent representing patients, not an individual representing a specific organisation.

4. Expected contribution from patients

Reference is made to the document 'The role of patients as members of the EMA Human Scientific Committees (EMA/351803/2010).

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/12/WC500119614.pdf

Although this document focuses on the role of patients as members of scientific committees, the principles laid down can be extrapolated and applied here.

Patients' main role at the Agency's discussions on benefit-risk is not expected to be of a scientific nature. Although experience has demonstrated that they very often are able to contribute scientifically into the discussion, the added value of having patients in benefit-risk discussions is to bring a unique and critical input based on their real-life experience of being affected by a disease and its current therapeutic environment. This element fills a gap which other (scientific) experts cannot fill, and which has proven necessary to achieve the best possible results within the regulatory process.

Patient involvement at this level is also expected to increase confidence and trust in the regulatory process and lead to higher level of transparency.

5. Ways of participation

Patients' representatives usually participate within the EMA scientific committees as:

Members, who act in the same way as all other members. Considering the scope of this document it only applies to the PRAC for the time being, or

Experts, who advise the committee on specific issues and are selected for their relevant expertise, experience or knowledge; they bring a real-life experience of the disease and its current therapeutic environment. They act on their own behalf. Experts usually only attend part of a meeting to answer specific questions raised by the committee and do not take part in committee conclusions or decisions. They must maintain confidentiality, declare any conflict of interest and abide by the EMA code of conduct. In accordance with article 62(2) of Regulation (EC) No 726/2004, when involved as an expert, the patient is entered into the EMA EU expert database.

Representatives of an organisation(s), who express the views of a patient organisation(s) related to a specific issue when requested by a committee. They have the responsibility to liaise with their organisation to ensure they present the views of the organisation on the questions to be addressed. Representatives of organisations are not bound by confidentiality and the agreement of the applicant/MAH should be sought prior to disclosure of any confidential data. Representatives are still expected to declare any conflict of interest and the organisations involved should be fully transparent with regard to their activities and funding sources.

When involving experts and representatives of organisations the 'Rules of involvement of members of patients/consumers and healthcare professionals in committees related activities' (EMEA/483439/2008 rev. 1) should apply.

When should patients be involved?

5.1. Upon request from scientific committees

1. Situations where patients should be consulted:

- When the CHMP is still undecided on a marketing authorisation application for a new medicinal product in an area where there remains an unmet medical need and would like to assess the impact of their recommendation on the relevant patient population;
- When the PRAC and/or the CHMP would like to assess the impact of their recommendation, to maintain, suspend, revoke a marketing authorisation, or to restrict the indication of an authorised medicine, on the relevant patient population.
- When a marketing authorisation holder informs of their intention to withdraw an authorised medicinal product or pharmaceutical form from the market; patients should be informed so that any concern from their side on the imminent withdrawal can be timely be brought forward;
- When a Marketing Authorisation Holder notifies of a potential shortage in supply/availability of an authorised medicinal product, which is likely to incur a significant EU-wide shortage.

2. Situations where patients may be consulted:

- Feasibility of Risk Management Plan in a "real life" environment (including feedback on its implementation).
- Positive opinion for 1st in class/breakthrough especially in case of specific contra-indication/warning
- Specific information to be included in the Package Leaflet and its wording;
- Any information on benefit-risk of a medicine which may be specifically addressed to patients.

3. Situations where a process already exists to consult patients systematically:

- Review of Package Leaflet during preparation (for new medicines and renewals);
- Review of EPAR summaries during preparation (new summaries and updates);
- Review of safety announcement following PRAC/CHMP¹ evaluation of a safety referral);
- When a Scientific Advisory Groups (SAG) / ad-hoc expert meeting is to be held;
- When a meeting of the Scientific Advice Working Party (SAWP) is to be held.

5.2. Request from patients' organisations

Occasionally, patient organisations may address directly an EMA scientific committee on a specific issue; the scientific committee will consider the matter and will decide whether further dialogue or

¹ By analogy, this may apply to safety announcements which follow CMDh evaluation

interaction is necessary. In all cases the scientific committee together with the EMA secretariat will acknowledge the request and will respond in writing to the patient organisation.

6. How should patients be involved?

- The table in section 6 should be used by EMA secretariat, Rapporteurs and committee members in order to identify when they should consult patients during benefit-risk evaluation.
- The table should be reviewed by the relevant EMA staff/Rapporteurs at least around day 180 for new applications evaluated by the CHMP or at the time of adoption of LoQ/LoI during PRAC evaluation.
- In all cases, the contribution from the patient should be incorporated to the CHMP/PRAC assessment report and the EPAR.
- For procedures involving both PRAC and CHMP, patients should be consulted during PRAC evaluation; by this means, when the issue reaches the CHMP, input from patient representatives will be already incorporated. However, if necessary the CHMP may decide to further consult patient representatives.
- For any further advice or clarification during the implementation of this process, PCWP secretariat (PCWPsecretariat@ema.europa.eu) can be contacted.
- The EMA/PCWP secretariat will identify relevant patient(s) in the disease area of concern via the EU network of experts to which the EMA has access (see below section 8).
- The EMA secretariat will inform the patient and if relevant, his/her organisation on the outcome.

6.1. Format of the interaction

Once it has been decided to hold a consultation with patients, the following will be used as guidance to choose the most adequate format for such consultation.

Flexibility should be applied in order to choose the most adequate format of the interaction, taking due consideration of resources as well as minimising interference in committee's normal operations.

Patients may participate either in writing, via teleconference or in a meeting at the EMA:

In writing

- EMA secretariat together with (Co) Rap will agree on the question(s) to be put to the patient(s). The question(s) will be circulated to the scientific committee for information;
- Sufficient background information will be provided by the EMA secretariat to the patient to allow for an adequate understanding of the issues related to the question(s) being asked;
- The relevant patient(s), as identified by EMA secretariat (see below section 8), is consulted and given a deadline for their response(s);
- Upon receipt of response to the question(s), and depending on the issues, the (Co) Rap and scientific committee may decide if there is a need for further discussions with the patient(s) either via teleconference or at a meeting;

Via teleconference

- The same procedure as described above applies, however, upon request of the (Co) Rapporteur and/or the scientific committee, the patient may join the scientific committee discussion via teleconference;
- When necessary, written responses may be received in advance of the discussion;
- Alternatively, a teleconference may be held only with a selected group of persons (e.g. (Co) Rapporteurs, assessors and EMA secretariat) without involving the whole committee; this is also regarded as a suitable way to clarify certain issues in the case of the interaction being requested by a patient organisation. The outcome of the discussion in every case will be fed back to the scientific committee.

Participation in a meeting at the EMA

- *Scientific committee meeting (PRAC and CHMP):*
 - Patient representatives are members of the PRAC. The role of patient representatives as PRAC members is described in the document 'The role of patients as members of the EMA Human Scientific Committees (EMA/351803/2010)'.
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/12/WC500119614.pdf
 - Having a patient as member of the scientific committee does not guarantee systematically the necessary input for every discussion in terms of experience and expertise (depending on the therapeutic area or condition being discussed). Analysis of experience indicates that the best results are obtained by, in addition to the member, having ad-hoc involvement of the most adequate patient coming from the patient's organisation in the field under discussion.
 - Ad-hoc participation of patient in specific discussions during a CHMP/PRAC meeting may follow previous written consultation on the specific issue;
 - Patients may also participate during an oral explanation with a marketing authorisation applicant/holder. In these cases, after agreement with the CHMP/PRAC, they may be able to put questions to the company. Patients would attend only the part of the meeting related to the specific issue under discussion.
- *SAG / Ad-hoc expert meetings:*
 - Following a successful pilot phase in 2011, patients participate routinely in SAGs meetings. This process has become normal practice and constitutes an ideal way to gather patient input during discussions on benefit-risk and to incorporate their views prior to decision-making.
 - Patients should participate in all SAGs and Ad-hoc expert meetings (unless a priori their attendance is thought not be useful; either due to the technical nature of the proposed discussions and/or where they do not specifically concern the benefit/risk of the product).
 - Participation will usually consist of 2 patients per meeting; identified by EMA secretariat via the EU network of experts to which the EMA has access (see below section 8).
 - Selected patients should have direct knowledge of the disease and of the issues faced by patients (as patients, carers or through their organisation).
 - Patient representatives should feel part of the meeting and be able to contribute to the discussion at any point. The patients appreciate being welcomed, acknowledged and

specifically asked if they have any comments; this encourages their involvement and their perspectives to be heard. It is recommended that SAG Chairs continue to devote efforts to involve and facilitate patient participation in the discussions.

- Patients contribute to the discussion and the outcome of the meeting as any other (scientific) expert.
- The scientific committee requesting the SAG meeting can take full advantage of patient participation and is encouraged to identify in advance any specific questions where patient input would be particularly valuable; however it is not expected as a routine.
- *Scientific advice meetings:*
 - Patients have attended protocol assistance meetings for many years with very positive results. Since 2013 they are also invited to attend scientific advice meetings, whenever a suitable patient can be found. Patients are invited to participate in Scientific Advice meetings to share their 'real-life' perspective and experience with the SAWP and the pharmaceutical company, in relation to a particular medicine in their disease area.
 - Patients in scientific advice participate similarly to the way they do at SAGs meetings and are identified in the same manner.
 - This paper proposes this activity to be continued over the coming years so that patient input can be incorporated to the advice given to companies during their drug development

7. Source of patients

Patients involved in benefit-risk evaluation at the EMA should preferably be identified through the so-called "eligible" patient's organisations. These organisations have fulfilled a set of defined criteria ("Criteria to be fulfilled by Patients' and Consumers' Organisations" involved in EMA Activities (EMA/24913/2005 - rev. 2):

http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/12/WC500018099.pdf. This system will ensure that patients come from the most appropriate European organisations, which are selected by the EMA in a transparent manner.

The current list of eligible organisations can be found on the Agency website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/q_and_a/q_and_a_detail_000082.jsp&mid=WC0b01ac0580035bf2

In certain cases, when no eligible organisation exists in a certain area, when no suitable patients are identified through the normal route or when interaction is requested by the organisation, patients may be contacted through other means (e.g. from a non-eligible organisations, other bodies, etc). Any organisation which is involved however should be fully transparent with regard to their activities and funding sources.

Additionally, Member States may propose patients sourced via their respective national competent authorities. The same principles will apply.

8. Confidentiality aspects and screening for conflicts of interest

Every patient will be required to complete a declaration of interest / confidentiality agreement prior to involvement. They undergo screening for conflicts of interest in the same manner as all other experts.

Patients must adhere to the confidentiality of the documentation they receive and the discussions they partake in. They participate as individuals and should not discuss the documents received with others.

9. Training and support for participation

Specific training to facilitate involvement and participation of patients will be provided. The EMA in collaboration with the Patients Consumers Working Party (PCWP) has developed a specific training strategy to support patients who are to be involved in any EMA activities. The role of the PCWP and other patients' organisations with experience in working with the EMA and regulatory environment has been critical in such design.

As part of this training strategy, specific consideration is paid to those activities related to benefit-risk evaluation by the PRAC and CHMP. In particular, individual support will be provided by the EMA secretariat to the patient(s) by ensuring that he/she receives at least 2 weeks in advance of the interaction (mostly when attending to meetings):

- 'Patient friendly' background information on the issues for discussion,
- An on-line "information pack" which includes:
 - General information on the Agency's work,
 - Specific information pack designed for a specific type of meeting or activity (e.g. SAG meetings, scientific advice, etc.), which includes patient friendly explanations, video tutorial, etc.
- Apart from written and on-line material, a conversation with an EMA member of staff will also take place via telephone, to manage their expectations and answer any queries prior to the meeting.
- Finally, EMA secretariat will always be on hand to respond to any additional queries from the patient and will accompany them to any EMA meetings.

10. Monitoring

The Agency continually monitors its interactions with patients and each year produces an annual report on the progress of the interaction.

In this regard, interactions with patients during benefit-risk evaluation will be monitored and a progress report will be prepared after one year which will be included within the annual report. This will be presented to the CHMP, PRAC and the Management Board.