EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 October 2014

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EU Pharmacovigilance public hearings should be as transparent and independent as in the US

Joint comments on EMA's public consultation on its 'Draft rules of procedures on the organisation and conduct of public hearings at the Pharmacovigilance Risk Assessment Committee (PRAC)' (EMA/624809/2013)

Comments from:

Name of organisation or individual
Health Action International (HAI) Europe International Society of Drug Bulletins (ISDB) Medicines in Europe Forum (MiEF) Nordic Cochrane Center (NCC)

Short presentation of the signatory organisations

HAI Europe. Health Action International (HAI) Europe is a non-profit, European network of consumers, public interest NGOs, health care providers, academics, media and individuals working to increase access to essential medicines and improve their rational use through research excellence and evidence-based advocacy. More info: www.haieurope.org; Contact: ancel.la@haieurope.org

ISDB. The International Society of Drug Bulletins, founded in 1986, is a worldwide network of bulletins and journals on drugs and therapeutics that are financially and intellectually independent of the pharmaceutical industry. Currently ISDB has about 80 members representing 41 countries around the world. More info: www.isdbweb.org; Contact: press@isdbweb.org

MiEF. The Medicines in Europe Forum (MiEF) was launched in March 2002 and reaches 12 European Member States. It includes more than 70 member organisations representing the four key players on the health field, i.e. patient groups, family and consumer bodies, social security systems, and health professionals. Such a grouping is unique in the history of the European Union and is testament to the importance of European medicines policy. More info: english.prescrire.org; Contact: pierrechirac@aol.com

NCC. The Nordic Cochrane Centre is part of the Cochrane Collaboration, an international not-for-profit international network of more than 28,000 dedicated people from over 100 countries preparing, maintaining and promoting the accessibility of systematic reviews of the effects of health care. More information: www.cochrane.org. Contact: Peter Gøtzsche (pcg@cochrane.dk)

1. General comments/Key points

Stakeholder number	General comment (if any)	Outcome (if applicable)
	In July 2014, almost 4 years after the adoption of the 2010 EU directive and EU regulation on pharmacovigilance, the European Medicines Agency (EMA) has finally launched a public consultation on its "draft rules of procedures on the organisation and conduct of public hearings at the Pharmacovigilance Risk Assessment Committee (PRAC)" (1). We welcome the opportunity to comment on this draft. We note that the EMA draft rules of procedure provide **no information on the timeline for the implementation of public hearings**. We hope that EU pharmacovigilance public hearings will be rolled out as soon as possible and at the latest during the 1st trimester of 2015. Our comments focus on several key issues, and where relevant, **compare** the EMA proposal **with the procedure in place for the open public hearings that are part of the advisory committees at the US Food and Drug Administration** (FDA) (2). Our **key messages** are as follow: - We strongly support the conduct of public hearings at the PRAC. However, the **aim of public hearings should be clarified**: "*to enhance EMA's ability to protect public health*" (to prevent or, at least, minimise harm, not only to "manage" risks). Moreover, in the framework of pharmacovigilance activities, it should be recognised and emphasised that **victims' testimonies** are of important added value (read on page 5); - We underline the need to ensure that public hearings are **independent**. The requirement that speakers have to declare their conflict of interest before speaking is welcomed but insufficient. Priority must always be given to independent speakers and participants, with no conflict of interest related to the marketing authorisation holder, rather than giving the floor only to patients' organisations with "EU representativeness" which are often heavily sponsored by	

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	pharmaceutical companies. Furthermore, public hearings should **not be used by marketing authorisation holders (MAH) as a platform** to downplay or deny genuine safety concerns or prevent scientific debate from occurring, when MAHs are granted *"the opportunity to present its/their view(s) to participants during the public hearing*" as proposed by the EMA (**a**). The US Food and Drug administration (FDA) guidance on advisory committee modalities opts, on the contrary, not to allow "*the sponsor whose product is under review*" to participate in the open public hearing (**b**) (read on page 7); - To strengthen speakers' and audience's representativeness, the EMA shall ensure a fair **balance between patient and consumer representatives** as well as between organisations acting at **EU level** and at **national/regional level**. Victims' testimonies must be at the core of public hearings (**c**); - In order to serve **transparency** and allow wider public participation, we encourage the EMA to make the most of **modern communication tools**: systematically live-broadcasting and web streaming public hearings; enabling participation via teleconferencing facilities; and providing **translation,** at least into English, for scheduled oral interventions so that speakers (consumers, victims) can intervene and testify in their own language (read on pages 7 and 8) ; - We question the **relevance of the criteria list as proposed by the EMA** to "*evaluate the need for a public hearing*" as it is particularly confusing. We propose greater transparency around the PRAC's process in deciding or not to hold a public hearing (e.g. PRAC minutes should include a summary of the discussion on the proposal to hold a public hearing, including the reasons why it was accepted/refused) (read on page 9 and 10); - We underline that **non-public hearings hinder public scrutiny** and should be **reserved in order to protect whistleblowers**. Non-public hearings should not be allowed for a MAH as they may influence the decision-making process. Clinical data, including pharmacovigilance data, should never be considered commercially confidential. They are scientific data of great public interest (read on page 11).	

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	In short. Several major improvements are needed to make the most of public hearings at the PRAC, a long awaited, welcomed initiative.	
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	Notes: **a-** To give the floor to MAH at crucial moments during the decision-making process is a tradition at the EMA that is a cause for concern. Such interventions offer MAH the possibility to influence the regulatory process. For example, MAH have a dedicated time called "oral explanations" to present their views to members of the Committee for Medicinal Products for Human Use (CHMP) before they decide on the granting or not a marketing authorisation. **b-** Evidence from the US shows the need not only to require advisory committee members to declare conflict of interests, but also for experts to avoid such conflict of interests (COI) in the first place. In addition, according to the US consumers' organization Public Citizen, former members of advisory committees should not be allowed to speak before their former colleagues at the same committees on behalf of companies seeking favourable committee votes (ref. 3). **c-** To facilitate attendance from relevant stakeholders and to provide equal opportunities, victims of drug-induced harm, patients, consumers and healthcare professionals and/or their representatives should be granted the opportunity to apply for justified reimbursement to cover travel expenses.	
	References: **1-** European Medicines Agency "Draft rules of procedures on the organisation and conduct of public hearings at the Pharmacovigilance Risk Assessment Committee (PRAC) (EMA/624809/2013) – draft for consultation" 24 July 2014: 9 pages. **2-** US Food and Drug Administration (FDA) "Guidance for the public, FDA advisory committee members, and FDA staff: the open public hearing at FDA advisory committee meetings" Final guidance; 15 May 2013: 13 pages. **3-** Public citizens "Public Citizen to FDA: Advisory Committee-Industry Revolving Door Should Be Closed" Press release 10 September 2014: 1 page (www.citizen.org/pressroom/pressroomredirect.cfm?ID=4278).	

2. Specific comments on text

Our specific comments are organised by key issues (words in **bold and in blue** at the beginning of each line).

Line number(s) of the relevant text	Stakeholder number	Comment and rationale; proposed changes	Outcome
33 to 37 (Purpose of a public hearing)		**Clarification of the purpose of public hearings** Comment: There is a need to emphasise that public hearings are a mean, amongst others, to enhance EMA's ability to protect public health. In addition, the notion of independent advice should be underlined. These two crucial issues (protection of public health and independence) are explicit in the US Guidance for FDA advisory committees. Moreover, in the framework of pharmacovigilance activities, it should be recognised and emphasised that victims' testimonies are important and of added value. Proposed changes: (additions in **bold**) The primary purpose of a public hearing ***is to enhance the agency's ability to protect public health by providing independent advice to the agency and*** hear**[ing]** ***victims testimonies and*** the public's view on the acceptability of the risks associated with the medicinal product/medicinal substance/class of medicinal products concerned, particularly in relation to its therapeutic effects and therapeutic alternatives available, as well as to seek suggestions and recommendations ~~***on the feasibility and acceptability***~~ of risk ~~***management and***~~ minimisation activities.	

49 200-201		**Ensuring public hearings' independence instead of publicly sponsoring a platform for MAH to influence the decision-making process** Comment: PRAC public hearings should not be used as a platform for the marketing authorisation holders to minimise/deny genuine safety concerns, and to prevent debate from occurring in an attempt to restore the trust of their shareholders or investors. The US Food and drug administration (FDA) guidance on advisory committee modalities prevent "*the sponsor whose product is under review*" to participate in the "open public hearing part" of the advisory committee. MAH should reply to PRAC questions in writing and provide scientific evidence, rather than being allowed to share "views" representing their own opinion with meeting participants. Proposed changes: ***The PRAC chairman may give the*** marketing authorisation holder(s) ~~***has***~~ the opportunity to ~~***present its/their view(s)***~~ ***answer some questions*** ~~***to the participants of***~~ ***in writing after*** the public hearing***. These documents are to be made available on the Agency website together with other supporting documentation***. Delete: ~~*The marketing authorisation holder(s) may be given the opportunity to present his(their) 200 view(s) to the participants of the public hearing.*~~	
54 (1.5. Language regime)		**Scheduled oral interventions to be translated** Comment: According to the EMA document, public hearings are to be conducted in English only. In order to maximise participation by European citizens participations from wide range of countries, simultaneous translation could be organised by the Agency, since speakers are required to submit their request for intervention in advance.	

99, 107, 116, 148 51 231 (4.7. Meeting records) 51		**Transparency** Comment: Public hearings about pharmacovigilance issues are of public interest. The agency should therefore allocate sufficient resources to **always live-broadcast and web stream** such hearings. The EMA has moved into new, modern offices in London, so we are reluctant to accept that IT infrastructures for live-broadcasting and web streaming are not in place. Moreover, all interventions/oral statements should be included in the transcript of the meeting and made publicly available on the agency website. The US FDA provides such a transcript within few weeks of the meeting. In addition, journalists should not be confined to an observer role but be allowed to speak or ask questions to speakers at the end of the meeting, if time allows. Proposed changes: Delete "~~when feasible~~" or "~~when technically feasible~~" Add the words in bold: "Specific arrangements **(systematic live-broadcasting and web streaming)** will be put in place to allow wide media coverage of the public hearing." Add the words in bold: "A ***complete*** record of the meeting ***(audio or video record, and transcript including all interventions/oral statements and declarations of interest)*** (…) will be made available ***as soon as possible*** after the public hearing on the Agency's website, ***no later than 5 calendar days for the video and no later than 4 weeks for the written transcript***" "~~The media may follow the public hearing as observers~~" to be replaced by "***To facilitate media coverage, public hearings will always be broadcasted live and web streamed, and participation will be made possible via teleconferencing facilities"***	

109 110		Comment: We welcome the proposal to publish supporting documentation presented by the speakers and the written contribution received on the Agency website. However, a deadline for the Agency to publish this supporting documentation is missing. According to its guidance document, the US Food and Drug Administration "*distributes to the advisory committee before or at the meeting those copies of handouts received from public speakers*". Proposed changes: "Supporting documentation presented by the speakers during the intervention will be published on the Agency's website ***before the public hearing when possible, and no later than 10 calendar days*** after the public hearing " "Participants can submit their contribution in writing for consideration by the PRAC. Contributions received in writing will be published on the Agency's website ***when possible before the public hearing and in any case no later than 10 calendar days*** following the public hearing. ***For participants attending the meeting the supporting documentation must be made available at the latest on the day of the meeting***".	

			Decision-making to conduct a public hearing Comment: The **list of criteria** used to "*evaluate the need for a public hearing*" (lines 73-84) seems particularly **confusing.** It is in fact unclear whether criteria such as "*expected impact on trust in the regulatory decision-making*" or "*scientific complexity of the issue discussed*" will be invoked to hold a public hearing when a controversial issue is at stake (e.g. on oral contraceptives, or HPV vaccines) or rather be used to prevent the public hearing from taking place. We also question EMA's choice of words and posture judging "*risk attitudes of the users of the medicine(s) concerned*" which sounds rather paternalistic. Moreover, we disagree that the "urgency of the matter" should be used as a criterion to decide whether a public hearing is "feasible" or not. When the matter is urgent, the EMA (PRAC and CHMP) should apply the precautionary principle without delay (e.g. suspend a marketing authorisation, issue a warning), and then organise a public hearing. Such public hearings would help to ensure EMA's decisions are well-informed and further supported by the additional information and advice received. The US FDA does not have a list of criteria and systematically organises advisory committees when approving a new drug in case there are safety concerns or when the drug uses a new mechanism of action (or, less often, when safety concerns arise for an already authorised drug). Proposed change: At the end of section "2.1. Proposal for a public hearing", add: "***The annual report of the EMA should detail the percentage of public hearings proposals that were accepted by consensus and by vote and the percentage of those refused together with details on the votes and reasons for refusal***". Delete the following criteria: ~~• Feasibility to hold a public hearing in the light of the urgency of the matter~~	
71				
73-84	(2.2.			

Evaluating the need for a public hearing)		~~• Risk attitudes of the users of the medicine(s) concerned vis à vis therapeutic areas~~ ~~• Expected impact of the feedback obtained through the public hearing on scientific decision-making~~ ~~• Expected impact on trust in the regulatory decision-making~~ ~~• Scientific complexity of the issue discussed~~ After the list of criteria, add the following statement: "***When a PRAC member proposes the conduct of a public hearing, PRAC minutes are to include a summary of the discussion of such proposal, including the reasons why a decision was made to organise or not the proposed hearing".***	
		Non-public hearings impair public scrutiny <u>Comment:</u> Clinical data should never be considered commercially confidential. Clinical data are scientific data of public interest and therefore to be considered as a public good. As a general principle, in order to guarantee the independence of the decision-making process and to allow for public scrutiny of the activities of the Agency, a public institution, a marketing authorisation holder should not be allowed to participate in non-public hearings. The only case where a non-public hearing can be justified is when whistle-blowers wish to alert the Agency (for example about adverse drug reactions withheld by the manufacturing authorisation holder). A whistleblower is a person who exposes misconduct, dishonesty or illegal activity occurring in an organisation. The European Ombudsman, who has underlined that whistleblowers are key in uncovering serious irregularities recently released a draft decision on internal rules concerning whistleblowing in order to raising awareness among other EU institutions[1].	

[1] -www.ombudsman.europa.eu/en/press/release.faces/en/54626/html.bookmark

216-218 223-224		Proposed changes: ***"As a general principle, clinical data should not be considered commercial data***. Where a ***~~marketing authorisation holder or another~~*** person intending to submit information ***~~that has confidential data~~*** relevant to the subject matter of the procedure***, especially in order to expose misconduct, dishonesty or illegal activity of the marketing authorisation holder or similar activities occurring in another organisation***, he or she may request permission to present that data to the PRAC in a non-public hearing." "The name and affiliation of anybody presenting ***~~confidential~~*** information in a non-public hearing shall be made public as part of the official record of the meeting, with the only exception being ***the name of a whistleblower, which must may be kept confidential by the PRAC to protect that person's security/career".***	