European Medicines Agency

London, 19 June 2009
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SUBMISSION OF COMMENTS ON
The Draft EMEA transparency policy[1]

Draft for public consultation

Brussels, 23 September 2009

EMEA transparency policy[1] falls short: a weak and irresponsible project

HAI Europe, ISDB and MiEF joint answer to "The EMEA transparency policy – draft for public consultation"

COMMENTS FROM:

Name of organisation or individual
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Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

Once completed, this form should be sent in Word format (not PDF) by e-mail to:
transparency@emea.europa.eu

This answer was also sent to Thomas Lönngren (EMEA executive Director)**, to Christine Link** (EMEA document management)**, to Androulla Vassiliou** (European Commissioner DG Health and Consumers)**, to Martin Terberger** (Head of Unit Pharmaceuticals), **Claire Joan Scharf-Kröner** (Unit Pharmaceuticals)**, Nikiforos Diamandouros** (European Ombudsman)**.**

1. GENERAL COMMENTS

Stakeholder No. <to be completed by EMEA>	**General comments (if any)**	**Outcome** <to be completed by EMEA>
	Drug regulatory agencies should function in an open and transparent manner in order to serve patients' and citizens' interests. Without transparency, there can be no accountability and no means to ensure trust in decision-making. Preventable public health disasters involving marketed drugs and devices, such as the continued marketing of Vioxx° (*rofecoxib*) in Europe for four years after the results of the VIGOR trial showing strong evidence of cardiovascular risks, have undermined public confidence in the pharmaceutical industry and in regulatory agencies' independence. The 1996 Uppsala Declaration had already denounced the excessive secrecy surrounding drug regulatory decisions[2]. Despite repeated claims by EMEA and national drug regulatory agencies, especially during the last years, that the situation would change, major improvements did not materialise. In this context, the development of a new transparency policy by the European Medicines Agency is welcome[1]. Unfortunately, the "European Medicines Agency new transparency policy" released for consultation the 19th of June 2009 remains disappointing, as was the "Draft EMEA policy on the practical operation of access to EMEA documents" released earlier this year[3]. **A situation that urgently needs to be improved** **EMEA overlooks its excessive secrecy.** EMEA presents its "transparency measures" as "*going beyond legislative requirements*".	

	This does not reflect the experience of European citizens and health professional organisations. In fact, from 2005 to 2008, several independent bulletins of the International Society of Drug Bulletins (ISDB) and members of the Medicines in Europe Forum (MiEF), particularly *Prescrire* and *Arznei-Telegramm*, submitted requests for: - documents that should have been made publicly available on the EMEA website, but that were missing (mainly European public assessment reports (EPARs) and their updates); - documents that the Agency is not legally required to post on its website but that were needed in order to understand the rationale behind regulatory decisions (mainly full assessment reports on which EPARs are based, and clinical data supporting major changes in the section on adverse effects in the summary of product characteristics (SPC)); - various other information[4]. Overall, their experience demonstrates the EMEA's reluctance to release information, and the delays and lack of cooperation when they request clinical data that are contained in national agency reports and documents prepared by drug companies, such as periodic safety update reports (PSURs). Some sections of documents containing important scientific information were simply censored in the name of commercial confidentiality, despite EMEA duty to protect European citizens' safety. A flagrant example of such censorship is presented on page 4 of Annex A (box "Censorship masquerading as transparency: the EMEA assessment report on rimonabant"). It involves a report about *rimonabant* (formerly Acomplia°) where 65 pages out of 68 pages were blacked out. ► **In order to improve procedures, the first step is to be aware of existing weaknesses. With this draft policy, the EMEA once again ignores its failure to adhere to transparency rules. And EMEA does not give priority to European citizens' interests.** **Secrecy on pharmacovigilance data puts patient safety at risk.** EMEA's secrecy, especially when it comes to pharmacovigilance data, puts patient safety at risk, delaying the provision of information that could have prevented adverse drug reactions to occur.	

	Despite Regulation (EC) 726/2004 requirements, there is still no "appropriate access" of the public to Eudravigilance, the European adverse drug reactions database[5]. EMEA also systematically refuses to release documents prepared by pharmaceutical companies, such as periodic safety update reports (PSURs). PSURs contain clinical data on adverse effects, which according to EMEA's own rules should not be considered confidential, whatever their source[6]. Moreover, as EMEA receives and retains copies of PSURs, they should be available under Regulation (EC) 1049/2001 relative to access to documents held by a European Institution[7]. And, regarding the use of "commercial confidentiality" as an excuse for the retention of safety information, Regulation 1049/2001 stipulates that the grounds for refusal are null and void when an overriding public interest justifies the document's disclosure[7]. This discrepancy between theory and practice in matters of transparency represents a major obstacle in access to documents and information. **Proposals for improvements of EMEA draft policy:** **► The EMEA transparency measures are by no means "*beyond legislative requirements*". Hence, this misleading statement, repeated several times in the document, must be deleted.** **► The EMEA must comply with its transparency regulatory requirements (read below "Unacceptable delays")[8].** **"Commercial confidentiality" too broadly defined allows for excessive secrecy.** EMEA sees "*finding the right balance between transparency and protection of confidential commerciality*" as a "*pre-requisite*" for a more proactive approach towards transparency. HAI Europe, ISDB and the Medicines in Europe Forum strongly disapprove this dangerous proposal to find a "*right balance between transparency and protection of confidential commerciality*", as it puts on the same level a general interest's principle (transparency) and a private economical interest (confidential commerciality). Such a wording implies that confidential commerciality could justify depriving patients and health professionals of drug safety information, which is	

	unacceptable. What commercial information could possibly override the need to protect public health? To overcome extensive secrecy, ***"commercial confidentiality of proprietary information"* must be redefined accurately**[9]. In its draft transparency policy, EMEA failed to propose a new, more restrictive, definition of "*commercial confidentiality of proprietary information*"[10]. It is unfortunate since it would have allowed for a wider debate and for more coherence. **Proposals for improvements of EMEA draft policy:** **► The basic principle that "transparency should be the rule" needs to be clearly stated: information available within regulatory agencies should be freely available to any party that requests it.** **► Exception to transparency, notably for "commercial confidentiality", must be defined and interpreted very strictly. The redefinition of "commercial confidentiality of proprietary information" requires a democratic process (public consultation on the basis of a document designed first for citizens' needs) (read below page 12).** **Unacceptable delays are disguised as "stepwise implementation"… without deadlines!** In September 2009, EMEA still fails to implement its transparency requirements as defined in Regulation (EC) 1049/2001[11,7] adopted in 2001; Directive 2001/83/EC, consolidated with Directive 2004/27/EC adopted in 2004[12]; and Regulation (EC) 726/2004/CE adopted in 2004[5]. For example, European citizens are entitled to access any documents produced or received by a European institution (article 2 point 3 of Regulation (EC) 1049/2001), thus including EMEA's Periodic Safety Update Reports (PSURs) and assessment reports from Drug Regulatory Agencies received by EMEA[7]. Articles 126b of Directive 2001/83/EC as amended by Directive 2004/27/EC states: "*the Member States shall ensure that the competent authority makes publicly accessible its rules of procedure and those of its committees, agendas for its meetings and records of its meetings, accompanied by decisions taken, details of votes and explanations of*	

	votes, including minority opinions". The EMEA should be at least as transparent as Member States, and publish online detailed minutes of its Committee and working group meetings[12]. Another problem is the way EMEA intends to meet legal requirements provided for in Regulation 726/2004 on updates for variations of European public assessment reports (EPARs). EMEA only publishes lists of "steps-taken" (summary of the rationale for variations) that are often not informative enough[5,13]. Moreover, EMEA's list of "key transparency initiatives" includes, once again, several measures that should have been implemented years ago in order to comply with legal requirements. Yet some of these "key initiatives" do not even meet transparency legal requirements (see our comments to annex 1 of the EMEA draft policy). Moreover, EMEA proposes "*a stepwise implementation*" and makes minimalist proposals for improvements. No timeline is provided for the implementation of these "key transparency initiatives", undermining EMEA credibility[14]. **Proposals for improvements of EMEA draft policy:** **► If public health is to be guaranteed, the basic consideration that "the thorough implementation of transparency measures is a priority that should not be delayed" needs to be clearly stated. EMEA must clearly engage to fully comply with transparency legal requirements before 2012.** **Unequal treatment among stakeholders.** EMEA recognises itself that "*the focus [in terms of interactions with its stakeholders] has been first on the pharmaceutical industry*" (III.2). That is to say that pharmaceutical companies are EMEA's key clients. This is unacceptable: the primary aim of drug regulation should be the protection of public health. European citizens, not the private sector, should be the EMEA's primary client. **This 'industry first' policy is a logical consequence of EMEA's current funding through licensing fees.** According to EMEA's 2008 annual report, the fees collected from drug companies represent 74% of its revenue, a percentage that is increasing over the years[15]. Funding by the pharmaceutical companies creates an obvious conflict of interests.	

This may contribute to explain the systematic refusal of EMEA to release documents prepared by pharmaceutical companies, such as Periodic Safety Update Reports (PSURs) (read above). Other consequences of this conflict of interests are the deletion of crucial information in the assessment reports transmitted by EMEA (i.e. deletion of "follow up measures" (FUM), precious information allowing drug regulatory agencies to ask for more information on adverse effects).

EMEA should also tackle inequalities between citizens from various Member States in its handling of public requests for documents and information. A simple measure would be to refrain from inviting European citizens to visit the EMEA's office in London in order to provide the requested documents, but rather to proactively supply them through the EMEA website, by post or by e-mail.

Proposals for improvements of EMEA draft policy:

► EMEA's conflict of interest needs to be tackled effectively. It necessitates political changes with regard to financing, namely public funding instead of a fee-for-service relationship with pharmaceutical companies.

► The basic consideration that EMEA should treat all European citizens equally needs to be clearly stated.

A minimalist policy compromises public health

This EMEA draft policy, with its vague objectives and an extensive list of excuses for not being able to meet citizens' needs, shows that EMEA fails to identify the fundamental changes needed to protect public health..

Unclear objectives. The EMEA intends to "*involve its partners and stakeholders in discussions on how to meet the increasing demands of civil society (...) for earlier information whilst respecting commercial confidentiality of proprietary information*", with no information on who are EMEA's "*partners and stakeholders"*. Such a vague objective is ineffective, if the aim is to increase transparency. *Prescrire*'s 4-year

	assessment of the agency's performance shows that the defence of commercial interests often supersedes access to relevant scientific information, thus overriding the rights and welfare of both patients and consumers (read Annex A to this joint answer). Mentioning that "*the main aim of the EMEA Transparency Policy (…) is to provide more clarity on the Agency's understanding of its responsibility as a public body in the field of medicines regulation*" is simply not enough and reveals a very limited outlook. **Transparency and accountability are duties for EMEA**, paramount principles to be routinely implemented by the Agency, and moreover indispensable criteria to justify its existence and EU citizens' confidence that public health authorities act as safeguards of public health. Full availability of information is essential to ensure rational use of medicines. European citizens are expecting results in real life, with as easy as possible access to the information they need. Don't expect them to acknowledge and accept EMEA's difficulties to fulfil its tasks. **European citizens have the right to access the information they need and to receive prompt feedback.** **Proposals for improvements of the EMEA draft policy:** **► the legal basis for this policy needs to be clearly stated in the document's rationale;** **► the aim of EMEA transparency policy must be "to guarantee full accountability of EMEA in the carrying out of its tasks (notably opinion and decision-making process) for European citizens".** **"Pretexts" or "prerequisites" meant to avoid taking responsibilities.** Instead of presenting an ambitious transparency policy, with a timeline for its implementation and an assessment of the required human resources, the EMEA has opted for a long list of excuses to justify its inertia (see part II dedicated to the policy rationale). This minimalist policy is being put forward using **a patronising argument**: "*it needs to be recognised that the EU Regulatory System is characterised by a quite complex architecture* (…)*"* and "*the Agency's role in the EU Regulatory System [is] often poorly understood by the*	

	general public and the media". The EMEA expressed its wish to provide "*targeted, understandable and accessible information on medicines*", as it has done with the summaries of the European public assessment reports (EPAR) since its creation in 1995 and which were a progress. However, "*translating [the EMEA processes for opinion/decision-making and (...) the (scientific) rationale for such opinion/decision making] in communication material better adapted and targeted to the various stakeholders*" can lead to insufficiently informative documents and to delays in their dissemination to the public and health professionals. Most notably, these **"tailored versions" must not be used as an excuse to restrict access to the original documents** (documents held by an institution such as full assessment reports, PSURs). As well, the planed **EMEA public register of documents must not serve as an excuse to refuse access to documents that would not be listed in this public register**. EMEA justifies the non-disclosure of documents on occasions, by the need for institutions to "*protect their internal consultations and deliberations (...) to safeguard their ability to carry their tasks*". This provision is being applied unevenly and appears to protect internal consultations and deliberation between companies and the regulator from the public, a situation that needs to change. Pharmaceutical companies are free to seek EMEA's advice and can request an appointment at almost any time, in order to negotiate any measure proposed by the drug regulatory agency (i.e. the need to carry out post-marketing studies or to develop a "risk management plan"). In order "*to safeguard their ability to carry their tasks*", Regulatory Agencies must be aware that **a culture of transparency protects conscientious staff members working in organisations of all kinds**. Another patronising practice is EMEA's refusal to provide requested information when it considers that the decision-making process is still ongoing. Our experience shows that **waiting for "the decision-making process" to be completed,** with its numerous steps, the last one being the formal administrative approval by the EU Commission of EMEA's recommendations, **can lead to unacceptable delays in providing clinical information.** For example, the referral	

	procedure on the combination *dextropropoxyphene + paracetamol* took more than one year and half before EMEA recommends its withdrawal, depriving the medical community and researchers of clinical data contained in the assessment reports provided to EMEA, which knowledge could have saved live. We therefore call for an **early release of clinical data, so that health professionals and patients can have the opportunity to intelligently contribute to the Agency's evaluation of drugs, thus enhancing the quality of EMEA decisions in the safety and quality of drugs.** Another disquieting point is the "*harmonised approach*" being proposed since EMEA is "*recognising the limitations provided by national legislation on freedom of information*". This **'lowest common denominator' approach** is unacceptable. Maximum transparency at the European level is key to encourage for more transparency in EU Member States. EMEA should take the lead and proactively promote best national transparency practices[16,17]. And European citizens should at least expect the EMEA to be as transparent as the most open National Agencies. For example, the MHRA, the UK Agency, clearly states: "*Subject to exceptions, the Freedom of information (FOI) Act gives individuals the right to request any information held by the MHRA. Requestors have the right: to be told whether the information exists; to receive the information*"[18]. **Bureaucratic habits, inertia, lack of resources or over-caution, with EMEA's exaggerated fear of upsetting commercial susceptibilities, must be tackled effectively.** **Proposals for improvements of EMEA draft policy:** **► EMEA should start with the presumption that information about the safety and efficacy of drugs should be available to the public at the earliest possible time.** **► Specify that "*targeted, understandable and accessible information on medicines*" produced by EMEA come in addition to other transparency requirements that concern documents being held by the Agency (in agreement with Regulation (EC) 1049/2001). Moreover, it should not restrict nor delay the access to "original documents" (drug assessment reports, clinical data).**	

	► Append to the EMEA transparency policy a 2nd annex listing the best practices in medicines' transparency in Europe and the US. **Clinical data belong to the public.** The information the EMEA holds mostly comes from clinical trials, which are conducted under the Helsinki Declaration. The Helsinki Declaration clearly states the ethical obligations to make publicly available the results of the research, and insists on the completeness and accuracy of the reports (articles 30 and 33)[19]. In fact, patients participate in clinical trials also because their participation will benefit the public through the advancement of science. But science is hampered if the data never come public. It is therefore particularly important to give access to the clinical data submitted to the EMEA because many studies submitted are never published (especially when their results are negative leading to "publication bias"), and published studies are generally less detailed than the data submitted to the EMEA[20]. Failure to make all the data available greatly diminishes the social value of research. Public access to detailed and summary raw data is particularly important to protect public health because it allows for independent analysis. For example, the identification of cardiovascular risks associated with *rosiglitazone* (Avandia°) in 2007 relied on an analysis mostly of unpublished data[21]. It is also an independent analysis based on published summary-level data, research abstracts and data submitted to the FDA that showed an increased risk of heart attacks among *rofecoxib* (formerly Vioxx°) recipients[22], while the manufacturer had re-classified a number of deaths in a peer review publications[23]. Moreover, industry-funded research benefits from publicly funded research bodies (access to investigators and research teams at publicly research sites; public funding for basic research, etc.). It is reasonable then to expect that data from all research be made publicly available. **Proposals for improvements of EMEA draft policy:** **► Clearly recognise citizens' right to have open access to clinical data.**	

Concrete proposals for a more ambitious strategy guarantying EMEA's accountability to citizens

Redefine "commercial confidentiality of proprietary information" accurately. EMEA's responses to requests for access to safety information, with documents extensively blacked out including the date of the report, illustrate the censorship practiced by the supranational agency (see Annex A). The EMEA alleges that these practices are in place to protect commercial interests and intellectual property rights. But what can possibly justify non-disclosure of important safety information about medicines to patients, consumers and health professionals?

Transparency should be the rule. **Any exception to transparency should require detailed justification and should be granted only temporarily**, **with the possibility to override such an exception in case of an "*overriding public interest*"** (in agreement with article 4 (2) of Regulation (EC) 1049/2001).

As the current definition of "commercial confidentiality" serves to justify undue secrecy, HAI Europe, ISDB and MiEF call for a **redefinition of "commercial confidentiality" through a public debate.** Such a redefinition should be accurate in order to prevent misinterpretations and consequently excessive administrative burden when dealing with requests for information/documents.

All data with a bearing on human health, notably clinical data, should be excluded from "commercial confidentiality" definition, whether or not it affects sales. It includes pre-clinical laboratory and animal data, pre-market clinical trial data, and post-market safety and effectiveness data. Additionally, data concerning the volume of sales should be publicly available.

Exceptions to transparency should only **involve removal of specific elements of information within a document** (for example when protection of individuals' privacy is required), **never apply to an entire document or certain type of documents**.

As to the protection of legitimate business interests, **when no overriding public interests are at stake**, **a feasible approach would**

	be for the manufacturer or the National agency to state, when submitting a document to EMEA, **the reasons why specific parts of a document are to be considered confidential, and for what period** (i.e. "unreasonable degree of prejudice to the commercial interests" duly documented during the 2 next years). A standard application form would allow the authority to confer in confidence the matters accepted under this exception. As to the protection of personal data, a feasible approach would be to ensure that personal data entering an agency (i.e. individual patient or health professional identity) is coded in advance so as to preclude any identification. **Guarantee public access, without delay, to the following documents.** Availability of information must include not only EMEA own deliberations, conclusions and actions as proposed in annex 1 ("*proactive disclosure of EMEA documents/information (...)*"). In agreement with the definition of a document in Regulation (EC) 1049/2001, availability of information also includes documents received by the agency from the outside (3rd party documents) (i.e. PSURs, National drug regulatory agencies's reports). And clinical data belong to the public. We recap below some examples of relevant data which should be made available to the public without delay. For each document we precise if they are currently available or not. **Concerning the initial marketing authorisation and variations to this authorisation:** - All **European Public Assessment Reports (EPARs) underlying the marketing authorisation** of a drug (in agreement with article 13 of Regulation (EC) 726/2004) (currently, EMEA publishes proactively most of them and there is an improvement of the delays[24]); - **Any condition attached to a marketing authorisation**: -- follow-up measures (FUM) (currently, EMEA fails to make these FUM available to the public); -- detailed requests by health authorities for post-authorisation studies or risk management programmes, together with: the pharmaceutical companies' responses to these requests; the justified decision of the	

	health authority to maintain or not its initial request; if maintained, the draft protocols of the post-authorisation studies or risk management plans proposed by the pharmaceutical company and posted for comments; and the final version of these detailed protocols (currently, even upon request, EMEA refuses to give access to the final version of the detailed protocol of post-marketing study and of risk management programmes); - All **updates of European Public Assessment Reports (EPARs) following a change in a marketing authorisation (variation)** (in agreement with article 21 of Directive 2001/83/EC consolidated). Such updates are currently provided in a summarised form so called "steps taken" only "*whenever new information becomes available which is of importance for the evaluation of the quality, safety or efficacy of the medicinal product concerned*"[25]; - **All review documents created by the Agency**: -- **assessment reports** produced by the Committee for Medicinal Products for Human Use (CHMP) (centralised procedure) or by the rapporteur (mutual recognition procedure), at least upon request. (currently, the assessment reports, if transmitted, are often extensively blacked out); -- as for variations, **complete reports** by the Committee for Medicinal Products for Human Use (CHMP), which provide the rationale for the **"steps taken" available online**[13]; -- reports relevant to the **refusal, suspension or withdrawal of marketing authorisations or of manufacturing licences,** including an explanation of the reasons underlying these decisions (currently available on EMEA website in agreement with article 12 of Regulation (EC) 726/2004); -- reports relevant to the **withdrawal of a marketing authorisation application** at any time (currently, in agreement with article 11 of Regulation (EC) 726/2004, reports relevant to the withdrawal of a marketing authorisation application are available only if the assessment was completed); -- **CHMP's complete referrals reports** (assessment report produced within an arbitration procedure in order to harmonise decisions	

	in all Member States). Referrals occur when a Member State cannot approve elements of the marketing authorisation (mutual recognition procedure and decentralised procedure) on the grounds of potential serious risk to public health (article 29 of Directive 2001/83/EC consolidated), when there is need for harmonisation of an old national marketing authorisation (article 30 of Directive 2001/83/EC consolidated), when there is a public health concern about a product already marketed (article 31 of Directive 2001/83/EC consolidated)[26], and when a so called "emergency procedure" is launched (article 107 of Directive 2001/83/CE consolidated)[27]. Currently, only a brief document with no clinical data entitled "background" is provided, too sparse to be of much value to health professionals and patients. - The copies of **non-clinical toxicological reports and detailed clinical reports (efficacy and safety)[28] submitted by the pharmaceutical companies** when applying for initial marketing authorisation or modifications of it, as well as those which are put forward at later stage (read above on the importance to give access to clinical data in order to allow for independent analysis); - The **copies of the packaging elements**: colour mock-ups, detailed description of dosing and/or delivery devices in order to prevent medication errors; - Items above should be accessible for the public at the latest from the date of marketing in Europe onwards (as should the approved data sheet and package insert). To this end, a **publicly available register of all marketing authorisations granted in Europe (centralised, decentralised or by mutual recognition)** should be established. It should include the date of approval. **Concerning post-marketing surveillance and pharmacovigilance:** - The **full content of the Eudravigilance database**[29] (currently, the public and the medical community still have no access to the Eudravigilance database despite legal requirements of an "appropriate level of access" (article 102 of consolidated Directive 2001/83/EC and with article 57 of Regulation (EC) 726/2004); and the European Commission's proposals on pharmacovigilance are very insufficient in terms of transparency[30]);	

	- **Periodic Safety Assessment Reports (PSUR)** prepared by the pharmaceutical companies, including collected data on pharmacoepidemiology, data on drug sales and drug consumption (currently non available even upon request); - **PSUR assessment reports** prepared by national health authorities accompanied by the internal evaluation of current adverse reaction reports by the relevant regulatory authority[31] (currently non available online and those transmitted after several demands were extensively blacked out (see Annex A)); **- Inspection reports** of manufacturing plants, subject only to the deletion of personal details and material details relating to individual privacy and industrial secrets. **Concerning EMEA decision making process:** - **Minutes (transcripts) of agency meetings** (meetings of scientific committees and all working groups) **and hearings**. The EMEA should be at least as transparent as National drug regulatory agencies, which have to publish detailed minutes of their Committee meetings in accordance with article 126b of Directive 2004/27/EC. The FDA's publicly accessible "transcripts" (word-for-word transcription of the meetings) are a useful model; - The **detailed agendas** for all Committee and working group meetings must be **published online prior to meetings**, at the latest on the day before the meetings take place. This would prevent items where it is considered that a "final decision" was not obtained to be removed from the minutes. The detailed agenda should be published **including the list of all experts participating and of experts not allowed to participate** due to conflicts of interests. **Make expert advisory committees public.** EMEA's expert advisory committees[32] should meet in public, on a similar model to the FDA's expert advisory committee meetings, with anyone able to apply to make a submission and attend meetings, and with full public access to background documents.	

	Conclusion Evidence demonstrates that several years after the adoption of European transparency regulations, the EMEA is still lagging behind. The Agency seems to be more concerned with upholding the interests of pharmaceutical companies than in disclosing information to protect patients and consumers. With such a minimalist policy, the EMEA fails to create a European "*culture of transparency*" in drug regulation. ISDB, HAI Europe and Medicines in Europe Forum strongly encourage the EMEA to further increment and advance its transparency policy in order to institute real accountability and restore public confidence. Moreover, HAI Europe, ISDB and Medicines in Europe Forum will closely follow on the ongoing revision of Regulation (EC) No 1049/2001/CE on access to documents[33]. Moreover, more transparency of drug regulatory authorities would mean a real progress in terms of patient information[34].	

2. SPECIFIC COMMENTS ON TEXT

EMEA transparency policy should be rewritten in a more ambitious (general principles clearly formulated) and pragmatic (timetable) manner (read our general comments above). However, we suggest below a few changes in order to help EMEA staff to include our proposals.

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
13		**Comments:** The EMEA has not yet implemented all transparency legal requirements (read general comments and annex 1 to this answer) **Proposed change (if any):** Delete "beyond legislative requirements" and replace it by "in order to comply with legislative requirements"	
18		**Comments:** The EMEA has not yet implemented all transparency legal requirements, which has negative consequences on public health (i.e. delay on information on patient safety issues) and on citizens' trust. **Proposed change (if any):** Before "in order to achieve this objective", add ", bearing in mind that EMEA compliance with transparency legal requirements is a priority in order to protect public health. EMEA compliance with current transparency legal requirements should be fully implemented before 2012"	
20		**Comments:** This formulation is too ambiguous. It conveys the meaning that EMEA willingness to protect drug companies' interests could supersede its willingness to provide access to scientific knowledge or to protect patients' interests. **Proposed change (if any):**	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		Replace "on how to meet the increasing demands of civil society (…) for earlier information whilst respecting commercial confidentiality of proprietary information" by "on how to guarantee full accountability of EMEA in the carrying out of its tasks (notably opinion and decision-making process) for European citizens"	
32		**Comments:** Transparency is not a gesture of goodwill that the EMEA could do without. Transparency is a duty for EMEA, a legal obligation, and this legal basis should be clearly highlighted in the section presenting the "rationale" for the policy proposal. **Proposed change (if any):** Replace the rationale "to be able to better address the increasing need for information from civil society" by "to be able to comply effectively with transparency legal requirements in order to better serve the civil society" and precise the legal basis for transparency in a footnote.	
37		**Comments:** Transparency, and accountability even more so, are duties for EMEA, and indispensable criteria in relation to justifying its existence. **Proposed change (if any):** Add after "transparency", "and accountability are 2 pivotal elements"	
38 - 39		**Comments**: All EU-citizens have a right for impartial and comprehensive information about the medicines regulated by EMEA, not only EMEA's stakeholders.	
41		**Comments:**	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		This formulation testifies to a too narrow outlook. Full availability of information is essential if all parties involved in health care are to participate effectively, and to improve rational use of medicines. Not only EMEA's credibility and accountability are at stake, but also citizens' confidence in health authorities. European citizens are expecting results in real life from EMEA policy, which means as easy as possible access to the information they need. **Proposed change (if any):** Replace "the main aim of the EMEA Transparency Policy, therefore, is to provide more clarity on the Agency's understanding of its responsibility as a public body in the field of medicines regulation" by "the main aim of the EMEA Transparency Policy, therefore, is to provide **total** clarity on **how EMEA guarantees full accountability to European citizens in the carrying out of its tasks (notably the opinion and decision-making process)**"	
56		**Comments:** EMEA should remember that transparency at a European level is key to encourage transparency at a National level in EU Member States. EMEA shouldn't choose the lowest common denominator among Member States. EMEA should take the lead to promote best national transparency practices and pick the best bits from the US Food and Drug Administration (FDA) transparency. **Proposed change (if any):** Add after "legislation": "and the best transparency practices among Member States and the USA, some of which are listed in annex 2"	
61		**Comments:** Transparency should be the rule: information available within regulatory agencies should be freely available to any party requesting it. Exceptions to this must be	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		defined very strictly, with accuracy, in order to improve the current situation where it is a main obstacle to access to data. **Proposed change (if any):** Replace "Transparency implies openness, communication and accountability, whilst respecting the protection of ~~both~~ personal data ~~as well as~~ commercially confidential information" by "Transparency implies openness, communication and accountability, whilst respecting the protection of personal data **as defined by specific regulation** *(precise reference to the text in a footnote)*, and the protection of commercially confidential information **that prejudice to an unreasonable degree the commercial interests (such a prejudice should by duly justified). The protection of commercially confidential information falls when there is overriding public interest at stake**."	
67		**Comments:** The EPARs were a great progress. To produce more of such documents adapted to users is a good initiative that should come in addition to existing obligations. There is a risk that this "*translating [the EMEA processes for opinion/decision-making and (...) the (scientific) rationale for such opinion/decisionmaking] in communication material better adapted and targeted to the various stakeholders*" can lead to insufficiently informative documents and to delays in information provision to the public (i.e. steps taken sometimes insufficiently informative). Moreover, these "public documents" must not serve as an excuse to refuse access to original documents (documents held by an institution such as full assessment reports, etc.) for citizens that ask for these original documents. **Proposed change (if any):** Add: "Such "public information" comes in addition to EMEA transparency	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		requirements concerning public access to documents it holds, and must not delay the access to such documents".	
71-74 217-219		**Comments:** EMEA proposes to adopt a policy with more openness towards stakeholders, including involvement in opinion/decision-making. We support the involvement of civil society representatives. At the same time we would like point out that it is crucial that such contacts with stakeholders are completely transparent for the general public. As for the scientific experts, each stakeholder delegate should declare any conflict of interest that should be made publicly available. The involvement of stakeholders in EMEA's activities should be defined by pre-established rules and transparent procedures and criteria.	
80		**Comments:** EMEA should remember that transparency at a European level is key to encouraging transparency at a National level in EU Member states. European citizens should at least expect the EMEA to be as transparent as National Agencies. For example, the MHRA, the UK Agency, clearly states: "*Subject to exceptions, the Freedom of information (FOI) Act gives individuals the right to request any information held by the MHRA. Requestors have the right: to be told whether the information exists; to receive the information*". **Proposed change (if any):** Delete "Whilst recognising the limitations provided by national legislation on freedom of information"	
Before line 89 Section III		**Comments:** There is a need to add a new section presenting the General Principles guiding the EMEA transparency policy in order to clarify the policy and to allow for a better	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	Stakeholder No. *<to be completed by EMEA>*	Comment and Rationale; proposed changes *<if changes to the wording are suggested, they should be highlighted using "track changes">*	Outcome *<to be completed by EMEA>*
		understanding of it (read above). **Proposed change (if any):** Addition of: "III – General Principles guiding the EMEA transparency policy EMEA transparency policy is based on the following general principle: **1- Transparency should be the norm** Information available within regulatory agencies should be freely available to any party requesting it. Exceptions to this must be defined very strictly and should never occur for certain types of document. Exceptions should occur only for some mentions or part of a document if they are explained and duly justified. A feasible approach would be for a manufacturer or a national Agency, when submitting a document to EMEA, to state, with reasons (i.e. *"an unreasonable degree of prejudice to commercial interests*" duly documented), which specific parts of the file are considered confidential and for what period. This specification would be made on a standard form allowing the authority to confer in confidence about the types of matters accepted as justified under this exception. Exception falls in the case of an "*overriding public interest*" (article 4 (2) of Regulation (EC) 1049/2001). A public consultation will be organised on that issue. **2- Transparency measures implementation are a priority** EMEA compliance with transparency legal requirements is a priority in order to protect public health. The "stepwise implementation" process should be speeded up in order to allow for EMEA compliance with current transparency legal requirements to be fully implemented before 2012. **3- Equality of treatment relative to access to information and documents for European citizens** EMEA aims to serve civil society interests. For the beginning of 2010, EMEA will organise the possibility for documents requested to be sent by post or by e-mail, so that citizens do not have to go to	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		London at EMEA office to have access to some document. EMEA can ask for reasonable copies and post fees to do so."	
94		**Comments:** Misleading statement (read above) **Proposed change (if any):** Delete "(often going beyond the legislative provisions in force" and replace it by "efforts still need to be done and"	
104		**Comments:** The review of the definition of commercial confidentiality is a key issue for transparency policy in Europe. A democratic process is indispensable. **Proposed change (if any):** Replace "through a dialogue" by "through a public consultation with all interested parties, particularly civil society and all responders to the consultation on the EMEA draft transparency policy"	
107		**Comments:** EMEA shouldn't choose the lowest common denominator among Member States. EMEA should take the lead to promote best national transparency practices and pick up the best from the US Food and Drug Administration (FDA) transparency policy. And European citizens should at least expect the EMEA and the co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh) to be as transparent as National Agencies. **Proposed change (if any):** Replace "a concerted action with the National Competent Authorities (NCAs) of the Member States in order to achieve a harmonised EU approach in this field" by:	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		"implementation of the best transparency practices of the National Competent Authorities (NCAs) of the Member States and of the US Food and Drug Administration (FDA) identified (see annex 2), in order to guarantee EMEA and the co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh) accountability at a high level of transparency"	
126		**Comments:** Transparency is not a gesture of goodwill the EMEA could do without. Transparency is a duty for EMEA, a legal obligation as it is for the other European institutions, and this legal basis should be clearly reminded**.** **Proposed change (if any):** Add after "a primary focus.": **"**This communication material comes in addition to EMEA transparency requirements concerning the documents it holds. The production of such material must not restrict or delay access to original documents".	
127		**Comments:** Transparency is not a gesture of goodwill EMEA could do without. Transparency is a duty for EMEA, a legal obligation as it is for the other European institutions, and this legal basis should be clearly reminded**.** **Proposed change (if any):** add "and fulfilling transparency legal requirements" to "promoting good administrative and regulatory practices"	
135		**Comments:**	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		EMEA compliance with transparency legal requirements is a priority in order to protect public health. **Proposed change (if any):** Replace "will need to be put in place" by: "will be put in place before January 2011".	
197		**Comments:** The proposal of EMEA to make further progress in order to "apply a more proactive approach towards transparency in the daily operation of the EMEA" is clearly insufficient considering regulatory requirements (read above in the general comments). It needs to be substantially rewritten. To specify that EMEA gives access to information and documents only "once the decision-making process has been concluded" is not appropriate since much information and many documents that EMEA should give access to (i.e. assessment reports, PSURs) are not subjected to decision making issues. Our experience also shows that the interpretation of the statement "once the decision-making process has been concluded" is often too extensive, leading to undue delays (i.e. need to wait for the European Commission signature, even if the CHMP adopted an assessment report, etc.). **Proposed change (if any):** Replace text from line 197 to 215 by the following (some modifications to the initial proposal are apparent): "To make further progress in this field the EMEA envisages: - An embedded culture of transparency in the Agency's operations, in order to achieve a consistent approach in the application of the various principles of the EMEA Transparency Policy **and to comply with the regulatory transparency requirements**;	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		- ~~Gradually~~ **Urgently** improve, **without undue delays especially when public health is at stake**~~, once the decision-making process has been concluded,~~ the proactive disclosure of EMEA documents/information throughout the lifecycle of medicines for human and veterinary use. - **Urgently** improve, ~~once the decision-making process has been concluded,~~ the proactive disclosure of EMEA documents/information throughout the lifecycle of medicines for human and veterinary use. The identification of key milestones for the disclosure **without undue delays** of such documents/information should facilitate this process. **According to transparency legal requirements, public access to documents held by the EMEA should be guaranteed even if they are not identified as "key milestones".** - ~~Review the balance between transparency and the protection of commercial confidentiality of proprietary information by~~ **Redefine** the notion of commercially confidential information **with accuracy through a public consultation process, taking into account that full transparency should be the norm.** ~~and subsequently arriving at a harmonised EU view on this topic.~~ This should preferably lead to the disclosure of ~~selected pieces of~~ information prior to decision-making, **since EMEA aims to serve civil society interests, notably by an Equality of treatment relative to access to information and documents for all European citizens. Exceptions should be justified with explicit reasons given (i.e. "an unreasonable degree of prejudice to commercial interests" duly documented), and fall in case of an "*overriding public interest*" (article 4 (2) of Regulation (EC) 1049/2001).** ~~, without undermining the decision-making process (e.g. the release of a minimum set of information on the submitted applications for marketing authorisation)~~. - Improve the visibility of the Agency and undertake efforts to better explain how conclusions are being reached at the EMEA, as well as the (scientific) rationale for these conclusions. This should lead to a further strengthening of the EMEA stakeholders' trust in the Agency's deliverables **but must not add delay to the**	

Line No of the first line(s) affected. *<e.g. Line 20-23>*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		release of information.	
219 and 221		**Comments:** Patient organisations are often heavily industry funded, particularly at International and European levels, for example, the IAPO (International Association of Patient Organisations),the "European Patient Forum" (EPF) and the "Friends of Europe". This dependence biases debate. Consumers' and users' organisations, however, are often less dependent on such industry funding, which allows them to represent civil society with a more critical point of view, which is very constructive and useful for debate. **Proposed change (if any):** Add "independent" between "civil society" and "representatives" Replace "EMEA Patients' Organisations Working Group" by: "EMEA Patients', Users' and Consumers' Organisations Working Group"	
245		**Comments:** "Consistent implementation across the EU" shouldn't serve as a pretext to adopt the lowest common denominator, thus jeopardising civil society information on important issues such as patient safety issues, and consequently public health.	

2. SPECIFIC COMMENTS ON ANNEX 1

This list is a good start for more transparency at a European level: "key transparency initiatives" proposed in order to achieve objective 2 and 3 are particularly welcome. However, no timetable is given, undermining EMEA credibility. The final version should integrate a timetable, bearing in mind that EMEA compliance with transparency legal requirements is a priority in order to protect public health.

We propose some changes below, mainly to make some points more compliant to legal transparency requirements: additions in bold, ~~deletions~~; no change means that we support the measure proposed as edited. For the rationale for theses changes, read the comments above.

Objective 1- To apply a more proactive approach towards transparency in the daily operation of the EMEA

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		~~**Balance between transparency and commercially confidential information**~~ **Restrict the definition and interpretation of commercial confidentiality** (*If the aim is to improve transparency at European level, this new formulation is needed to clarify the objective*) **Proposed changes:** 1. Redefine the notion of commercially confidential information **in order to improve transparency and through a public consultation process**~~, in close collaboration with the NCAs, leading to a harmonised EU view in this field,~~ taking due account of the outcome of the public consultation on the EMEA Access to Documents Policy **and to the outcome of this public consultation on EMEA transparency policy**. 2. Progress the implementation of the EMEA Access to Documents Policy **and transparency regulatory requirements**, taking into account the outcome of the public consultation, including the establishment of the EMEA public register of documents.	

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		Proactive disclosure of ~~EMEA~~ documents/information throughout the product lifecycle *(Regulation (EC) 1049/2001 applies to the documents hold by the EMEA and not only to "EMEA documents/information")* **Proposed changes:** 3. Proactively publish additional product related documents: - **Detailed** agendas of EMEA Scientific Committees' meetings **and of EMEA Working group meetings (which should be available, at the latest, by the day before the meetings take place, so that issues where it is considered that a "final decision" was not obtained cannot be removed from the minutes);** - Detailed minutes **(transcripts)** of EMEA Scientific Committees' meetings and **of EMEA Working group meetings accompanied by decisions taken, details of votes and explanations of votes, including minority opinions** (article 126b of Directive 2004/27/EC); - PhVWP **agendas and transcript of meetings**, Monthly Reports (for medicines for human use). **- All review documents created by the Agency:** **-- assessment reports produced by the Committee for Medicinal Products for Human Use (CHMP) (centralised procedure) or by the rapporteur (mutual recognition procedure);** **-- as for variations, complete reports by the Committee for Medicinal Products for Human Use (CHMP), which provide the rationale for the "steps taken" available online;** **-- reports relevant to the withdrawal of a marketing authorisation**	

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		application at any time; **-- PSUR assessment reports**; **-- CHMP's complete referrals reports (articles 29, 30, 31 and 107 of Directive 2001/83/CE consolidated);** **- The copies of the packaging elements;** **- Establish a publicly available register of all marketing authorisations granted in Europe (centralised, decentralised or by mutual recognition) including the date of approval.** 5. Proactively publish additional information elaborating on the benefit/risk of medicinal products for human use: - Pharmacovigilance Newsletters/Safety Bulletins in relation to emerging safety information for centrally authorised products. - Information stemming from the assessment of Periodic Safety Update Reports (PSURs) and the subsequent variation procedures for centrally authorised products through the updating of EPARs (joint HMA/EMEA initiative which should be considered within the wider context of efforts to improve transparency on safety related aspects); **- Any conditions attached to a marketing authorisation:** **-- follow-up measures (FUM);** **-- detailed requests by health authorities for post-authorisation studies or risk management programmes, together with: the pharmaceutical companies' responses to these requests; the justified decision of the health authority to maintain or not its initial request; if maintained, the draft protocols of the post-authorisation studies or risk management plans proposed by the pharmaceutical company and posted for comments; and the final version of these detailed protocols;** **- Full Periodic Safety Assessment Reports (PSUR);** **- PSUR assessment reports**;	

Objective No and key transparency initiative No. <e.g. 2.7 >	Stakeholder No. <to be completed by EMEA>	Comment and Rationale; proposed changes <if changes to the wording are suggested, they should be highlighted using "track changes">	Outcome <to be completed by EMEA>
		- The **full content of the Eudravigilance database**; **6. Make publicly available without delay upon request:** - The copies of **non-clinical toxicological reports and detailed clinical reports (efficacy and safety) submitted by the pharmaceutical companies**; ~~- Direct healthcare Professional Communications proposed by the Marketing Authorisation holders and discussed by the CHMP.~~ **??** **Comment:** About the documents that should be made available see our general comments above ("clinical data belong to the public"). "Direct healthcare Professional Communications proposed by the Marketing Authorisation holders" needs to be clarified. Where is the transparency (access to clinical data) and independence of the information in this process? Direct communication can be a tool for advertising from opinion leaders.	
		Visibility of the EMEA and understanding the Agency's opinion/decision making **Comments** Points 1, and 9: We are wondering why the proposals refer to collaboration with some UK universities (What was the motivation? Who made this choice and based on which criteria (London School of Economics, Kings College)? What about the connection with the EUnetHTA in order to identify National Drug regulatory agencies best practices? What about the connection with ISDB bulletins, which assess drugs and	

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		routinely use EMEA's documentation? Does a collaboration with the LSE implies that EMEA's evaluations would integrate a medico economic approach? EMEA's mission is rather to assess drugs on scientifically and regulatory aspects, not to do medico economic assessments. Confusion between the roles of the different bodies could lead to opacity of decisions. **Proposed changes:** EMEA's approach should start with an exhaustive inventory of assessment best practices (National Drug regulatory agencies, independent teams such as ISDB editorial staff). **Comments** Point 11. "Assess the content of benefit-risk communication – expectations from key opinion leaders (in collaboration with the Kings College, UK)" is unclear. What would be the aim of this assessment? Who and how would these experts be chosen? (on which criteria?) **Proposed changes:** 16. Review the lay-out and content of EPARs to better describe the rationale for opinion-making and to better reflect ethical issues related to clinical trials conducted in non-EU countries that are included in an initial application for marketing authorisation. **Add a new section listing the experts involved in the assessment including additional experts questioned, with a link to their updated conflict of interest declarations;**	

Objective 2- To further strengthen interaction with EMEA stakeholders

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		Proposed changes: 1. Revise existing formal interactions with Patients'/Consumers' Organisations by reflecting on how to further increase patients' **and consumers'** involvement in EMEA activities, resulting in amendments to the current framework on interaction. 2. Involve Patients'/Consumers' **independent** representatives more systematically in the activities of the Pharmacovigilance Working Party (PhVWP) (for human medicines), taking into account the outcome of a 3 months pilot phase introduced in April 2009.	

Objective 3 - To enhance and promote closer interaction with the NCAs within the frame of the EU Regulatory System Network on transparency related aspects

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		2. Proactively publish **detailed** agendas at least one day before the meeting takes place and ~~Minutes~~ **transcripts** of EMEA Scientific Committees' meetings **and of working groups accompanied by decisions taken, details of votes and explanations of votes, including minority opinions, and by the list of the names of all experts that participated and by that of experts not allowed to participate because of their conflict of interests** ~~as per the agreement with the NCAs for a coordinated approach within the EU~~. ; 3. Achieve a coordinated approach within the EU Pharmacovigilance System on	

Objective No and key transparency initiative No. *<e.g. 2.7 >*	**Stakeholder No.** *<to be completed by EMEA>*	**Comment and Rationale; proposed changes** *<if changes to the wording are suggested, they should be highlighted using "track changes">*	**Outcome** *<to be completed by EMEA>*
		safety related aspects as regards: - The provision of information stemming from the assessment of PSURs (joint HMA/EMEA initiative). - Transparency on the ~~outcome of discussions at the level of the~~ PhVWP **work** (e.g. **publication of detailed agenda and transcripts of the meeting**, the publication of PhVWP Monthly Reports for medicines for human use and the publication of Executive Summaries of Pharmacovigilance Assessment Reports), taking into account the outcome of the PhVWP survey on pharmacovigilance transparency and public communication policies in the Member States (medicines for human use). These transparency initiatives should be considered within the wider context of efforts to improve transparency on safety related aspects.	

Annexe A to our HAI Europe, ISDB and MiEF joint answer:

Prescrire Editorial Staff "**Legal obligations for transparency at the European Medicines Agency: Prescrire's assessment over four years**" *Prescrire International* 2009; **18** (103): 228-234.

Notes and references to our general comments:

[1]- European Medicines Agency "The EMEA transparency policy – draft for public consultation" London, 19 June 2009 (Ref. EMEA/232037/2009). Available at: http://www.emea.europa.eu/pdfs/human/transparency/23203709en.pdf: 12 pages.

[2]- "Statement of the international working group on transparency and accountability in drug regulation: Uppsala Declaration". Uppsala, Sweden, 11-14 September 1996. Available at www.isdbweb.org/pag/uppsala.php.

[3]- The ISDB answered this consultation on "EMEA policy on the practical operation of access to EMEA documents". ISDB "EMEA: excessive secrecy beyond the law! Transparency should be the norm" Press release; 2 March 2009: 3 pages. Available at: http://www.isdbweb.org/pag/documents/200903_ISDB_TransparencyPR_001.pdf.

[4]- EMEA developed different procedures to deal with the different kinds of information, which are either contained in documents (and in electronic registers of documents), or in databases, or which are considered as "requests for information". Our experience is that such a distinction makes it very difficult to make a request. Faced with a request for information, EMEA should try to tailor its answer to meet this need with a real commitment to serve public interests.

[5]- "Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency" Consolidated version dated 26 January 2007. ec.europa.eu accessed 15 February 2009: 51 pages

[6]- European Medicines Agency "Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents" 15 April 2007: 8 pages.

[7]- "Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents" Official Journal of the European Communities, 31 May 2001: L 145/43-L 145/48: art. 4-2.

[8]- In addition, if patient safety is to be improved, the transparency provisions contained in the "pharmacovigilance proposals" (http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/pharmpack_en.htm), have to be strengthened by citizens' Representatives in the EU Parliament during the coming legislative process.

[9]- An example of the too broad interpretation of "commercial confidentiality" by EMEA was its refusal, at the first place, to answer information requests on consumption data, which is essential for evaluating the level of exposure of the population and assessing the harm-benefit balance of a medicine. Consumption data should not be considered as "confidential" if EMEA applied its own rules: they are in fact already available from public databases in some Member States (i.e. Medicam in France).

[10]- Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents (Doc. Ref.: EMEA/45422/2006). Available at: http://www.emea.europa.eu/pdfs/human/euleg/4542206en.pdf.

[11]- Article 73 of Regulation (EC) 726/2004 foresees that Regulation (EC) 1049/2001 applies to EMEA.

[12]- "Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use" Consolidated version dated 30 December 2009. ec.europa.eu accessed 9 April 2009: 129 pages.

[13]- The “steps taken” posted online for several variations are often too sparse to be of much value to health professionals and patients, even if patient safety is at stake: no details on the 4 cases of osteonecrosis affecting bones other than the jaw with *zoledronic acid*; no details on *rimonabant* (formerly Acomplia°), a psychotropic marketed for the treatment of obesity, adverse effects when its risk-benefit balance was becoming increasingly unfavourable (the drug has since been withdrawn from the market); no explanation of the *ethinylestradiol* dose reduction from 750 µg to 600 µg in Evra° patches (*norelgestromin+ethinylestradiol*), etc.

[14]- The vague wording that “*necessary (technical) tools (…) will need to be put in place*”, without timetables or additional details on the nature of these tools, is not reassuring.

[15]- European Medicines Agency (EMEA) "Statement of revenue and expenditure of the European Medicines Agency for the financial year 2009" 2009. Site internet eur-lex.europa.eu consulté le 1er juillet 2009: 6 pages.

[16]- Examples of good transparency practices among Member States: obligation for health professionals to declare conflicts of interests when speaking to the media in France (www.formindep.org), access to adverse drug reactions information in the Netherlands (www.lareb.nl), Freedom of information act giving individuals the right to request any information held by the MHRA in United Kingdom (www.mhra.gov.uk/), etc.

[17]- More information on FDA’s new blog on transparency: http://fdatransparencyblog.fda.gov/comment-policy.html.

[18]- MHRA Freedom of information (FOI) Act http://www.mhra.gov.uk/Aboutus/Freedomofinformationanddataprotection/Freedomofinformation/index.htm
Guidance on the Disclosure of Types of Human and Veterinary Medicines - Information Held by the Human and Veterinary Regulatory Authorities:
http://www.mhra.gov.uk/home/groups/l-unit1/documents/websiteresources/con2033020.pdf.

[19]- Helsinki Declaration available at: www.wma.net/e/policy/b3.htm.

[20]- The European Clinical Trials Database (Eudra CT) is limited to a relatively small number of data fields and to summary treatments of data. Eudra CT provides no raw data that is needed by the medical community and drug safety and pharmacoepidemiology experts to conduct effective original analysis.

[21]- Nissen SE et coll. “Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes” NEJM 2007; 356: 2457-71.

[22]- Jüni P et coll “Risk of cardiovascular events and rofecoxib: cumulative meta-analysis” Lancet 2004; 364 : 2021-2029.

[23]- Egilman DS et Presler AH “*Missing* Safety Data and Merck-y Ethics in the ADVANTAGE trial” Ann Int Med. 3 Aug 2005.

[24]- A new section should be created in each EPAR containing lists of all experts involved in the assessment of medicines (including additional experts questioned), with a link to their updated conflict of interest declarations (in agreement with Article 63 of Regulation (EC) 726/2004). Currently, such declarations are only available online for members of the Management Board and of the committees and for rapporteurs, but not for members of working groups and experts, making them difficult to obtain.

[25]- The selection criteria of such relevant information are disputable, product centred but not patient centred. For example, no information was made available about the risk of contraceptive loss of effectiveness when taking *tériparatide* (Forsteo°) (an osteoporosis treatment) in the EPAR of the product. In fact, this information does not directly concern the product itself…

[26]- An example of a referral using article 31 of the Directive 2001/83/CE consolidated is the one on the dextropropoxyphene + paracetamol combination that leads to EMEA’s recommendation to withdraw it from the European market in June 2009.

[27]- The urgent referral procedure under Article 107 of Directive 2001/83/EC is launched when a Member State decides to suspend a marketing authorisation, considering that "*urgent action to protect public health is necessary".*

[28]-.The detailed clinical reports are sometimes "called the clinical study report", which should include information about the study's protocol, raw data submitted in support to the study after deletion of nominative information, and any information provided to an EMEA Committee).

[29]- The USA Food and Drug Administration (FDA) already provides this type of information through quarterly data extracts from its Adverse Event Reporting System (AERS) database.

[30]- AIM, ESIP, HAI Europe, ISDB, and MiEF joint analysis of the pharmacovigilance proposals are available at: http://www.isdbweb.org/pag/documents/En_CEProposals_June2009.pdf.

[31]- See the European Commission legal proposals on pharmacovigilance (released in December 2008):
- Proposed Directive: http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0665:FIN:EN:PDF
- Proposed Regulation: http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0664:FIN:EN:PDF.

[32]- Committee for Medicinal Products for Human Use (CHMP), Committee for Medicinal Products for Veterinary Use (CVMP), Committee for Orphan Medicinal Products (COMP), Committee on Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), Committee for Advanced Therapies (CAT) and future Pharmacovigilance Committee.

[33]- A regression in transparency is feared by the European ombudsman itself (http://www.statewatch.org/news/2008/jun/eu-ep-ombudsman-on-com-proposals-speech.pdf) and by the European Parliament Committee responsible (Committee on Civil Liberties, Justice and Home Affairs) because of the restrictive definition of a document proposed in the European Commission proposals (www.europarl.europa.eu/oeil/FindByProcnum.do?lang=1&procnum=COD/2008/0090). Regulation (EC) 1049/2001 shouldn't be weakened but on the contrary strengthened and apply to all communitarian marketing authorisation procedures (i.e. not only centralised procedures, but also decentralised procedures or by mutual recognition).

[34]- Transparency of drug regulatory authorities is one key measure in order to really improve patients' access to relevant health information. For more details, read our joint position on the European proposals on patient information: "Legal proposals on "information" to patients by pharmaceutical companies: a threat to public health". Available at: http://www.isdbweb.org/pag/documents/LegalProposalsInfofinaleeee.pdf.