



The Cochrane Adverse Effects
Methods Group



Transparency of adverse drug reactions in Europe: Proactive public access to qualitative data is needed, pharmacovigilance data are not “trade secrets”

Submission of comments on 'Revision of EudraVigilance access policy for medicines for human use' (EMA/759287/2009 Revision 1)

Comments from:

Name of organisation or individual

Cochrane Adverse Effects Methods Group (AEMG)
Health Action International (HAI) Europe
International Society of Drug Bulletins (ISDB)
Medicines in Europe Forum (MIEF)

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Transparency of adverse drug reactions in Europe: Proactive public access to qualitative data is needed, pharmacovigilance data are not “trade secrets”

Summary/Key points

- In August 2014, the European Medicines Agency (EMA) organised a public consultation on the revision of its 2011 policy on the access to the European pharmacovigilance database EudraVigilance, which created the public interface adrreports.eu.
- Reports of suspected adverse drug reactions are coded using standardised terminology and then registered in EudraVigilance as “Individual Case Safety Reports, ICSR”. In practice, however, this process can strip spontaneous reports of individual cases of clinical significance. That is why access to narrative summaries of individual cases needs to be provided along with quantitative data.
- Unfortunately since 2012, the public interface Adrreports (www.adrreports.eu) has provided access to only a limited number of quantitative information, e.g. the number of suspected adverse reactions associated with a given substance, but it does not give access to a listing of case summaries (“Narrative Case Summary”).

According to Pierre Chirac, Medicines in Europe Forum coordinator:

“In the EU, health professionals and patients, who are major contributors to the EudraVigilance database through the spontaneous reports they send to their national drug authorities, are paradoxically the actors who access the least information.”

- In its draft revision document, the EMA proposes to share more data with marketing authorisation holders (MAH), which makes sense since they are required to develop periodic benefit-risk evaluation reports about their drugs. Nevertheless, drug regulatory agencies have to closely monitor the MAH pharmacovigilance activities in order to avoid data being misinterpreted or withheld as recently happened on several occasions.
- The EMA also proposes to give research organisations, on request, “access to ICSR data sets similar to those provided for MAHs in response to justified research requests”. However, the EMA sets up restrictive conditions for granting access to researchers, e.g. the signature of confidentiality agreements. The EMA also demands to “view any publication resulting from EudraVigilance data before submission (...). [and that] any issues raised by the Agency (...) must be addressed to the satisfaction of the Agency before submission for publication”. However, EMA’s central role does not give it the right to control how the data are used or to censor scientific discussion.
- Another change of concern is that the description of access for each stakeholder now makes them responsible for applying “appropriate technical and organisational measures to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss”.

Ancel.la Santos, Health Action International (HAI) Europe policy advisor, comments:

“There are standards in place for de-identifying personal data and additional measures can be explored for particular cases (rare diseases). But data protection cannot be used as a pretext to protect commercial interests. Pharmacovigilance data are not trade secrets, but information that is of the utmost relevance to protect public health.”

- We encourage the EMA in its policy to support public health by:
 - proactively providing public access to **useful qualitative data** such as anonymised summaries of cases;
 - granting public access to **consumption data** of drugs in the EU;
 - providing access to all **drug regulatory authorities’ assessment reports of MAH’s periodic benefit-risk evaluation reports** (former Periodic safety update reports);
 - **not** forcing researchers to sign “**confidentiality agreements**”.

1. General comments

Stakeholder number	General comment	Outcome (if applicable)
	<p data-bbox="757 475 1391 576">Transparency of adverse drug reactions in Europe: Proactive public access to qualitative data is needed, pharmacovigilance data are not “trade secrets”</p> <p data-bbox="483 619 1666 754">We welcome the opportunity to contribute to the European Medicines Agency (EMA) public consultation on the revision of its policy on the access to the European pharmacovigilance database EudraVigilance (1). This draft policy aims to update the previous EMA EudraVigilance access policy from 2011, which created the public interface adrreports.eu (a).</p> <p data-bbox="483 791 1666 995">Created in 2001, the EudraVigilance database is a central database holding reports on suspected adverse drug reactions in Europe (b). Until the 2010 EU pharmacovigilance legislation (directive 2010/84/EC and regulation (EC) 1235/2010), the data in EudraVigilance were submitted electronically by national medicines regulatory authorities on the basis on spontaneous reports from health professionals (and from patients in Member States already allowing patient reporting), and on the basis of reports submitted to medicines regulatory authorities by pharmaceutical</p>	

a- Unfortunately, despite the short consultation period (4 August until 15 September 2014), the consultation document does not allow readers to identify clearly the changes proposed to the 2011 policy (no apparent modifications, even in the tables on pages 29 to 51). Holding a consultation in such a short timeline during summer recess is not consistent with the actual purpose of a consultation, which is to obtain an adequate and representative feedback from the public.

b- “Taking into account the pharmacovigilance activities in the pre- and post- authorisation phase, EudraVigilance provides two reporting modules:
- The EudraVigilance Clinical Trial Module (EVCTM) to facilitate the electronic reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) as required by Directive 2001/20/EC;
- and the EudraVigilance Post-Authorisation Module (EVPAM) for post-authorisation Individual Case Safety Reports (ICSRs) as required by Regulation (EC) No 726/2004, Directive 2001/83/EC as amended.”
(ref. <https://EudraVigilance.ema.europa.eu/human/index.asp>)

companies. With the implementation of the 2010 pharmacovigilance legislation, the pharmaceutical companies are now allowed to submit data on their medicines directly in EudraVigilance (2).

EMA's question: *As regards stakeholder group II "Healthcare professionals and the public" would you consider it useful to obtain additional data outputs from the European database of suspected adverse reactions such as tabular presentations or outputs presented as individual cases whilst fully respecting personal data protection?*

Our answer:

Spontaneous reports of suspected adverse drug reactions are registered in EudraVigilance as "**Individual Case Safety Reports, ICSR**". ICSR are the result of a coding of spontaneous reports using standardised terminology (c). In the registration process, one spontaneous report about a patient suffering several suspected adverse drug reaction will be coded into several ICSR, one for each suspected adverse reaction. In practice, the registration process can strip spontaneous reports of individual cases of clinical meaning, resulting in data being minimised or misinterpreted (3). **That is why access to comprehensive summaries of individual cases needs to be provided along with quantitative data.**

Proactive disclosure of pharmacovigilance data: qualitative data is needed

According to the draft document, there will be "*no changes in the EudraVigilance Access Policy (...) for (...) healthcare professionals, consumers and patients*" who "*maintain the possibility to search and screen ICSR data*" using Adrreports. Adrreports (www.adrreports.eu) is the public interface of the EudraVigilance database set up by EMA's 2011 access to EudraVigilance policy.

Since May 2012 (d), Adrreports (www.adrreports.eu) provides access to **only a limited amount of quantitative information** and only for centrally approved medicines, e.g. the number of

c- The coding of spontaneous reports is done using the Medical Dictionary for Regulatory Activities (MedRA) dictionary developed under the auspices of International Conference on Harmonisation (ICH).

d- Adopted in 2004, regulation (EC) N°726/2004 already stated that "*the Agency shall ensure that healthcare professionals and the public have appropriate levels of access to the EudraVigilance database*". However, until 2012 and the setting up of the interface [adrreports.eu](http://www.adrreports.eu), 'appropriate access' meant no access at all.

individual cases associated with a given substance. The database is also searchable by adverse reaction groups or for a selected adverse reaction (the adverse reactions are coded using the MedDRA dictionary). The number of individual cases is available by age group, sex, reporter group (e.g. health professional, patient, or MAH) and geographic origin.

Since the registration process can strip spontaneous reports of individual cases of clinical meaning, comprehensive qualitative data are essential in order to better understand quantitative data. That is why the publicly accessible database of the Dutch pharmacovigilance centre, Lareb (www.lareb.nl), gives access to **anonymised summaries of cases**. Unfortunately, despite the work being done when ICSR are registered in EudraVigilance (e), the adrreports interface does not give health professionals and patients access to such a listing of summaries of cases. Health professionals and patients, who are major contributors to the EudraVigilance database by sending their spontaneous reports to their national drug authorities, are paradoxically denied access to any information about the context of occurrence of adverse reactions (f).

There is no information either on the consumption data of a given drug in the EU or in the different EU Member States, making it impossible to have an idea of the incidence of a given adverse drug reaction associated with a given drug. This information is however easily available to the EMA since it is given by the pharmaceutical companies in their periodic benefit-risk evaluation reports (former periodic safety update reports, PSUR).

And finally the Adrreports interface is not user friendly:

- it is not compatible with several common internet navigators;
- since the summer of 2014, it has been no longer possible to download and register requests in pdf format, only as an Excel file;
- it provides only cumulative data on the total number of adverse drug reactions being registered in the EudraVigilance database, without the possibility of identifying new cases.

e- See the lines “ICH H - Narrative Case Summary and Further Information, including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information” and “Reporter’s comments” on page 50.

f- Spontaneous reporting remains the main resource for bringing safety signals to light, despite the fact that adverse effects are vastly under-reported. This is because spontaneous reports are often very specific: a small series of properly documented cases can suffice to constitute a signal, and to enable health authorities to take whatever decisions are required to protect public health.

Our proposals for improvements through proactive disclosure of pharmacovigilance data include:

- ▶ Extend the possibility to search and screen Individual Case Safety Reports (ICSR): data should be extended to **all medicinal products authorised in the EU**, not only to centrally authorised medicines (**g**); when searching by brand names, the results should include the other brands for the same substance and same pharmaceutical form;
- ▶ Since EudraVigilance comprises a Clinical Trial Module (EVCTM), reports of suspected unexpected serious adverse reactions (SUSARs) should be included within the scope of the EudraVigilance access policy (**h**);
- ▶ Grant public access to duly anonymised **“Narrative Case Summary”** for each ICSR;
- ▶ Grant public access to **consumption data** of a given drug in the EU and in the different Member States, in order to give an estimate of the incidence of a given adverse drug reaction associated with a given drug;
- ▶ Redesign the Adrreports database to make it **more user friendly** (e.g. with a list of clickable “Narrative Case Summaries” made available for each request; with the official information about a medicine (packaging leaflet, SPC) being accessible by a simple click on the brand name of the medicine);
- ▶ For each substance, provide a **link to drug regulatory authorities’ assessment reports of the Periodic benefit-risk evaluation reports** (former Periodic safety update reports) (e.g. link to be made to the registry to be set up in accordance to Regulation (EC) N°1235/2010, article 25a (**i**));
- ▶ Regarding proactive publication, if there are concerns about personal data protection for specific cases (rare diseases or very rare adverse drug reactions), the public (group II) as well as the other groups could be required to agree to a clause which states that they will comply with regulations on personal data protection and will not try to re-identify patients.

g- The extension of ADRreports to include non-centrally approved medicines was announced for Spring 2013. But in September 2014, it has still not been implemented.

h- According to the draft revision document, *“Access to reports of suspected unexpected serious adverse reactions (SUSARs) based on the provisions set out in Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC will be subject to a later consultation.”*

i- *“Article 25a: The Agency shall, in collaboration with the national competent authorities and the Commission, set up and maintain a repository for periodic safety update reports (hereinafter the ‘repository’) and the corresponding assessment reports (...).”* (ref. Regulation (EC) No 726/2004)

More data sharing, but new worrying juridical data protection wording

In its draft revision document, the EMA proposes several amendments which are welcomed to allow for more efficient pharmacovigilance:

- **Setting up proactive and regular data sharing with the World Health Organization (WHO) Uppsala Monitoring Centre and with other Medicine Regulatory Authorities;** however, the “confidentiality agreements” of these institutions with the EMA (page 17) should not prevent them from making relevant information and analysis available to the public and to health professionals;
- **Increasing proactive access to extensive ICSR information to marketing authorisation holders (MAH).** This proposal makes sense since MAH are required to develop the periodic benefit-risk evaluation reports about their own drugs (4); nevertheless, drug regulatory agencies have to take very seriously their responsibilities to check that MAH effectively report ADR to EudraVigilance and do not withhold the data (5,6). Drug regulatory agencies must also control the interpretation of data by the MAH to avoid data being minimised (e.g. suicide attempts coded as “emotional liability”) (7);
- **Giving research organisations, on request, “access to ICSR data sets similar to those provided for MAHs in response to justified research requests”.** However, this access would be granted only under conditions which could threaten their independence (see below).

Nevertheless, we identified **two important reasons for concern:**

- creating confusion between the need to protect personal data and the consideration of pharmacovigilance data as “commercially confidential information” or even “trade secrets” in order to protect commercial interests;
- setting up very restrictive conditions for granting access to researchers and over controlling the publication of results.

“Protection of personal data”: a pretext to justify opacity of pharmacovigilance data. According to the draft revision document, *“The need to maintain the confidentiality of the identity of patients and reporters in accordance with EU data protection law is being further emphasised including the responsibility of concerned stakeholders to apply appropriate technical and*

organisational measures to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss (text integrated in the description of access for each stakeholder)” (page 5).

This general statement raises serious concerns. In fact, the consultation takes place in a particular context that needs to be taken into account. After claiming that it would widely open up proactive access to clinical data in November 2012, it seems that the EMA gave in to pharmaceutical companies’ pressure and watered down its draft policy on proactive access to clinical data (j). Moreover, in late November 2013, when both the European Parliament and the Council representing the 28 European Member States showed strong political support for transparency of clinical data during the new EU Regulation on clinical trials legislative process, the European Commission made public a new directive proposal “*on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure*”. According to the trade association of the European pharmaceutical industry, clinical data would fall into the scope of this directive (k) (8,9). We strongly disagree: clinical data are not proprietary information.

Restrictions on access to researchers and publication of results: patronizing is outdated and not acceptable. The parallel of EMA’s general statement that there is a need “*to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss*” with the title of the new directive on trade secrets (read above) is even more disturbing when analysing what it means in practice for researchers. In fact, according to the EMA’s draft revision documents, the “*pre-requisites for granting access*” to researcher organisations would encompass:

– “*Researches to sign confidentiality undertaking*” (without stating whether such confidentiality

j- Made public in May 2014, the EMA revised draft policy on proactive access to clinical data forced data users to enter into legal agreements with pharmaceutical companies and allowed systematic censorship by pharmaceutical companies under the pretext of commercial confidentiality. Formal adoption of this controversial draft policy was delayed and should take place at a scheduled board meeting in October 2014 (ref. 14,15).

k- As a result of the Transatlantic Trade and Investment Partnership (TTIP), this proposed directive includes a very broad definition of trade secrets. According to the trade association of the European pharmaceutical industry “*Almost every aspect of the drug development process involves the generation and application of substantial amounts of technical information and know-how, including the (...) clinical trials phase.*” (ref. 16). And according to an industry responsible, pharmacovigilance data are commercially confidential information (ref. 17).

undertaking would be signed with the EMA or with the marketing authorisation holder) (page 15);

- “Researchers to sign agreement that EMA exercises the right of review for publications based on EudraVigilance data (...)” (page 15).

Moreover, the EMA proposes that:

- “The Agency has the right to view any publication resulting from EudraVigilance data before submission (...). [and that] Any issues raised by the Agency concerning incorrect analyses, unsupported inferences, misleading statements or the protection of personal data must be addressed to the satisfaction of the Agency before submission for publication”;
- “A confidentiality agreement must be signed by the party applying for extended data access for research purposes. Data may not be transferred to any third party” (page 23).

Several of the EMA’s requirements go too far and can be seen as an opportunity for censorship (10). In fact, proportionality in ethics has to be taken into account (11). “Unlikely to happen” risks need to be weighed against the current situation, where millions of otherwise avoidable adverse drug reactions are occurring, sometimes because the pharmaceutical industry routinely hides drug-induced harms (5to7,12).

To claim that the disclosure of clinical trial data could lead to misinterpretation of data and to the dissemination of skewed information that would scare the public reflects an outdated paternalistic attitude. There is no example of misinterpretation of data and misuse from recent years (2010 to 2013) during which the European Medicines Agency has released clinical data to researchers on request without insisting on such restrictions.

Moreover, the statement that “Data may not be transferred to any third party” forbids researchers to publish the raw data along with their paper, a practice increasingly growing in order to avoid fraud and allow other researchers and the scientific community to reanalyse data.

Our proposals for greater disclosure of pharmacovigilance data on request include:

- ▶ Making clear that this policy can only **apply without prejudice to the European Freedom of Information Regulation (Regulation (EC) N°1049/2001)**. European citizens, including researchers not wishing to sign confidentiality agreements, should still be able to access pharmacovigilance data using Regulation (EC) N°1049/2001 (page 8);
- ▶ Replacing the wording ‘Research Organisations’ by ‘interested third parties making a research

request justified on the grounds of public health' to ensure that healthcare professionals, students, public health organisations or patients/victims/consumer associations can qualify;

► **No longer forcing researchers to sign “confidentiality agreements”**, to be replaced by an agreement including a clause stating that they will comply with regulations on personal data protection and will not seek to re-identify patients.

To conclude

When medicines agencies publicly disclose important efficacy and safety information to potential users and the public at large, they fulfil their mandate to contribute to rational medicine use, and to safeguard and uphold public health.

We therefore encourage the EMA to take into account our proposals, notably by:

- proactively giving public access to useful qualitative data such as anonymised summaries of cases (a list of clickable “Narrative Case Summaries” should be made available for each request);
- granting public access to consumption data of a given drug in the different EU Member States;
- providing access to the drug regulatory authorities’ assessment reports of Periodic benefit-risk evaluation reports (former Periodic safety update reports, PSUR) ;
- ending “confidentiality agreements”, to be replaced by an agreement including a clause stating that the persons accessing the data will comply with regulations on personal data protection and will not seek to re-identify patients.

2. Specific comments on text

Line number(s) of the text	Stakeholder number	Comment and rationale; proposed changes	Outcome
Page 5 and tables on pages 12 and 14 to 17		<p><u>Comment:</u> Pharmacovigilance data are scientific data and belong to the public; they are not a “trade secret”. Pharmacovigilance data are information of public interest, they are not “commercially confidential information”.</p> <p>Health professionals and patients who report adverse drug reactions (ADR) do so in order to advance science and to prevent other patients experience the same ADR where other treatment alternatives exist.</p> <p><u>Proposed changes:</u></p> <ul style="list-style-type: none"> - delete the term information in the sentence: <p>“The need to maintain the confidentiality of the identity of patients and reporters in accordance with EU data protection law is being further emphasised including the responsibility of concerned stakeholders to apply appropriate technical and organisational measures to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss”.</p> <ul style="list-style-type: none"> - on page 5 add a statement that: “In general, pharmacovigilance data should not be considered commercially confidential”. 	
All over the text		<p><u>Comment:</u> Healthcare professionals, students, public health organisations or patients/victims/consumer associations who wish to conduct research on pharmacovigilance data should be entitled to request data from the EMA.</p>	

Line number(s) of the text	Stakeholder number	Comment and rationale; proposed changes	Outcome
		<p><u>Proposed change:</u></p> <ul style="list-style-type: none"> - Replace the wording ‘Research Organisations’ by “interested third parties making a research request justified by a public health reason” - or add a definition of a “research organization” specifying that it comprises “healthcare professionals, students, public health organisations or patients/victims/consumer associations who wish to conduct research on pharmacovigilance data”. 	
Page 8		<p><u>Comment:</u> European citizens, including researchers who do not wish to sign confidentiality agreements, should still be able to access pharmacovigilance data using Regulation (EC) N°1049/2001.</p> <p><u>Proposal for change:</u> Make clear that this policy can only apply without prejudice to the European Freedom of Information Regulation (Regulation (EC) N°1049/2001).</p>	
Page 15		<p><u>Comment:</u> The EMA is the institution collecting adverse drug reactions reports from all Member States, the final aim being to protect public health by early signal detection and large communication to the public and health professionals on suspected risks. This central position does not give the EMA the right to control how the data are used or to censor scientific discussion. In case of over- or under-interpretation of risk signals, scientific discussion and public debate will contribute to knowledge building. Moreover, public access to safety data should be rapid and not slowed down by the EMA.</p> <p><u>Proposed change:</u> delete the following “Pre-requisites for granting access”:</p> <p>“Researches to sign confidentiality undertaking “Researchers to sign agreement that EMA exercises the right of review for publications based on EudraVigilance data including a privacy check (possible</p>	

Line number(s) of the text	Stakeholder number	Comment and rationale; proposed changes	Outcome
<p>Pages 22 and 23</p> <p>5.4. Access by Stakeholder Group</p> <p>-> 5.4.4. Group IV: Research Organisations</p>		<p><i>re-identification of patients)</i>"</p> <p><u>Comment:</u> All along the consultation text, there is confusion between the need to protect personal data and the notion of protection of intellectual property. Referring to Regulation (EC) N° 1049/2001 would be clarifying (commercially confidential information is covered as an exception to the disclosure principle where there is no overriding public interest at stake).</p> <p><u>Proposed changes:</u> deletions in bold, ital and crossed; additions in bold and ital</p> <ul style="list-style-type: none"> • Data access should observe EU legislation on protection of personal data and commercially confidential data comply with Regulation (EC) N° 1049/2001. • The Agency has the right to view any publication resulting from EudraVigilance data before submission (maximum period for initial Agency review will be six weeks) including a privacy check as regards possible re-identification of patients. Any issues raised by the Agency concerning incorrect analyses, unsupported inferences, misleading statements or the protection of personal data must be addressed to the satisfaction of the Agency before submission for publication. • A standard Agency disclaimer must be added to the manuscript to explain that the analysis of the data represent the view of the authors but not the position of the Agency which simply provided the data. The Agency reserves the right to reword the disclaimer to the manuscript in cases of unresolved disagreement over the interpretation of the data. The manuscript or its conclusions must not be disseminated in any way without the disclaimer. • A confidentiality agreement must be signed by the party applying for extended data access for research purposes. Data may not be transferred to any third party. 	

Line number(s) of the text	Stakeholder number	Comment and rationale; proposed changes	Outcome
Pages 30, 32, 36, 38, 39, 42, 43, 45, 47, 48, 49, 50, 51,		<p>Complements to the answer to EMA's question: <i>As regards stakeholder group II "Healthcare professionals and the public" would you consider it useful to obtain additional data outputs from the European database of suspected adverse reactions such as tabular presentations or outputs presented as individual cases whilst fully respecting personal data protection?</i></p> <p><u>Comment:</u> There is no reason to restrict access to stakeholder group II to several items of ICSR. Several databases worldwide give public access to such information (e.g. US Food and Drug Administration, Lareb in the NL, UK Drug Regulatory Agency MHRA, etc.) (13). We therefore propose that these items are publicly disclosed.</p> <p><u>Proposed change:</u> Change No to "Yes" for the following items of the ICSR:</p> <ul style="list-style-type: none"> - Date of creation (Data element ICH C.1.2 on page 30) (to be able to identify new cases) - Case identifier(s) (Data element ICH C.1.9.1.r.2 on page 32) (to be able to identify if an individual case was registered under different ICSR, e.g. in case of several ADR occurring in a patient) - Gestation period when reaction/event was observed in the fetus (Data element ICH D.2.2.1a and 1b on page 36) - Body weight (kg) and height (cm) (Data element ICH D.3 and D.4 on page 36) - Date of death (Data element ICH D.9.1 on page 38) + Reported cause(s) of death (free text) (Data element ICH D.9.2.r.2 on page 39) + Autopsy-determined cause of death (MedRA code) (data element ICH D.9.2.r.1b on page 39) - All items from the list classified under ICH E.i. Reaction(s)/event(s) on pages 42 to 44, especially: 	

Line number(s) of the text	Stakeholder number	Comment and rationale; proposed changes	Outcome
		<ul style="list-style-type: none"> - Reaction/Event as reported by the primary source in native language (ICH E.i.1.1a) + Reaction/Event as reported by the primary source for translation (ICH E.i.1.2) - Term highlighted by the reporter (ICH E.i.3.1) - Date of start of Reaction/Event (ICH E.i.4) + Date of enf of Reaction/Event (ICH E.i.5) - Name part – scientific name + Trademark name + Strength + Form + Device name (ICH G.k.2.2 on page 45) - Route of administration (Data element G.k.4.r.10.1 on page 47) - Gestation Period at time of exposure (ICH G.k.6 on page 48) - Result of assessment (ICH G.k.9.i.2.r.3 on page 49) + EU Result of assessment (ICH G.k.9.i.2.r.3.EU.1 on page 49) - Case summary's and reporter's comments (Data element H.1 e H.2 on page 50) + Case summary's and reporter's comments in native language (Data element H.5.r.1a and H.5.r.1b on page 51) - Add the Consumption data 	

Short presentation of the signatory organisations

Cochrane Adverse Effects Methods Group (AEMG). Registered with the Cochrane Collaboration in 2007, the Cochrane Adverse Effects Methods Group (AEMG) aims to develop the methods for producing high quality systematic reviews and to advise the Cochrane Collaboration on how the validity and precision of systematic reviews can be improved. More info: aemg.cochrane.org; Contact: a.herxheimer@ntlworld.com

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.

References:

- 1- European Medicines Agency "Revision of EudraVigilance access policy for medicines for human use" Released 4 August 2014.
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/08/WC500170699.pdf
- 2- ISDB & MIEF "Pharmacovigilance in Europe: the European Commission's proposals endanger the population" Joint analysis; October 2009.
- 3- Prescrire Editorial Staff "Patient reporting improves pharmacovigilance" *Prescrire International* 2008; 17 (98): 241-242.
- 4- Prescrire Rédaction "Réorganisation de la pharmacovigilance européenne. Première partie: pharmacovigilance européenne: sous-traitance accrue aux firmes" *Rev Prescrire* 2014 ; **34** (369) : 536-544.
- 5- "GlaxoSmithKline to plead guilty and pay \$3 billion to resolve fraud allegations and failure to report safety data". www.justice.gov accessed 30 July 2012: 3 pages.
- 6- "European Medicines Agency acts on deficiencies in Roche medicine-safety reporting" www.ema.europa.eu accessed 26 July 2012: 2 pages.
- 7- Healy D "Let them eat Prozac" New York: New York University Press, 2004.
- 8- The European Federation of Pharmaceutical Industries and Associations "EFPIA welcomes the Commission's Proposal on the protection of undisclosed know-how and business information ("Trade Secrets")" press release published on 28 November 2013. www.efpia.eu: 1 page.
- 9- European Commission (Directorate General Internal Market and Services) "Proposal for a Directive of the European Parliament and of the Council on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure COM(2013) 813 final - 2013/0402 (COD)" Brussels, 28.11.2013: 26 pages.
- 10- Kmietowicz Z "EMA's proposal to vet drug research that uses its data is "outdated," say critics" *BMJ* 2014 ; 349 (11 August 2014): 1 page.
- 11- Strech D et Littmann J "Lack of proportionality. Seven specifications of public interest that override post-approval commercial interests on limited access to clinical data" *Trials* 2012 ; **13** : 100.
- 12- Gøtzsche P "Deadly Medicines and Organised Crime: How Big Pharma Has Corrupted Health Care" ISBN: 9781846198847 ; Published: Aug 2013.
- 13- Prescrire Editorial Staff "Publicly accessible pharmacovigilance databases" *Prescrire Int* 2012; 21 (126): 99.
- 14- AIM, HAI, ISDB, MiEF, NCC "Backpedalling on EMA's "proactive publication of clinical-data" draft policy: Was it all just a window-dressing exercise? Who or what is the EMA afraid of?" Joint Press Release; 20 May 2014: 4 pages.
- 15- AIM, HAI Europe, ISDB, MiEF, NCC "EMA's new policy on access to clinical data: About to privatise pharmaceutical knowledge? The proof will be in the pudding (June 2014) Brussels, 24 June 2014.
- 16- AIM, HAI Europe, ISDB, MiEF, NCC, TACD, Wemos "EU Regulation on clinical trials: close to the finish line" press release Brussels, 17 March 2014: 3 pages.
- 17- "Neal Parker on AbbVie's Mission to Discover New Diseases" transcript published on 13 September 2013 from a speech during a conference organized by EFPIA on 27 August 2013 in Brussels. Website davidhealy.org: 4 pages.