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Obstacles to transparency over pharmacovigilance data within the EMA

Abstract

● **In July and August 2014, the European Medicines Agency (EMA) organised two public consultations concerning European pharmacovigilance. These two consultations reveal a number of EMA proposals that are counterproductive to the objective of improving transparency over pharmacovigilance data.**

● **The EMA's proposals offer pharmaceutical companies an opportunity to participate in public hearings held by the European Pharmacovigilance Risk Assessment Committee (PRAC), in order to defend their drug. They also provide for the possibility of holding non-public hearings to discuss public data. There is a great risk that the drug industry might use these provisions to influence the debate.**

● **The strings attached to the access that the EMA proposes to grant researchers to data contained in the centralised European pharmacovigilance database would allow the EMA to censor the publication of their findings. The EMA seems to regard pharmacovigilance data as commercially confidential information.**

● **Responding to these consultations provided an opportunity to remind the EMA that data about adverse effects are a public good, in the common interest, and that it is unacceptable to keep this information confidential.**

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The regulations reorganising European pharmacovigilance, adopted in late 2010, included several measures that should increase transparency (1,2). One of these measures was that the new European Pharmacovigilance Risk Assessment Committee (PRAC) would hold public hearings.

In mid-2014, almost four years later, the European Medicines Agency (EMA) finally launched a public consultation on how these public hearings would be organised and conducted (3). And in another consultation, the EMA proposed to revise its policy on access to pharmacovigilance data (4).

The Medicines in Europe Forum, the International Society of Drug Bulletins (ISDB) and Health Action International (HAI) Europe (three networks of which *Prescrire* is an active member), and the Cochrane Collaboration submitted joint responses to these consultations. This article summarises the key points of these responses (**a**)(5,6).

The final versions of the documents released for consultation were still not available as of late June 2015.

Pharmacovigilance hearings: industry influence and uncertain transparency. Several of the provisions proposed by the EMA concerning the organisation of public hearings are counterproductive (3,5).

In its draft document, the EMA proposed giving pharmaceutical companies "*the opportunity to present its/their view(s) to the participants of the public hearing*". The EMA would thus offer drug companies an ideal platform from which to downplay concerns over the adverse effect profiles of their drugs, despite the risk of influencing the debate (**b**).

The EMA also proposed holding non-public hearings when a company or another person "*intending to submit information has confidential data relevant to the subject matter of the procedure*". This provision would undermine the transparency of the debates and the independence of the EMA's decision-making process. Non-public hearings are only acceptable for protection of the identity of a whistle-blower (**c**)(3).

The joint response to which *Prescrire* contributed urged the EMA to systematically broadcast live videos of public hearings on its website. And to prevent hearings from being monopolised by European patient groups that are heavily funded by the pharmaceutical industry, the EMA was also encouraged to ensure that representatives of independent patient groups (victims of adverse effects, consumers, patients and their relatives) are heard, and allowed to testify in their own language (5).

Access to pharmacovigilance data: too limited. Since 2012, the public has been able to access some quantitative data extracted from the centralised European pharmacovigilance database, Eudravigilance, through the unfortunately rather unwieldy ADRreports interface (www.adrreports.eu). For example, the public can find out how many spontaneous reports were recorded in Eudravigilance in which a specified adverse effect was associated with a given drug (**d**)(1,6). In practice, these data are too limited (6,7). In order to interpret spontaneous reports and ensure that individual cases are not stripped of their full clinical significance through the use of inappropriate terms when they are entered in the database, anonymised narrative case summaries must also be made publicly available (**e**)(1,6).

In the draft revision of its policy on access to pharmacovigilance data, the EMA proposed granting greater access to Eudravigilance data to researchers, on request (4). In exchange, however, the EMA would require them to sign confidentiality agreements. It also has the option of censoring scientific debate by demanding "*the right 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 (…)*" (4,6). These proposals speak volumes about the EMA's commitment to transparency.

In addition, despite the fact that pharmacovigilance data are a public

good, in the common interest, statements about the need to protect intellectual property have appeared, such as the responsibility to apply "*appropriate technical and organisational measures to protect information and personal data (…) against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss*" (4).

This wording, which resembles the title of the proposal for a European directive on "trade secrets" currently under review by the European Parliament, reveals that the EMA now seems to regard pharmacovigilance data as commercially confidential information or even "trade secrets", and has taken on board the pharmaceutical industry's willingness to control these data and their dissemination (6,8,9).

In summary: erosion of transparency. These two consultations reveal that the EMA's approach to transparency over pharmacovigilance data is even more timid than its approach to clinical trial results (7). The final versions the EMA adopts for its rules of procedure on the organisation and conduct of public hearings and for its policy on access to pharmacovigilance data will need to be examined carefully.

We will continue to monitor the situation.

a- *The full versions of these responses are freely available on the Prescrire website (english.prescrire.org).*

b- *In the United States, "the sponsor whose product is under review" is not allowed to speak during the open public hearings of the Food and Drug Administration's advisory committee meetings (ref 5).*

c- *For example, an employee of a pharmaceutical company who is aware of illegal practices, such as concealment of adverse effects (ref 10).*

d- *The public cannot access data on drug consumption, yet they are essential for evaluating population exposure to a particular adverse effect.*

e- *The Medicines in Europe Forum, HAI Europe and the ISDB have also called for public access to drug regulatory agencies' assessment reports on the Periodic Benefit-Risk Evaluation Reports (PBRERs) that pharmaceutical companies are required to submit (ref 6).*

Selected references from Prescrire's literature search.

1- Prescrire Editorial Staff "European pharmacovigilance: increasingly outsourced to drug companies" *Prescrire Int* 2014; **23** (155): 302-307.

2- Prescrire Editorial Staff "The reorganisation of European pharmacovigilance. Part 2: from spontaneous reports to agency reviews and decisions" *Prescrire Int* 2015; **24** (157): 50-54.

3- European Medicines Agency "Draft rules of procedures on the organisation and conduct of public hearings at the Pharmacovigilance Risk Assessment Committee (PRAC) (EMA/624809/2013) - draft for consultation" 24 July 2014: 9 pages.

4- European Medicines Agency "Revision of EudraVigilance access policy for medicines for human use (EMA/759287/2009 Revision 1)" 4 August 2014: 53 pages.

5- Medicines in Europe Forum, HAI Europe, ISDB, Nordic Cochrane Centre "EU Pharmacovigilance public hearings should be as transparent and independent as in the US" Brussels, 14 October 2014: 11 pages. www.prescrire.org

6- Cochrane AEMG, Medicines in Europe Forum, HAI Europe, ISDB "Transparency of adverse drug reactions in Europe: Proactive public access to qualitative data is needed, pharmacovigilance data are not trade secrets" Paris, 15 September 2014: 17 pages. english.prescrire.org

7- AIM, Medicines in Europe Forum, HAI Europe, ISDB, Nordic Cochrane Centre "EMA's final policy on access to clinical data: proactive access to some data, but strings attached" 16 October 2014: 4 pages.

8- European Commission "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 November 2013: 28 pages.

9- "Neal Parker on AbbVie's mission to discover new diseases" transcript published on 13 September 2013 of a talk given during a meeting organised by the EFPIA on 27 August 2013 in Brussels. davidhealy.org accessed 30 June 2015: 4 pages.

10- Jiji Press "Novartis fails to report side effects, fatality" 30 August 2014. pharmagossip.blogspot.fr accessed 30 June 2015: 1 page.

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Pay for performance: financial rewards without improving quality of care

"Pay-for-performance" systems offer healthcare professionals financial incentives intended to support public health initiatives, to reduce health care spending, or to apply "best" practices (1). Yet according to various analyses, pay-for-performance programmes yield mixed and often disappointing results (2,3). The effects of one such programme involving benzodiazepine prescribing in France show that the reality can be complex.

Reduced benzodiazepine use? In 2009, one of the objectives of the French National Health Insurance Fund's pay-for-performance programme "CAPI" (Contracts for Improved Individual Practice) was to reduce the proportion of persons aged over 65 years taking long half-life benzodiazepines to less than 5%. A reduction in the duration of benzodiazepine treatment would have been a more relevant measure for patients, however (4). In 2011, the "ROSP" programme (Payment for Public Health Objectives), which replaced the CAPI programme, addressed this issue by encouraging prescribers to limit benzodiazepine treatment to less than 12 weeks (5,6).

In a report on the ROSP programme published in 2015, the National Health Insurance Fund congratulated itself on a reduction in the proportion of persons aged over 65 years taking long half-life benzodiazepines from 13.7% in late 2011 to 10.8% in late 2014 (5). However, the programme failed to reduce the proportion of patients newly treated with benzodiazepines who continued treatment for more than 12 weeks; this proportion remained unchanged in 2014, at about 15%.

Counterproductive. The results of a study conducted in the Pays de la Loire region of France may explain this phenomenon. The reduction in the proportion of prescriptions for long half-life benzodiazepines between 2011 and 2012 was associated with an increase in prescriptions for short half-life benzodiazepines (7). And a greater proportion of patients over the age of 65 years who were prescribed short half-life benzodiazepines continued treatment for more than 12 weeks compared with those who were prescribed long half-life benzodiazepines. This seems "*counterproductive*".

This pay-for-performance programme therefore altered benzodiazepine prescribing patterns without leading to any real improvement in the quality of health care. Protecting patients from adverse effects requires more than payments for meeting measurable performance targets.

Selected references from Prescrire's literature search.

1- Prescrire Rédaction "Contrats d'amélioration des pratiques individuelles (CAPI) (suite et fin): un essai de rémunération "à la performance" à amender pour la qualité des soins" *Rev Prescrire* 2010; **30** (326): 932-935.

2- "Health Policy Brief: Pay-for-Performance" *Health Affairs*, October 11, 2012: 6 pages.

3- Cashin C et al. "Paying for performance in health care. Implications for health system performance and accountability" European Observatory on Health Systems and Policies 2014: 338 pages.

4- Prescrire Rédaction "CAPI - Objectif n° 4" *Rev Prescrire* 2010; **30** (325): 862.

5- "La rémunération sur objectifs de santé publique. Une amélioration continue en faveur de la qualité et de la pertinence des soins. Bilan à 3 ans" Assurance Maladie 27 April 2015: 40 pages.

6- Prescrire Rédaction "Rémunération sur résultats: objectifs de soins et de coûts (n° 14 à n° 24)" *Rev Prescrire* 2013; **33** (356): 456-463.

7- Rat C et al. "Did the new French pay-for-performance system modify benzodiazepine prescribing practices?" *BMC Health services research* 2014; **14** (301): 7 pages.