PCIM/11/01 – Public Consultation on implementing measures for pharmacovigilance

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General comments

Although communication is an essential part of pharmacovigilance and patient safety, it does not have a prominent place in the consultation document. Also, when communication is mentioned, it refers to *information giving*, rather than *dialogue*. There is nothing on how to encourage and invite a dialogue between stakeholders, nor on how to create a pharmacovigilance culture which actively involves patients and health care professionals in an exchange that is meaningful to them. Maybe this is (intended to be) covered elsewhere, but the picture emerging from this consultation paper is that the only real pharmacovigilance stakeholders in the EU are regulators and MAHs.

Naturally, in Europe there will be a strong focus on the Eudravigilance system, and undoubtedly EMA has a key role in supporting pharmacovigilance in the EU, but since most major medicinal products available in the EU are sold and used in many countries outside the EU it would seem appropriate to include the consultation of other sources of data and knowledge than those available inside the EU, e.g. for signal detection and risk identification. Pharmacovigilance activities that relate to stakeholders, data and knowledge from outside the European Union are scarcely mentioned at all (only in the phrase "marketing authorisation holders shall monitor the data to the extent of their accessibility to the Eudravigilance database, as part of their *broader monitoring of all emerging data and global signal detection activities"*). Should that be interpreted as if EMA and national competent authorities do not have the same responsibility to engage in a broad monitoring of all emerging data on products available in the European Union? It could be argued that the current wording does not exclude such consultation and exchange, but there is a risk that the absence of specific mention is taken as a recommendation not to engage in certain activities. This logic applies also to regional pharmacovigilance centres (not mentioned as a possibility) and the need for a constant search for novel methods and ways in which pharmacovigilance will better support patients and public health into the future.

Specific comments

Consultation item 1

The scope of the 2010 Regulation and Directive covers the detection, assessment, understanding and prevention of adverse reactions, and the identification of and action taken to reduce the risks of, and increase the benefits from, medicinal products for human use for the purpose of safeguarding public health. The Directive defines a Risk management system as "a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those activities and interventions".

The list in A.3(6) refers to "A description of the process, data handling and records *for the fulfilment of pharmacovigilance*". It does cover some of the activities which contribute to the fulfilment of the goals of pharmacovigilance/risk management, but the activities are secondary to the goals. It would be clearer if the goals were specifically stated, and in a logical order:

(a) Detection of adverse reactions/new risks
(b) Characterisation and assessment of adverse reactions/new risks
(c) Understanding of adverse reactions/new risks
(d) Prevention of adverse reactions/new risks
(e) Actions taken to reduce risks, including communication
(f) Actions taken to increase benefits, including communication
(g) Assessment of the effectiveness of interventions

Legally required activities and reporting could be mentioned, e.g. PSUR production and submission, preferably with a statement as to how a particular activity/report achieves the goal. For example, "ICSR collection, assessment and reporting" is not an end in itself – these are activities aimed at fulfilling (a) – (d) above.

There should also be a mention of the need of links between pharmacovigilance and existing knowledge from toxicology and premarketing studies.

Consultation item 3

There is no need to be more precise. The responsibility of the MAH is clear.

Consultation item 4

A copy of the audit report should be retained. The ability to learn from mistakes is an essential part of process improvement; to be able to do so one must keep a historic record of audit findings and the measures taken to correct or improve processes. Although A.7 relates to audits and not specifically to quality management systems, the same concepts are applicable – see below for comments specifically on quality systems.

Consultation item 11

It is difficult to agree or disagree with the proposed terminologies in (c) – (g) since the terminologies resulting from the ISO IDMP standards are not yet available, nor is there currently an agreed mechanism for their being made available and updated on a regular basis. An assessment of their fitness for purpose cannot realistically be made until the terminologies are available and tested, both regarding scientific content and usability.

Quality systems (section B, C and D)

According to ISO 9000 the four cornerstones of a quality management system are

- *quality planning* - setting quality objectives and specifying necessary operational processes and resources to fulfil the quality objectives
- *quality control* - the fulfilment of quality requirements
- *quality assurance* - providing confidence that quality requirements will be fulfilled
- *quality improvement* - increasing the ability to fulfil quality requirements.

Since ISO 9000 is an international standard, which is well known and widely used, it would be helpful if section B, C and D were structured around these concepts, clearly defining the goals and activities of each step.

Audits should aim both at fulfilling the *quality control* function (compliance and correction), but also serve as input to *quality improvement* (lessons learnt and the building of a better system).

Regarding pharmacovigilance performance indicators, this is an area where substantial work has been done for some years within the WHO Programme for International Drug Monitoring, by Professor Ambrose Isah and his group. The proposed WHO pharmacovigilance indicators are awaiting final approval by WHO and its Advisory Committee on the Safety of Medicinal Products (ACSoMP), after which they will be made publicly available. A recent paper published in Drug Safety, with Professor Isah as one of the authors, gives a good picture of the main features of the WHO pharmacovigilance indicators. *The paper is enclosed as a separate attachment in the same email as this comment document (pharmacovigilance indicators.pdf).*

E. Signal detection and risk identification

22. Methodology

Does the application of a "common methodology" for the determination of the evidence contained in a signal mean that, in the future, there will only be one allowed way of detecting and assessing signals in the EU, including choice of disproportionality measure, triage algorithms etc? Or does this only refer to the signal detection on data in Eudravigilance performed by EMA, and not the national competent authorities? This should be clarified.