RESPONSE TO:

Commission Public Consultation: An Assessment of the Community System of Pharmacovigilance

Name: BPI (Bundesverband der Pharmazeutischen Industrie)
Type of stakeholder : Industry Association
Organisation: German Pharmaceutical Industry Association

Comments:

The BPI comments relate principally to three areas:

1. Harmonisation of pharmacovigilance requirements
2. Procedures
3. Responsibilities

According to the comments already made by the EFPIA the BPI suggests the following main points

- One Pharmacovigilance system in one language
- One set of binding rules to all stakeholders
- One assessment (rapporteur/lead member state)
- One voice (in pharmacovigilance communication)

1. Harmonisation of pharmacovigilance requirements

The assessment of the Community System of Pharmacovigilance presents an excellent opportunity to improve harmonisation of pharmacovigilance standards across the European Union. In order for this objective to be achieved, BPI would like to propose that the requirements should be more specific and binding also to regulators in order to achieve unified rules throughout the EU for the best interest of the protection of public health. At the moment Member States define additional national requirements resulting in a patchwork situation. Therefore it is essential to have a direct binding peace of legislation in place. It is required to have a unified EU-Regulation mandatory to all Member States, Commission and EMEA and available in all languages of the member States.

In addition it is crucial to streamline the EU requirements, i. e.

- reporting of cases of serious and unexpected ADR from third countries to all EU Member States and EMEA;
- ADR / SUSAR reporting pre- and post- authorisation and
- PSUR/yearly reports have to be discussed in an overall approach.
- There is not only an overlapping in phase IV studies but in addition if the status of authorization is different in several countries.

BPI thinks it is crucial to have a harmonized EU-system which reflects all situations pre-, during and post-authorisation.

2. Procedures

The current version of Volume 9A does not properly clarify some important aspects and there are specific approaches of Member States to handle the reporting requirements. Companies are focussing on how to report and not on the much more important medical issues.

In order to this BPI would like to propose the following aspects concerning the utilisation of Eudravigilance and how to use this database as a unique powerful tool for data mining and signal detection in Europe.

2. 1. Electronic Reporting Measures

We have significant concerns regarding practicability and requirements of electronic submission established by Nov. 25, 2005. There are many problems associated with managing electronic submission, especially for micro, small and medium sized companies.

In practise, for MAHs with less than 10 cases per year it is still difficult and unreasonable expensive to establish an electronic reporting system. According to German Drug Law § 80, there has to be an exception due to “undue hardship for some reasons” e.g., costs of the system. Neither they are able to use the EVWEB nor any other system nor is Germany (health Authorities) planning to set up a system (DIMDI Tool, MEDRA) even for local reporting.

Although the usual regulatory requirements for reporting of adverse reactions must be fulfilled, there has to be a way to facilitate the electronic submission of ADR cases. To support the overall implementation of electronic submission BPI suggests the following

- there has to be an acceptable licence policy for the use of MedDRA for every MAH, which better refers to the actual usage of MedDRA terms in reporting activities instead of referring to the turn over of a company; the turn over is in many cases not connected to the ADR reporting activities (i. e. with regard to herbal medicinal products or OTC medicinal products)
- in addition possibilities of group licenses are not available
- training courses for the use of EVWEB have to be conducted on a national level
- training courses for the use of EVWEB have to be available in all languages of the member States.

2. 2. Reports published in worldwide literature

Volume 9A (Draft) points out that the Marketing Authorisation Holder is expected to maintain awareness of possible publications by accessing a widely used systematic literature review and reference database no less frequently than once a week and to ensure that relevant publications in each Member State are appropriately reviewed. In addition, all company offices are encouraged to be aware of publications in their local journals in the Member State and bring them to the attention of the Qualified Person Responsible for Pharmacovigilance as appropriate. These cases might qualify for expedited reporting.

Article 104 (3) Directive 2001/83/EC defines no specific timelines for this literature search. The proposed time interval in the Draft Volume 9A is **"no less frequently than once a week"** irrespective from the type of the medicinal product. In principle, this seems adequate for medicinal products with new active ingredients.

For other products this weekly literature search seems to be disproportionate particularly for well established medicinal products, with a known risk-benefit ratio, traditional herbal medicinal products and homeopathic / anthroposophic medicinal products.

Reasoning: Experiences with publications show that adverse reactions normally occurred several months very often more then a year before they are published. Sometimes adverse reactions are collected and released in one publication with the result that the published cases are quite old. In addition for i. e. well established medicinal products there is only some new information, with the likelihood that weekly searches do not bring new information. With hundreds of pharmaceutical companies in the EU searching the relevant literature in parallel the timeline from one week represents an extremely high and cost-intensive expenditure, without any improvement of Pharmacovigilance.

BPI has established a project to coordinate literature searches for smaller companies. Our experience shows that searches every three months are resulting in an acceptable safety for well established medicinal products, traditional herbal medicinal products and homeopathic / anthroposophic medicinal products. With regard to the experiences with these medicinal products over many years the German Ministry of Health has accepted a three monthly search in interpreting the legal basis in Directive 2001/83/EC.

To enhance information from publications it should be considered that physicians possibly inform Competent Authorities in advance about publications, which refer to observed adverse reactions. The legal basis for this could be Article 101 of Directive 2001/83: "The Member States shall take all appropriate measures to encourage doctors and other health care professionals to report suspected adverse reactions to the competent authorities. The Member States may impose specific requirements on doctors and other health-care professionals in respect of the reporting of suspected serious or unexpected adverse reactions."

BPI therefore proposes for all medicinal products with well established medical use, for traditional herbal medicinal products and homeopathic / anthroposophic

medicinal products a time interval of three months for literature searches with regard to suspected serious adverse reactions.

3. Responsibilities

24-hours-availibilty of the Qualified Person

EU legislation requires all MAHs to have a qualified person responsible for pharmacovigilance within the Community. This person must be permanently and continuously at the disposal of the MAH.

National regulations in some Member States require a nominated individual in that country who has specific legal obligations in respect of pharmacovigilance at a national level.

According to the “GUIDELINE ON MONITORING OF COMPLIANCE WITH PHARMACOVIGILANCE REGULATORY OBLIGATIONS AND PHARMACOVIGILANCE INSPECTIONS” the MAHs should ensure that they have an appropriate system of pharmacovigilance in place in order to assure responsibility for their products on the market and to ensure that appropriate action can be taken, when necessary. This includes the MAH having at its disposal permanently and continuously an appropriately qualified person (QP) responsible for pharmacovigilance residing within the European Economic Area, and there has to be a description of the back-up procedure to apply in the absence of the QPP.

Concerning this back-up procedure the BPI proposes to differentiate between regular deputyship and procedure during normal absence (over the night and the weekend). According to our main statement, this has to be harmonised for all member states even on a local level.