COMMENTS ON LEGISLATIVE PROPOSALS TO BETTER PROTECT PUBLIC HEALTH BY STRENGTHEN AND RATIONALISE THE EU SYSTEM OF PHARMACOVIGILANCE

Bundesverband der Pharmazeutischen Industrie e.V.
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BPI, the German Pharmaceutical Industry Association, represents more than 260 Companies in Germany, including both small and medium sized Pharmaceutical Enterprises and multinational companies.

BPI welcomes the opportunity to comment on the European Commission's draft legislative proposals to strengthen and rationalise the EU system of Pharmacovigilance.

International harmonisation of Pharmacovigilance requirements, clear definition of roles and responsibilities and rationalising administrative processes should be an objective in all new or revised regulations and guidance as it would reduce the current administrative burden.

In addition BPI fully supports the European Federation of Pharmaceutical Industries and Associations' (EFPIA) response to this consultation as our member companies have also contributed comments via EFPIA.

The BPI Comments are focussing on 12 key issues:

1. **Pharmacovigilance Committee**

   Roles and responsibilities and interrelation with other EMEA Committees and the national competent authorities/CMD: We appreciate the establishment of a Pharmacovigilance Committee that should replace the informal Pharmacovigilance Working Party. Nevertheless, it needs to be ensured that overall evaluation and continuous monitoring of benefits and risks rests with the CHMP and the national competent authorities/CMD (if no referral procedure). The new Committee would be responsible for a wide range of Pharmacovigilance tasks this may result in new administrative burden and significant fees. To cover differences in local medical practice and/or specific national legislated requirements and/or other national particularities (e.g. homeopathics), the national competent authority still needs to be responsible. For the new committee (as the others within the EMEA) names of members, rules of procedures etc. and contact details should be published on the EMEA website.

2. **Safety Communication & Transparency:** all information on medicinal products should be available on **one single European website** (i.e. interlinkage of Eudrapharm, Eudravigilance, and the publicly available portal). Public availability of safety information should only be provided in **close connection with education of the public** and in **context of the overall benefit risk profile** of a medicinal product.

Information should be managed by **1 single agency lead in EU per medicinal product,** ie. it would be helpful and potentially more efficient to have the **RMS or Rapporteur** review the PV aspects of a product to allow continued knowledge management. The implementation of the use of electronic data submission and review tools will improve the efficiency and effectiveness of all regulatory processes. The publication of key elements of non-interventional post-authorisation studies protocols might be possible via a study registry compatible with all registries in the WHO-network.

3. Proposed amendments regarding the new Article 101 k directive 2001/83/EC

With respect to Article 101 k the principles of subsidiarity and proportionality under EC law should be taken into account. Under paragraph 1 of this Article a member state shall notify other member states, the Agency and the Commission about certain circumstances. Following this verification a Community assessment and binding decisions by the Community shall take place. The Committee on Pharmacovigilance shall make a recommendation the CHMP (free Art. 101 k Paragraph 9) and the CHMP shall adopt an opinion.
Given its legal basis in Article 95 EC the provision of Article 101 k has to be on line with the objective of removing trade barriers. If no relevance to the common market is given Article 101 k cannot serve as legal basis for community acts.
It should therefore be ensured that the Article 101 k procedure is only applicable if the substance is on the market in other Member States as well. In case of purely and unique national marketing authorizations the issue lacks community relevance. In addition, the goal of the legislative strategy (implementing and improving a fast and robust decision making process on safety issues) is better served on the national level in this case.

4. Procedural rights of marketing authorization holders

Given the Commission's general endeavour to guarantee a good administration practice public hearing rights, the right of participation for concerned stakeholders should be ensured in the new Commission strategy to the degree it existed before. The same is the case for the duty to give reasons for Commission decisions, the Committee on Pharmacovigilance recommendations under Article 101 k paragraph 9 and on the opinion by the CHMP under Article 101 k paragraph 10. The degree of procedural rights under Article 31 of directive 2001/83/ECshould at least is implemented in the procedure of Article 101 k if not increased.

5. **New labelling information**: Further definition and clarification of the criteria for intensive monitoring is required; the wording proposed on the package and in the SmPC for intensive monitoring seems not appropriate to ensure patient compliance. In order to convey appropriately the benefit risk profile of the product, it is important to clarify the positioning and content of the '**key safety information**' within the SmPC to allow an informed decision of physicians and patients based on an adequate description of benefits and risks. Products not listed in the **European list of intensively monitored products** might be wrongly regarded as "safe" which might lead to unconsidered use. **It is important to define the criteria for including products and how they will be excluded from the list.**

6. **PSUR obligation should not be dependant from the legal base of the marketing authorisation (MA)** (101f does not reflect Article 8 of the Community Code as amended). PSUR review procedures for all products should be based on the CP review procedure model (i.e. best available expertise of agency and transparent appointment process). It is scientifically not justified to regard products like generics as generally "safe" just because they have passed the 10-year limit. Innovator and generic products have to be treated equally. It has to taken into consideration that in the situation of a generic market the innovator product only has a reduced markt share. PSURs have to be submitted electronically as stated in Article 101f (2). An internationally agreed structure and format for electronic submission of PSURs has still to be defined.

7. Instead of **all reports (including non-serious) to be reportable within 15 days**, focus should be on serious cases. The added value of expedited reporting of non-serious reports for Pharmacovigilance purposes, e.g. for signal detection, is very limited. Non-serious cases should be submitted in line-listings every 12 months. Timelines could be reduced on a risk based approach. Wih regard to PhV activities ist is crucial to focus in serious cases, which have to be worked on very intensivly.

8. To avoid duplicate reporting of literature cases for active ingredients with well established safety profile EMEA wants to conduct **medical literature reviews**. This is a very innovative and interesting approach. It is important, that these reviews are focussing on the world-wide literature and are available for all interested parties nationally, EU- and World-wide. Otherwise this will bring only partial advantage to MAHs, because the necessity of full reviews for authorities outside of the EU. It would be another interesting approach if physicians could be obliged to inform competent authorities about planned publications in parallel.

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9. **Non-interventional post-authorisation safety studies (articles 101g and 101h):** the scope and "light oversight" need to be further defined. Clarification is required on how EMEA will work in coordination with the product specific Rapporteur or RMS. The proposed timeline of 60 days in which the competent authorities has to respond to the submission of non-interventional studies is too long, specially compared with the timelines in the Clinical Trial Directive (2001/20/EC. Submission of an abstract in addition to study reports and the general requirements on the publication of trial results seems to be redundant. The publication of key elements of non-interventional post-authorisation studies protocols might be possible via a study registry compatible with all registries in the WHO-network.

10. **Submission of one single global risk management plan (RMP) acceptable to a NCE (if necessary)**, which should cover the **entire EU perspective: T**he transposition of global RMP actions into **national mitigation activities** can then be used to cover differences in local medical practice and/or specific national legislated requirements. Wording: Both RMP (Risk Management Plan) and RMS (Risk Management System) are used in the Commission paper. Using RMP throughout the legislation avoid misunderstandings. The abbreviation “RMS” is frequently used for “Reference Member State”. Consequently the newly defined term “Risk Management System (RMS)” (definition in Article 1 para 33) should be replaced by “Risk Management Plan (RMP)” to avoid any confusion between the overall Pharmacovigilance system and product specific activities.

11. The concept of the **Pharmacovigilance Master File** is already implemented with great success for national authorisations in Germany (Identification of the supervisory authority for QP and PhV System based on authority inspection expertise, company location). This approach is very helpful and unbureaucratic and BPI welcomes that the Commission has included this in its proposal. Therefore it is confusing, that the Commission is still asking for exact information about for responsible person for Pharmacovigilance (i. e. name and address) as part of the marketing authorisation application with the problem of multiple parallel variations. BPI therefore proposes to implement an EU-wide database were the information on the responsible person for PV should be available for competent authorities.

12. **Roles and responsibilities of PhV Committee and interrelation with other EMEA Committees and the national competent authorities/CMD**: It needs to be ensured that overall evaluation and continuous monitoring of benefits and risks rests with the CHMP and the national competent authorities/CMD (if no referral procedure). For the new committee (as the others within the EMEA) names of members, rules of procedures etc. and contact details should be published on the EMEA website. To

cover differences in local medical practice and/or specific national legislated requirements and/or other national particularities (e.g. homeopathics), the national competent authority needs to be still responsible.

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