EuropaBio's contribution to the public consultation on a concept paper on implementing measures in order to harmonise the performance of the pharmacovigilance activities provided for in Directive 2001/83/EC and Regulation (EC) NO 726/2004[1]

General comments:
EuropaBio member companies welcome the opportunity to contribute to the public consultation on the implementing measures related to the Pharmacovigilance Directive. We fully endorse the comments made by the European Federation of Pharmaceutical Industries and Associations (EFPIA) and would like to add some comments for selected topics which are specific to our members. You will find these comments below.

Comment on specific consultation items:

Consultation item no. 2: The aim of the pharmacovigilance master file is two-fold: to concentrate information in one global document and to facilitate maintenance by uncoupling it from the marketing authorisation. Therefore changes to the content of the master file will be no longer subject to variation obligations. Would it be nevertheless appropriate to require the marketing authorisation holder to notify significant changes/modifications to the master file to the competent authorities in order to facilitate supervision tasks? If so, how should this be done? Should the master file contain a date when it was last reviewed?

The Marketing Authorisation Holder (MAH) should only need to notify the Regulatory Authorities of significant changes to the master file as per Article 23 of Directive 2001/83[2] i.e. for a change of EUQPPV. This should be done by notification letter or template without any further administrative process.

Consultation item no. 5: Overall, do you agree with the requirements as regards the content and maintenance of the pharmacovigilance master file? Please comment.

Yes, EuropaBio members companies endorse the concept as i) it reduces regulatory burden for cumbersome notifications through variations and ii) it centralises information. The concept will also facilitate harmonisation and simplification, assuming there will be no expectation from individual competent authorities to include detailed country level information as per the pre-inspection "Specification of Pharmacovigilance System".

Consultation item no. 9: For efficiency reasons a 'work sharing' procedure could be appropriate for the monitoring of medicinal products or active substances contained in several medicinal product. However, do you see a risk in cumulating all tasks (for the

[1] http://ec.europa.eu/health/files/pharmacovigilance/2011-09_concept-paper.pdf
[2] Directive 2001/83/EC on the Community code relating to medicinal products for human use. Available at: http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_cons2009/2001_83_cons2009_en.pdf

authorisation, PSUR scrutiny and Eudravigilance monitoring) in one Member State, as thereby the benefits of parallel monitoring may be lost ("peer review" system)? Additionally, it may be envisaged to extend 'work sharing' to all medicinal products (including all centrally approved products) and to appoint a lead Member State in addition to EMA (Article 28a(1)(c) of Regulation (EC) No 726/2004). Please comment.

EuropaBio member companies support the "work sharing" concept and the role and tasks of the leading Member State. This concept should be adopted for all products registered in the European Union (EU) regardless of their registration route.

Other comments related to this section:
Please delete "or beneficial" from the definition of what constitutes a signal (p. 14, section E. 21 in the Concept Paper) as the purpose of signalling is aimed towards identifying safety issues.

Consultation item no. 10: In the Commission's view the aim of this part is to establish common triggers for signal detection; to clarify the respective monitoring roles of marketing authorisation holders, national competent authorities and EMA; and to identify how signals are picked up? Are the proposed provision sufficiently clear and transparent or should they be more detailed? If so, which aspects require additional considerations and what should be required? Please comment.

EuropaBio member companies agree that the specific roles of MAH, European Medicines Agency (EMA) and National Competent Authorities (NCAs) must be clarified regarding signal detection to avoid missed signals or false positives. This can be done in the Good Vigilance Practice (GVP) guidance. Please consider for the implementing guidance that the requirements with regard to signal detection should take into account that complicated statistical systems should not apply for products with low volumes of Adverse Drug Reaction (ADRs) reports. In addition we would like to raise some concerns on automatic signal detection on spontaneous data, which is significantly biased by large numbers of simulated reports

Consultation item no. 13: Is there additionally a need for transitional provisions as regards certain aspects of this implementing measure, especially in relation to the specifications on format and content? Please comment.

Specific transitional provisions should be provided in the GVP guidance. A discussion of realistic transition periods should be held with stakeholders to ensure practicability.

Consultation item no. 17: Do you agree with the proposed format? Please comment.

Post-authorisation safety studies (PASS) can be very different in nature and range from Randomised Clinical Trials to observational studies and registries.

EuropaBio member companies recommend that the level of detail in this section regarding format and content of protocols and reports which will be inflexible to address the different types of studies. Defining those details in the implementing Regulation will make amendments to the requirements very cumbersome. Guidelines may be a better tool to define more level of detail for specific types of studies.

We recommend that for the purpose of these measures, reference to appropriate standards such as the existing ISPE Good Pharmaco-epidemiology Practice (GPP) guidelines[3] and the EU Data Protection Directive[4] are included instead of such details.

~ENDS~

About EuropaBio:
EuropaBio's mission is to promote an innovative and dynamic biotechnology based industry in Europe. EuropaBio, (the European Association for Bioindustries), has 62 corporate and 7 associate members operating worldwide, 2 Bioregions and 19 national biotechnology associations representing some 1800 small and medium sized enterprises.

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[3] http://www.pharmacoepi.org/resources/guidelines_08027.cfm#1
[4] Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31995L0046:en:HTML