IMPLEMENTING MEASURES IN ORDER TO HARMONISE THE PERFORMANCE OF THE PHARMACOVIGILANCE ACTIVITIES PROVIDED FOR IN DIRECTIVE 2001/83/EC AND REGULATION (EC) ° No726/2004.

Reference: PCIM/11/01-Public consultation on implementing measures for Pharmacovigilance

Company: CIS bio international-IBA Pharma S.A. (not belonging to small-medium sized enterprise)

A- Pharmacovigilance system master file:

- Definition
- Location
- Content

Consultation item no.1: Should additional processes and Pharmacovigilance tasks be covered:

Answer: National Competent Authorities that require nomination of a local responsible person for Pharmacovigilance at a national level should be included in a comprehensive list.

- Maintenance

Consultation item no.2: The aim of Pharmacovigilance master file is twofold: to concentrate information in one global document and to facilitate maintenance by uncoupling it from the marketing authorization. Therefore changes to the content of the master file will be no longer subject to variations obligations. Would it be nevertheless appropriate to require the marketing authorization 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?

Answer: It would be appropriate to notify significant modifications to EMA through an immediate notification; for tracking purpose, the master file should contain a date of revision.

- Delegation

Consultation item no.3: Is it necessary to be more precise on potential delegation, e.g. in the case of co-marketing of products. Please comment.

Answer: France is a specific country with the role of the “exploitant”. When a company is exploitant on behalf of a non-European Marketing Authorization holder, the responsibilities as for Pharmacovigilance should be described precisely.

- Audit

Consultation item no.4: Should a copy of the audit report be retained in the master file? Would it be appropriate to require documentation of audit schedules?

Answer: Audit reports are internal documents; therefore they should not be retained in the master file. Audit schedules are likely to move and should not be included.

- Inspection

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

Answer: Overall we agree with the contents and maintenance of the master file (with comments above).

B- Quality systems for the performance of Pharmacovigilance activities - Common obligations
- Scope
- Audit

Complementary comment:

"Quality audits shall be conducted by individuals who do not have direct responsibility for the matters being audited":

Answer: This should more precisely made explicit. Does that mean that Pharmacovigilance Department members should not audit subsidiary/ distributor Pharmacovigilance organization?

- Performance indicators

C- Quality systems for the performance of Pharmacovigilance activities by marketing authorization holders
- General
- Resource management
- Compliance management

Consultation item no.6: Is there a need for additional quality procedures, e.g. in relation to study reporting in accordance with article 107p of the Directive, in relation to communication on Pharmacovigilance between the marketing authorization holder and patients/health professionals; in relation to processes for taking corrective and improvement actions or in relation to the detection of duplicates of suspected adverse reaction reports in the Eudravigilance database.

Answer: Duplicates can be created through the direct Health Professional reporting (either to NCA or to companies) and further literature search done by companies. Only a centralized detection can solve this issue.

- Record management

Consultation item no.7: Do you agree with the requirements for marketing authorization holders?

Answer: it should be clarified that is under "at least 30 years" for product related documents retaining. Does that mean "indefinitely"?

D- Quality systems for the performance of Pharmacovigilance activities by national competent authorities and EMA

- General
- Resource management
- Record management

Consultation item no.8: Do you agree with the quality system requirements? Please comment, if appropriate separately as regards requirements for MAH, national authorities and EMA.

Answer: Overall we agree with the quality system requirements.

E- Signal detection and risk identification

- General
- Changed risks/new risks
- Methodology
- Signal management procedure
- Work sharing of signal management

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 authorization, 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

Answer: This is an important improvement thus avoiding inconsistency between core SPC, PSUR work sharing etc. On the other hand, one can expect a quicker process.

- Signal detection support
- Signal detection audit

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 authorization 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

Answer: the role/responsibility of each Party 'MAH, NCA, EMA should be more precisely addressed in the signal detection process.

F- Use of terminology

- Use of internationally agreed terminology

Consultation item no.11: Do you agree with the proposed terminology? Please comment

Answer: no comment.

- Use of internationally agreed formats and standards

Consultation item no.11: Do you agree with the proposed terminology? Please comment

Answer: no comment.

G- Transmission and Submission requirements

- Transmission of suspected adverse reactions
- Risk management plans
- Periodic safety update reports
- Post authorization safety studies

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

Answer: no comment.

Annex I-Electronic submissions of suspected adverse reactions

Consultation item no.14: Do you agree with the proposed format and content? Please comment.

Answer: we agree.

Annex II-Risk management plans

Consultation item no.15: Do you agree with the proposed format and content? Please comment

Answer: we agree.

Annex III-Electronic periodic safety update reports

Consultation item no.16: Do you agree with the proposed format and content? Please comment

Answer: It can be difficult to quantify the actual use from indicated use. (Section 3)
It should be clearly addressed what is needed: line listings, narratives etc. (section 5)
Appropriate/detailed templates would be appreciated.

Annex IV-Protocols, abstracts and final study reports for the post-authorization safety studies

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

Answer: We agree.