European Federation of Pharmaceutical Industries and Associations

New EU Pharmacovigilance Legislation

Early Industry Experience, Challenges for Implementation and some Proposals

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Industry Aims and Concerns

- Industry Aims
  - Better protection of public health
  - Robust and efficient pharmacovigilance system
  - Transparency which is consistent for all stakeholders
  - Simplification of processes and systems which facilitates a focus on public health vs non value added bureaucracy

- Industry Concerns
  - Anything that impedes industry`s ability to achieve these aims.

General Challenges

- "Pharmacovigilance" legislation in name only
  - Global impact; leaves virtually no function untouched
  - Massive changes in multiple processes required
  - Extensive education and training for non PV functions
  - New skill sets required e.g. lay summary for RMP
- Delay in transposition of Directive in most Member States
  - Inconsistencies already apparent in adoption
  - Rejections of requests in line with Directive but not national law
- Inconsistencies between finalised modules
  - Consequences of choosing one interpretation over another on compliance and resources
- Lack of harmonisation with non-EEA countries
  - Increased bureaucratic burden with no contribution towards promoting patient safety.

Specific Challenges

- Individual Case Safety Reports (ICSRs)
- PSURs/PBRERs
- Risk Management Plans (RMPs)
- PRAC

Specific Challenges - ICSRs

- Non serious case collection from **all** PAS
  - Number 1 EFPIA concern
  - Article 107(1) :

    Marketing authorisation holders shall record all suspected adverse reactions in the Union or in third countries ***which are brought to their attention****, whether reported spontaneously by patients or healthcare professionals, or occurring in the context of a post-authorisation study.* GVP Module VI implies only if actively sought i.e. protocol driven
  - Q&A (July 2012) implies that all AEs should be collected by MAH and assessed but does not address whether required by all protocols
  - Significant impact on studies which do not actively solicit safety data e.g. health outcomes studies

Specific Challenges - ICSRs

- Reports from Patient Support Programmes (PSPs)
  - **All** to be classified as solicited in final GVP Module
  - Poorly documented reports; impossible to make informed causality assessment and attempts to follow up nearly always unsuccessful
  - Significant bureaucratic burden with no contribution to patient safety
  - Said to be based on FDA position but not consistent with 1997 guidance :

III. INDIVIDUAL CASE REPORTS BASED ON SOLICITED INFORMATION

The FDA has determined, for purposes of post-marketing safety reporting…. that information concerning potential adverse experiences derived during planned contacts and ***active solicitation of information from patients*** *(e.g., company-sponsored patient support programs….) should be handled as safety information obtained from a post-marketing study*

Specific Challenges - ICSRs

- Off label use without adverse outcomes
  - Significant implications for companies with respect to corporate integrity laws
  - Active solicitation, particularly if by sales representatives not permitted.
- Inconsistent requirements across Member States already apparent
  - Reporting requirements of ICSRs revised 3 times since July 2012
  - Significant implications for ability to monitor /maintain compliance
  - Does not seem to be consistent with legislation with respect to no additional requirements

EFPIA Proposals - ICSRs

- Non serious case collection from **all** PAS
  - Clarify that requirement to collect AEs applies to protocols where AEs are actively sought (i.e. protocol driven)
  - Even if AEs are not actively sought by protocol, if received should be collected and processed as spontaneous reports (not solicited)
- Reports from Patient Support Programmes (PSPs)
  - Actively sought = solicited
  - Others = implied causality
  - Longer term - collect data to assess impact on signal detection
- Off label use without adverse outcomes
  - Clarify that there is no requirement to actively solicit
  - Collect only if become aware through existing processes
- Inconsistent requirements across MSs already apparent
  - Refer to CMDh for resolution

Specific Challenges – PSURs/PBRERs

- Ad hoc requests for spontaneous data reviews that are not consistent with new principles, format and content e.g.
  - Requests to continue cumulative /interval reviews of spontaneous data even when these have been negative on many previous occasions
  - Provision of line listings of cases reports with a fatal outcome
- International harmonisation
  - EURD not always based on IBD; increased bureaucratic burden
  - PSUR or PBRER (per ICH E2C (R2) given that the new report is neither periodic/ focussed solely on safety nor an update……

EFPIA Proposals – PSURs/PBRERs

- Ad hoc requests for reviews that are not consistent with new principles, content and format
  - Fulfil commitments or requests to conduct reviews
  - If results are negative – include this information in a covering letter
  - If results conclude a new signal or new information on a known risk etc., discuss in appropriate section of the report
- International harmonisation
  - Harmonise with Step 4 ICH E2C (R2) guideline
  - PSUR rebranding ?????

Specific Wish List – RMPs

- New RMP template format still not published
  - Amendments post consultation version unknown
  - Insufficient time to implement final version for RMPs due in January 2013
  - EFPIA understand that there are legitimate reasons for this but…….
- RMP requirements for new applications involving generics without risk management beyond routine
  - May become an administrative burden for no added value
- Wish List
  - If it could be released yesterday, that would facilitate compliance
  - When released, Word format to facilitate efficient implementation
  - Reasonable and consistent approach across EU for generic new applications

Specific Challenges – PRAC

- Transparency with MAHs appears to be selective:
  - Publication of PRAC agenda or minutes with outcome without prior communication
  - Unclear prioritisation of signals brought forward for PRAC consideration
  - No scientific rationale provided e.g. for requested update to the SmPC
- Proportionality principle does not seem to apply :
  - Very short timeframe for responses regardless of medical importance or public health impact of the signal
  - Statistical signal generation can cause huge increase in the number of false signals that have to be verified by MAH
- Inability to prepare if signal has global implications
  - Medically significant event
  - High profile product

EFPIA Proposals – PRAC

- Transparency with MAHs appears to be selective:
  - Prior to web portal availability, easily identified area on EMA website to find this information
  - MAHs notified 24 hours ahead of publication if significant signal
  - All signals published on a predefined date
  - Clear scientific rationale provided
  - Transparent communication of prioritisation
- Proportionality principle does not seem to apply :
  - Timeframe for responses to take into account medical importance and public health impact of the signal