The European Commission's Proposal to Re-design Existing European Drug Safety Rules

An Industry View on Practical Implications

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Initial Position / Understanding:

- The proposals are generally very positive, and industry strongly supports measures aimed at:
  - Improving robustness of the EU PV process and systems
  - Ensuring a clear and supportive legal framework
  - Rationalising EU decision-making on drug safety
  - Optimising the use of available resources
- Per informal feedback, seems industry request for a single binding Regulation is not possible within EU legislative framework – awaiting confirmation?
- Finalisation through to the EU Parliament and sign-off by the EU Commission will take until at least 2010
  - Post-publication period for industry implementation not known

From Experience Gained With Implementing Volume 9A (Dec 2006):

- What you see/think you understand is not always what is expected, i.e.
  - Interpretation by MAHs Vs Regulators (and PV Inspectors)
  - Status of guidance Vs. true legal requirements
- Lead times for implementation can be extensive for
  - Internal process and procedural changes
  - Updates to databases (both ‘off the shelf’ and ‘in-house’)
  - Update of business partner and contractor agreements
- May also take time to test and/or confirm technical changes with authorities

From Experience Gained With Implementing Volume 9A (Dec 2006):

- The ‘devil is in the detail’
  - Questions remain long after initial publication
- Communication is key, both internally and externally
- Hence investment in consultation to gain clarity ***now*** is essential!

Initial Review and Actions Steps As Proposals Released:

- Internally:
  - Prepare and submit specific company comments and questions
  - Consider overlap with global requirements
  - Identify areas definitely and potentially requiring process, procedure and system changes
- Externally:
  - Seek clarity through the wider EU consultation process
  - Collaborate on follow-up with industry associations (EFPIA, PhRMA etc.)
  - Monitor individual Member State implementation discussions

Pro-active Assessment Of Implementation Needs:

- Given plans can only be ‘best guess’ at present with respect to what will actually be implemented
  - Assess changes to internal processes and procedures
  - Identify implications for safety database
  - Review agreements with business partners and contractors
  - Consider/track pilot schemes
  - Estimate lead time to implement changes
  - Assess resources required
  - Identify any barriers

- Decide which areas need action now Vs. those where we need to await more clarity….

Proposals for Pharmacovigilance Committee:

- Supportive of new PV committee at EMEA
  - And for maximising expertise on this committee
- However, clarification of practical aspects requested
  - Need to clarify/confirm Risk Benefit decision making will remain the responsibility of the CHMP
  - What will fall within the scope and decision making authority of this new Committee? e.g. RMP reviews, signal detection, risk-benefit analysis etc.
  - Will their processes be transparent in terms of agenda, input etc.
- Next steps for industry:
  - Seek further clarification of intent, structure etc.

Proposals To Simplify Referrals:

- Supportive of proposals to:
  - Simplify referrals and rationalise decision making
  - Establish an automatic PV referral procedure with non-discretional referral triggers
  - Have the outcome become legally binding
- Comments/Questions:
  - Request inclusion of an appeals procedure
  - The process around public hearings is not clearly defined e.g. what are the triggers, does this apply to all routes of approval?
- Next steps for industry:
  - Await further clarification

Proposals On Strengthening Risk Management Planning:

- Strongly support for proposals, though clarity required:
  - Focus on true Public Health issues with scientific justification
  - Commitments must be practical and achievable.
  - MAH compliant if all efforts made to conduct RMP obligations.
  - Have one EU Risk Management Plan acceptable in all Member States *and* within a global context
- Next steps for industry:
  - Continue development and tracking of RMP process, both in the EU and Global environment

Proposals On Post Authorisation Safety Studies (PASS):

- Support legal basis for authorities to request PASS
  - Is the aim to clarify basis on which they can be requested?
  - And for those requested, a sub-group having ‘light’ oversight
- Real need for further clarity
  - Under what circumstances should Non-EU studies be included?
  - Handling PASS studies conducted by external agents
  - If not clarified, risk of non-inclusion of relevant studies in RMPs and PSURs Vs. MAHs including all
- Next steps for industry:
  - Await guidance/feedback further to regulator consideration of EFPIA position paper
  - Collaborate towards ensuring clarity in new proposals

Proposals On Systems and Inspections:

- Strongly support
  - Clarifying roles and remits
  - Establishing clear standards & drawing up GVP
  - Harmonising inspections
  - ‘PV Master File’ plus declaration of risk status
- Comments/Questions:
  - Clarify use of ‘Master File’ Vs. local file pre-inspection
  - Concern on inclusion of internal audit reports in Master File
  - Request option to link inspection to MS of QP residence *or* to main EEA PV activity site
  - QP contact details should not be made public.
- Next steps for industry:
  - Await further information on ‘PV Master File’ format and application, plus monitor any MS pilots in this area.

Proposals On Rationalising ADR Reporting:

- Support simplification of ICSR reporting requirements:
  - Fully support sending 3rd country reports *only* to EV
  - Noting that to maximise effectiveness it is essential that the individual CAs commit
  - Concern with change to all ICSRs required in 15 days, timeframes for reporting should continue to reflect the seriousness of the ICSR in question
  - Request that non-serious ICSR submissions should be in line with current Volume 9A (i.e. periodic).
- Next steps for industry:
  - Continue with existing requirements, but review potential changes required in order to expedite all serious ICSRs (in 15 days?) and non-serious periodically.

Proposals On Rationalising ADR Reporting:

- Support intensive monitoring linked to RMP milestones but clarification requested:
  - All new, all routes, method of removal?
  - Alert to intensive monitoring on package to be symbol rather than a (boxed) warning
  - Support variety of methods of reporting, directly to regulators
  - Public education needed to avoid unwarranted concerns
- If literature to be handled by EMEA:
  - Suggest useful for old products only, and ICSRs must be rapidly available (<<15days) to MAHs for onward expedited reporting to Ex-EU Agencies
- Next steps for industry:
  - Await clarification of proposals

Proposals Relating to Periodic Safety Update Reports (PSURs):

- Proposals generally supported, noting:
  - Would be good to build on recently introduced work-share process
  - Conclusions of PSUR assessments and recommendations must be provided in lay language adapted to the audience and be available to the applicable MAH when posted.

- Next Steps:
  - Continue to follow existing requirements (including workshare) and await further clarification

Proposals With Respect to Transparency and Communication:

- Support proposals, however,
  - Essential that Risk information is not presented in isolation
  - Need for close consultation between parties
  - Formats for EV data release should put in context
  - Clarification of roles and timing of increased transparency and communication & proposal for EU Portal needed
- Support enhanced co-ordination of important safety messages
  - accepting importance of local factors and cultural elements
- Next steps for industry:
  - Await further information on proposals

Proposals With Respect to Strengthening Product Information:

- Supported, noting that:
  - information must be presented in a balanced manner
  - Proposal for SPC to have new 'key safety' information section needs clarification
  - Would support this to be 'key information' rather than just 'safety information'
- Next steps for industry:
  - Await further information on proposals

Other Considerations And Next Steps:

- These proposals, given some changes from feedback are accepted, should be positive towards
  - Reducing workload (for both regulators and industry)
  - Increasing the efficiency of PV systems
  - Freeing up resources for signal detection and risk minimisation
  - Towards the goal of protecting of public health
- MAHs will need to consider other initiatives impacting on company systems and procedures, e.g.
  - Overlap with existing and updated Ex-EU PV requirements (e.g. changing F&DA PV requirements)
  - Overlap with existing and changing clinical trial requirements (e.g. development of DSURs)
  - Rapidly developing global data privacy requirements

Moving Forwards:

- Industry is assessing changes which will be needed internally if proposals implemented 'as is', as well as with requested changes
- Clarity is essential before MAHs can effectively plan for timely and effective implementation, particularly for:
  - The role and remit of the new PV Committee and it's relationship to the CHMP for decisions on Risk benefit
  - Definitions and requirements for PASS
  - Transparency / information release in appropriate formats
- Harmonised MS implementation will also be critical to achieving the stated goals of the proposals
  - Towards the ultimate goal of protection of Public Health