EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Implementation of Regulation 1235/2010, Article 57(2)

Stakeholders forum on the implementation of the new Pharmacovigilance legislation

Presented by: Sabine Brosch
Pharmacovigilance and Risk Management Sector, Patient Health Protection Unit

Introduction

- New legislative provisions:
  - (a) EMA shall make public a format for the electronic submission of information on medicinal products for human use (by 2 July 2011)
  - (b) MAHs shall electronically submit to the Agency information on all medicinal products for human use authorised or registered in the Union, using the format referred to in point (a) (by 2 July 2012 at the latest)
  - (c) MAHs shall inform the Agency of any new or varied marketing authorisations granted in the Union, using the format referred to in point (a) from the date set out in point (b)

Introduction

International Standardisation Activities

- At the request of the European Commission the Agency engaged in international standardisation activities
- ICH Steering Committee decision in 2006 to collaborate with Standard Development Organisations (SDOs) for development of technical standards
- ICH E2B Individual Case Safety Reports (ICSR) and ICH M5 Identification of Medicinal Products (IDMP) topics were adopted by SDOs as part of a Joint Initiative
- ISO is lead SDO, electronic messaging developed by HL7:
  - ISO ICSR standard – standard finalised December 2011
  - Five ISO IDMP standards – final standard expected 2nd half 2012

Agency's Deliverables on 1 July 2011 (1/2)

- Agency delivered on time in accordance with the legal requirements
- Legal Notice: defines high level content and phased implementation
- Detailed Guidance: format for electronic submission of medicinal product information (Extended EudraVigilance Medicinal Product Message)
  - Data elements that characterise a medicinal product
    - 30% of ISO IDMP standard (FDIS 11615) chosen for the following reason:
      - Corresponds to EVMPD data set already in use with a number of modifications to ensure ISO IDMP compliance (e.g. expression of strength)

Agency's Deliverables on 1 July 2011 (2/2)

- Detailed Guidance: format for electronic submission of medicinal product information (Extended EudraVigilance Medicinal Product Message) (cont'd)
  - Data elements that characterise the substances contained in a medicinal product
    - 90% of ISO IDMP standard (FDIS 11238) chosen for the following reasons:
      - Substance identification is building block for maintaining information on medicinal products
      - Important for the regulation of medicines including support of pharmacovigilance (coding of ICSRs, signal detection, EV Access Policy implementation, PSUR work sharing)
- The XML Schema Definition (XSD) for the individual data elements

Agency's Deliverables

- On 1 September 2011:
  - Update to the Detailed Guidance
  - Publication of the XML Schema Definition (XSD) for the individual data elements
  - Controlled Vocabularies for structured substance information
  - XSD schema files and naming conventions for substances
- Until January 2012:
  - 2 ISO IDMP Information Days
  - 1 Article 57 Information Day
  - 5 meetings with interested stakeholders
  - 7 Training courses
  - 409 responses to Help Desk requests

Main Concerns Raised by Pharmaceutical Industry

- Timelines
  - Short timeline to comply with e-submission requirements
    - High workload
    - Timing of availability of IT tools for industry (EMA data entry tool (although no legal obligation for EMA to develop) and private initiatives)
- Content (not always harmonised view by all Pharmaceutical Industry Associations)
  - Structured information contested vs. non-structured information (SPC, PL, labeling)
  - Duplication of efforts for generic substances
  - SPC, PL, labeling - which documents to be submitted and in which language?
  - Manufacturing information for non-biologicals (extension of deadline)
  - Excipients (extension of deadline)
  - Extension of timelines for notifying variations

Considerations for a Revised Approach

- The legal deadline for submission of information cannot be extended
- A 2011 Member State survey in relation to pharmacovigilance data and fees has allowed to better quantify the workload: 263,444 medicinal products are authorised in 21 MSs
- A stepwise approach to move towards ISO IDMP implementation as ultimate and longer term objective
- Focus short term is on the submission of information necessary to support pharmacovigilance
- As a result there is a substantial reduction of the mandatory data set for July 2012

Options for a Revised Approach (1/2)

- Three options have been elaborated by EMA for discussion with pharmaceutical industry
- For each option pros, cons and risks have been identified to facilitate informed decision-making
- For each option there has been a further reduction of the mandatory data set for medicinal products compared to July 2011 (20% medicinal products ISO IDMP compliance compared to 30% in July 2011)

Options for a Revised Approach (2/2)

- Option 1: reduction of the mandatory data set for structured substances (60% versus 90% in July 2011)
- Option 2: restricted to structured substance data set for biological products only (10% versus 90% in July 2011)
- Option 3: no structured substance data set

Agreed Approach (1/4)

- The various options were presented to the European Industry Associations (AESGP, EFPIA, EGA, EUCOPE, EBE, EVM, Europabio) during a workshop on 30 January 2012
- Meeting was attended by an HMA representative (from MHRA)
- Approach favoured by pharmaceutical industry is based on option 3

Agreed Approach (2/4)

- Characteristics of favoured approach:
  - Reduction of the mandatory data set for medicinal products compared to July 2011
  - Are not mandatory
    - Additional monitoring
    - Location of pharmacovigilance system master file
    - Description of the packaging information
    - Regulated documents (condition of MA, labelling, PL)
  - Structured substance information: no such information to be submitted until an agreement is reached on a collaborative way forward to coordinate the entry of high-quality structured substance information
  - SPC to be submitted for validation purpose

Agreed Approach (3/4)

Pros	Cons	Risks
• Significant reduced burden for MAHs making it most likely to meet the legal deadline • Allows the Agency to establish a complete list of medicinal products authorized and registered in the EU	• Substance data set not compliant with ISO IDMP standard – will require duplication of efforts by MAHs (data entry and re-linking of substances and products) and the Agency (validation) at time of ISO IDMP implementation • Agency cannot establish comprehensive substance registration system • Delay of the release of the EMA data entry tool/DB for MAHs due to necessary adaptation (15 April 2012 at the latest) • Delays for vendors and MAHs to further adapt and test their IT systems based on proposed solution • Requires updates to the Legal Notice, Detailed Guidance and schema	• No improvement of current deficiencies in signal detection for the Agency and the EU Regulatory Network • Complaints from IT vendors and MAHs that already invested in IT tools and resources to comply with format published on 1 July 2011 • Collaboration/harmonisation with FDA on substance maintenance at risk due to lack of data in the EU

Agreed Approach (4/4)

- Next steps:
  - Dedicated virtual workshop with Industry Associations on 9 February 2012 to clarify remaining questions (on the XEVPRM format, on the language requirements depending on the authorisation procedure)
  - Communication of the outcome of the workshop (including revised Legal Notice, updated Detailed Guidance/Q&A document) and afterwards regular updates on progress made
  - Data entry tool to be made available by 15 April 2012 at the latest
  - Testing by pharmaceutical industry: gateway connection testing, message submission testing, UAT of the data entry tool prior to release (nominations from Industry Associations invited)
  - Other follow-up workshops will be organised (e.g. to discuss maintenance of data)

Follow-up to 30 January 2012 Workshop

- Virtual technical workshop with Industry Associations held on 9 February 2012
  - All Industry Associations participated
  - 170 questions were submitted by industry
- All questions raised by pharmaceutical industry were discussed during the teleconference and the outcome of the discussions will be reflected in a revised Detailed Guidance and Q&A document

Next Steps

- EMA will at regular intervals communicate on progress made, including the release date of the data entry tool and the dates for testing
- EMA will consult first with the Network and subsequently with all stakeholders over the next months to develop a longer term strategic vision towards implementing the IDMP standards and ICH5