S&P Subgroup

Report for the EU ISO IDMP Task Force – 19 February 2016

Presented by S&P subgroup on 19 February 2016

Contents

- EU IG framework development
- Analysis for the stability of the PMS IT1 draft scope
- Next steps

EU Implementation Guide Framework Development: Review of Current Article 57 Guidance Content

User Guide & Training

- XEVMPD Data-Entry Tool (EVWEB) User Manual;
- XEVMPD training presentations;
- Step-by-step guides
- Guidance on submission of Investigational Medicinal Products (IMPs)

Detailed guidance

Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2), second subparagraph of Regulation (EC) No. 726/2004:

- *Chapter 1: Introduction*
- *Chapter 2: Electronic submission of information on medicinal products by MAHs*
- *Chapter 3: Extended EudraVigilance product report message (XEVPRM) technical specifications, user guidance and practical examples*
  - *Chapter 3.I:... technical specifications 08/01/15*
  - *Chapter 3.II: ... user guidance*
  - *Chapter 3.III: Practical examples*
- *Chapter 4: Structured Substance Information (currently not applicable)*
- *Chapter 5: Extended EudraVigilance product report acknowledgement message*
- *Chapter 6: Annex: Definitions*

Data quality-control methodology

Quality control of medicinal-product data submitted as per the legal requirement introduced by Article 57(2) of Regulation (EC) No. 726/2004

Coding of indications in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)

European Medicines Agency substance names best practice: Procedure and principles to handle substance name in the substance management system

15 Controlled vocabularies

European Medicines Agency splitting of the full presentation name of the medicinal product best practice: Procedure and principles to handle product name in the EudraVigilance Medicinal Product Dictionary (XEVMPD)

Data quality control methodology for data submitted under Article 57(2) of Regulation (EC) No.726/2004

Measures for Article 57 data quality assurance

Controlled vocabularies: quality control *e.g.*

Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information

Legacy product data in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)

Frequently asked questions

Electronic submission of Article 57(2) data: questions and answers

Learnings from Article 57 Guidance

Difficult to find information between many documents

- Proposal for IDMP to not have a linear document, but rather a modular document with the information that can be searched and navigated
- Practical challenges to pursuing this approach may exist, review ongoing

Special situations are incorporated into the general content

- Propose pulling special situations (e.g., Lichtenstein; multiple language countries, etc) into separate topics, referenced as appropriate in the main document content

Guidance is field-oriented rather than business-process oriented

- This worked for Art 57 where the product record is created after approval and content changes to the records are fairly simple. In full IDMP implementation, records will be created well before approval, and will be maintained/changed over the course of the lifecycle more dynamically.
- Bringing a product lifecycle/process approach to the document content will help ensure Industry understand the expectations for submission and ongoing maintenance

Guiding Principles for EU IG Design: Framework for Evolving Implementation

Begin with the end in mind

- While the first iteration is very similar to Art 57, subsequent iterations will introduce greater scale and breadth of data content as well as additional complexity around maintenance instructions.

Business process focus

- Clear orientation in the IG around simple and streamlined business processes will best establish understanding in Industry and support compliance as future iterations are implemented
- E.g., Create new record, maintain record, withdraw record; new development product, clinical trial application, initial marketing authorization, variation, renewal, etc
- Once data is entered it will not have to be re-entered

Change Management process

- Establish a process for how the future versions of the IG will be managed

Comprehensive and Consistent

- EU IG will cover all of SPOR with individual sections to be updated by working groups in a consistent format
- Other Activities of interest need to align with IDMP e.g. FMD

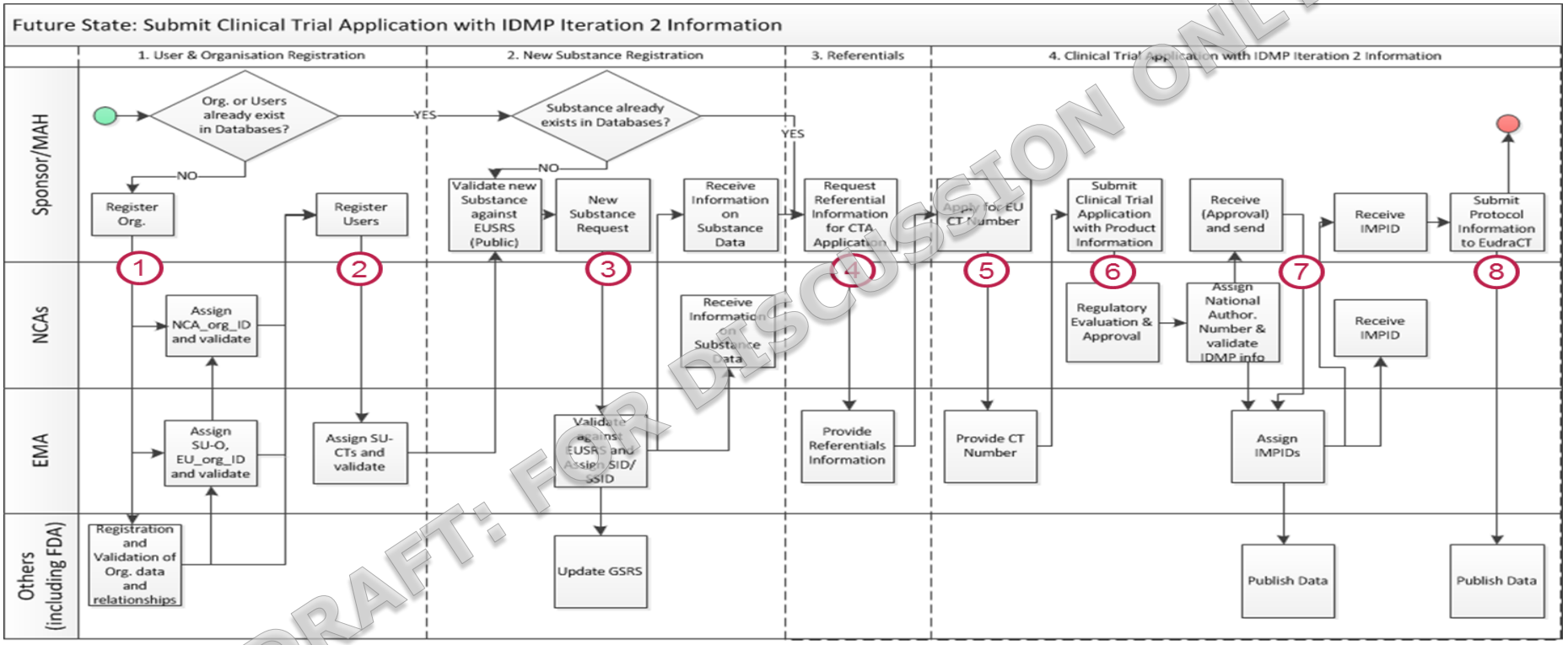
EU Implementation Guide Development

- IG Deliverables will include
  - Process-oriented implementation guide for business
  - Technical guide for IT/technical audiences
- IG will incorporate all components of SPOR
- IG will require input from all IDMP sub-teams for completeness and accuracy
- Business process details will need to be worked out as input into the guidance content, this work is beginning now (see next slides)

Potential IDMP Process Impact

#	Process	Description	IDMP	#	Process	Description	IDMP
1	Pre-Trial	Scientific Advice	?	7	Safety Reporting	Submit ICSRs Maintain PSMF (GVP Inspections) Investigator Initiated Studies/P4	Y
2	CTA/IND	Organization and User Registration New Substance Registration (SID) Submit CTAs and INDs (IMPID) Publish CT Information	Y	8	Manufacturing/CMC	Update BAIDs Update Manufacturing Information GMP Inspections	Y
3	Development	Submit CTA/IND Amendments Submit ATC/INN Requests Provide GCP Information Maintain Trial Master File Submit PIPs/DSURs/PSRs	Y	9	Variations	Submit Variations (Update Clinical Particulars etc) Maintain XEVMPD Information Maintain PACs/FUMs	Y
4	MA Submission	Submit MAA Orphan Drug Designation MAPPs/Breakthrough	Y	10	New Country MAA	Submit MAA in new Country Apply for new MPID, PCID, BAID?	Y
5	MA Review	Maintain current CTD File during Q&A Request MPID and PhPID	Y	11	MAH Transfer	Apply for License transfer (new IDs?)	Y
6	Approval to Launch	Submit XEVMPD Data Request PCID and BAID Linguistic Review/Translate Label	Y	12	Withdrawal	Update Marketing Status of Product (retire IDs?)	Y

2. What does a Sponsor need to do to file a CTA?



- Process Diagram is under discussion and may contain inaccuracies
- Numbers correspond to Information Flow steps (details on next slide)
- Process Flows consolidated from SPOR and Clinical Trial Draft Processes (see back up slides)
- This process flow only covers a simple initial Clinical Trial Application assuming approval with no additional communication between NCA and Sponsor. It does not cover subsequent amendments, questions, end of trial notifications, results disclosure etc

2. What does a Sponsor need to do to file a CTA?

Step	Description	From	To	Format	(IDMP) Attributes
1	Register Organisation	Sponsor	NCA EMA Other	CT Portal? CT Portal? Web Interface?	Org Name, Org Address, Org Relationship etc*
2	Register Users	Sponsor	EMA	CT Portal?	User Name, Email Address etc*
3	New Substance Request	Sponsor	EMA	HL7/SPL?	Substance Attributes etc*
4	Referentials Information	Sponsor	EMA	Export/Download from Referentials Database?	Clinical Particulars, units of measurement, dosage forms, routes of administration etc*
5	Apply for EU CT Number	Sponsor	EMA	CT Portal?	
6	Clinical Trial Application with IDMP Iteration 2 Product Information	Sponsor	NCA	CT Portal? Data Entry? eAF? PDFs? HL7/SPL?	All Iteration 2 attributes and supporting common documentation (Protocol, IB, IMPD) and local documentation (country specific requirements?)
7	Submit CTA Approval	Sponsor	EMA	HL7/SPL? Email?	Update on Approval of CTA and IMPID Attributes
8	Submit Protocol Information to EUdraCT	Sponsor	EMA/ Public	EUdraCT?	Which IDMP Attributes will be published and how will confidentiality field work?

Analysis for the stability of the PMS IT1 draft scope

Analysis for the stability of the PMS IT1 draft scope

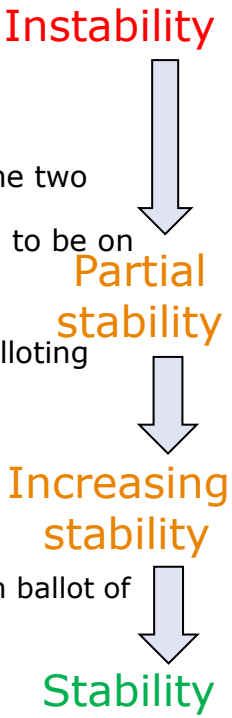
Objective: To assess the stability of the sections of the ISO Medicinal Product IG (DTS20443) relevant for EU Iteration 1

Process: Assessment of comments received, per ISO DTS section, which have then been categorised based on ongoing discussions and progress within ISO Expert Group

ISO Technical Specification (Implementation Guide) and revised Standard - Status

Progress on addressing ~1000 ballot comments has been good

- Most key issues have been resolved
- Still some points to consider but anticipate resolution
- Technical Specification and Standard are being revised in parallel – content being reassigned between the two
- Good drafts plus ballot disposition documents need to be sent to the Technical Committee by mid-March to be on agenda for May 2016 meeting in Amsterdam
- Revised Standard must be balloted but an additional ballot for Technical Specification is optional (but balloting again would open up TS to further change)
  - Decision to be taken on balloting in Amsterdam (May 2016)
  - Ballot for standard (potentially June-September 2016)
  - Balloting of Standard also opens up TS to further change (so TS should not be published before results on ballot of Standard known and addressed)
  - Published versions of TS and Standard not anticipated until 1Q 2017 if published in parallel



Process details

Reviewed each comment for EU Iteration 1 relevance/comment on issue

Reorganised ISO comments sheet

Split into

- Main body
- Individual Annexes (A-H)
- Organised sequentially by Section Number (Field name)
- Does not cover IMPs (I), SPL (J), CVs (K), Abbreviations (L)

Created new worksheets to define *At Risk* sections

- Main body and Annexes A-H

Section Number	Section Title/Field	In scope for Iteration 1	Key Issues from ISO Ballot relevant to EU Guidance	At Risk Section for EU for Iteration 1 Guidance	ID# for industry analyses document
A.1	General	Yes	None	No	
A.2	Medicinal Product	Yes	None	No	
A.2.1	MPID	Yes	None	No	1

Section Number & Title from DTS20443 (July 2015 edition)

In scope for Iteration 1 ('92+' fields list used)

- Yes, No, Maybe (where there was/is some uncertainty)

Key Issues relevant to Iteration 1

- Does not include e.g. Cardinality, conformance, snippets, typos, minor
- Does include key business issues where solution not yet discussed, proposed solution is judged likely to raise further comments either during a 2nd DTS ballot or ballot of the Standard

At Risk Section for Iteration 1 Guidance

- No
- Potentially – requires more definition from ISO, or more consideration inside EU as to actual requirement
- Yes – more likely that section would need to undergo further consideration after ballot comments

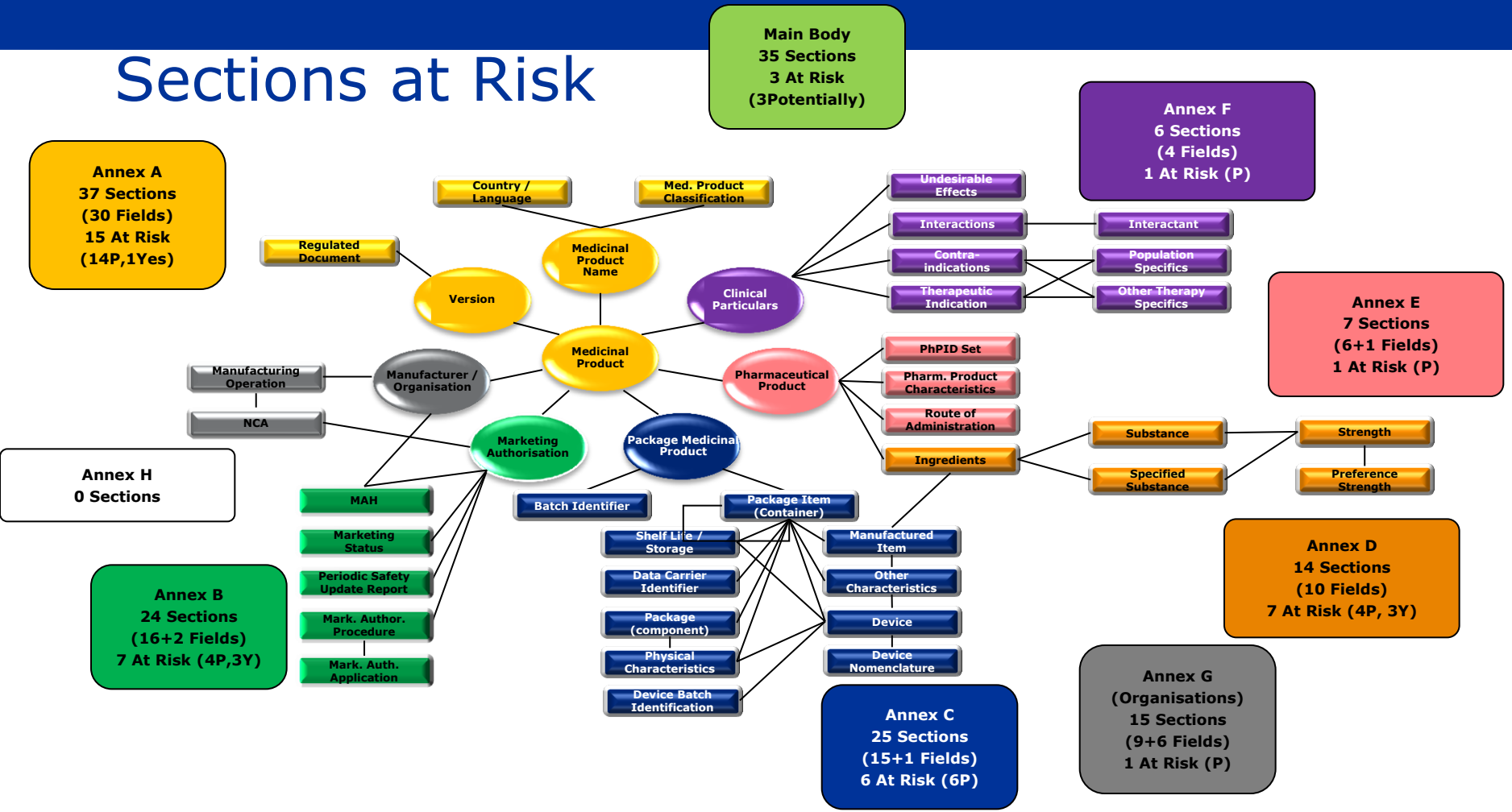
Linked to Industry analysis comments

Filterable

Annex A – Medicinal Product – partial example

#	Section Name	Key Issues	At Risk
A.2.12	Medicinal Product Name	Clarification that multiple names can be included for a single medicinal product for countries where more that one language is used	Potentially
A.2.12.1	Name	SPL implementation does not appear to allow the Full Name (as per XEVMPD) to be provided and seems to expect that it is a concatenation of the parts The full and complete Medicinal Product Name as approved by the Medicines Regulatory Agency in a jurisdiction shall be specified as text, with parts of the name tagged as appropriate. Not all name parts appear to be tagged independently eg. brand name not represented if scientific name not provided	Yes
A.2.12.2	Invented Name Part	Invented name cannot be mandatory	Potentially
A.2.12.3	Scientific Name Part	Redefine the model so that the Invented Name uses the Name tag (or a newly defined Invented Name tag) and the generic name uses the Scientific Name on all occasions	Potentially
A.2.12.4	Strength Part	For a product name like Seretide® Accuhaler® 50 microgram /100 microgram /dose inhalation powder, pre-dispensed how would the model support Strength? Would the strength be "50 microgram /100 microgram /dose" without reference to the ingredients?	Potentially
A.2.12.14.1	Country	Clarification of EU as a country and not a jurisdiction	Potentially
A.2.12.16	Language	Clarification that multiple languages can be used for names for a single medicinal product for countries where more that one language is used	Potentially

Sections at Risk

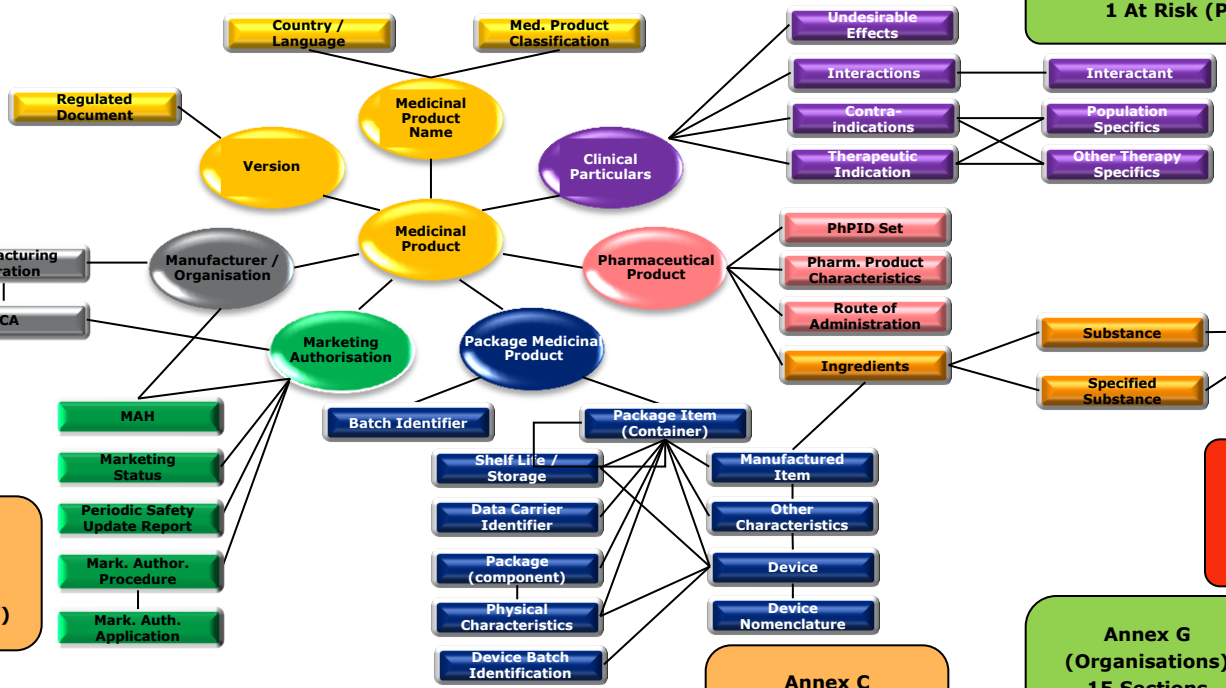


Sections to Progress

Main Body
35 Sections
3 At Risk
(3Potentially)

Annex A
37 Sections
(30 Fields)
15 At Risk
(14P,1Yes)

Annex F
6 Sections
(4 Fields)
1 At Risk (P)



Annex E
7 Sections
(6+1 Fields)
1 At Risk (P)

Annex H
0 Sections

Annex D
14 Sections
(10 Fields)
7 At Risk (4P, 3Y)

Annex B
24 Sections
(16+2 Fields)
7 At Risk (4P,3Y)

Annex C
25 Sections
(15+1 Fields)
6 At Risk (6P)

Annex G
(Organisations)
15 Sections
(9+6 Fields)
1 At Risk (P)

Next Steps

Note: The number of potential issues will reduce with time as further ballot resolution continues and documents are redrafted

Initiate EU IG on basis of mid-March 2016 draft of ISO document for

- Main body, Organisations, Pharmaceutical Product, Clinical Particulars (1st priority)

Utilise ‘ballot’ or ‘draft for publication’

- Marketing Authorisation, Packaged Medicinal Product (2nd priority)
- Medicinal Product, Ingredients (3rd priority)

S&P Subgroup - Next Steps

In order to progress with the EU IGs drafting, the progress should be on the two aspects:

- data content consolidation
- submission business process definition

Therefore , the following next steps are envisaged:

1. EUNDB/Regulators to confirm PMS It1 scope
2. S&P Subgroup to map risk analysis file against the scope
3. EUNDB/Regulators to provide the business case per data elements
4. Link the business case data elements with risks analysis and the EU IG framework/chapters for prioritisation of future activities and drafting of the document
5. To assess benefit realisation sequence (i.e. when each process can be implemented to support which business cases)

Thank you for your attention