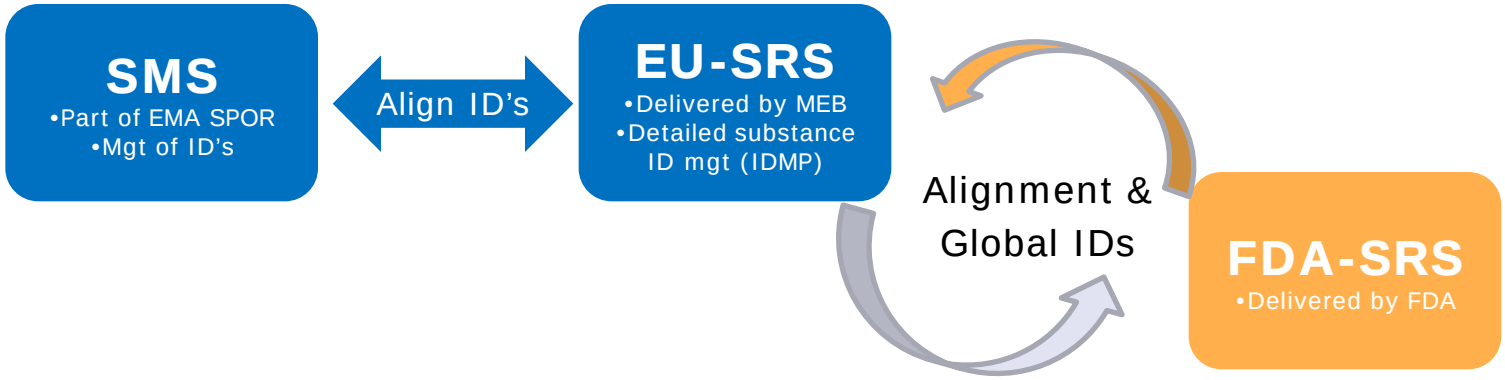
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

SMS / EU-SRS Update

SPOR Task Force meeting March 2018
Frits Stulp, Project Manager EU-SRS

Precise substance identification supports clinical safety and minimized toxicological risk



- The EU-SRS database will support identification of structurally diverse substances as in this area SMS is not equipped to capture the level of detail that is required.
- These areas include:
  - Vaccines
  - Biologicals
  - Herbals
  - Homeopathics

For SPOR TF input

EU Substance Systems

EUROPEAN MEDICINES AGENCY

SMS
"IDMP light"

- **Who:** Implemented by EMA
- **Data:** SMS data is the "simplified" PUBLIC substance data, that supports selection in regulatory processes and therefore enables you to distinguish two or more similar substances
- **Technology:** SMS solution covers:
  - Search, browse and export of PUBLIC substance data
  - Management of substance change requests
  - Translation management
- **Process/People:** EMA provides a broker service by managing substance requests, supporting translations and assuring data quality.

EU SRS
ISO IDMP compliant

- **Who:** Implemented by MEB (NL)
- **Data:** EU SRS contains ISO IDMP substance data that supports scientific identification of substances. It includes PUBLIC and CONFIDENTIAL information subject to controlled access
- **Technology:** EU SRS solution covers only Substance data management
  - Software development/implementation led by NL in the short term in collaboration with EMA, under EU Telematics governance
  - Software maintenance to be transferred to EMA
- **Process/People:** This project is responsible to set up the EU Substance Validation Group (SVG) who will:
  - Prepare the EU substance list
  - Maintain the EU list by approving substance requests and managing substance data

Current project status and plans

Overall

- Endorsed at HMA (Talinn)
- Carried by MEB
- Run under Telematics governance

Phase 0: Project set-up

- EU-SRS project manager started per February 1st (Frits Stulp, fa.stulp@CBG-MEB.nl)
- Responsible to achieve agreed deliverables and inform stakeholders

Phase 1: Business case

- Agreed deliverable to HMA (Q2 2018) for further decision-making
- Describes scope, plan and effort to deliver EU-SRS

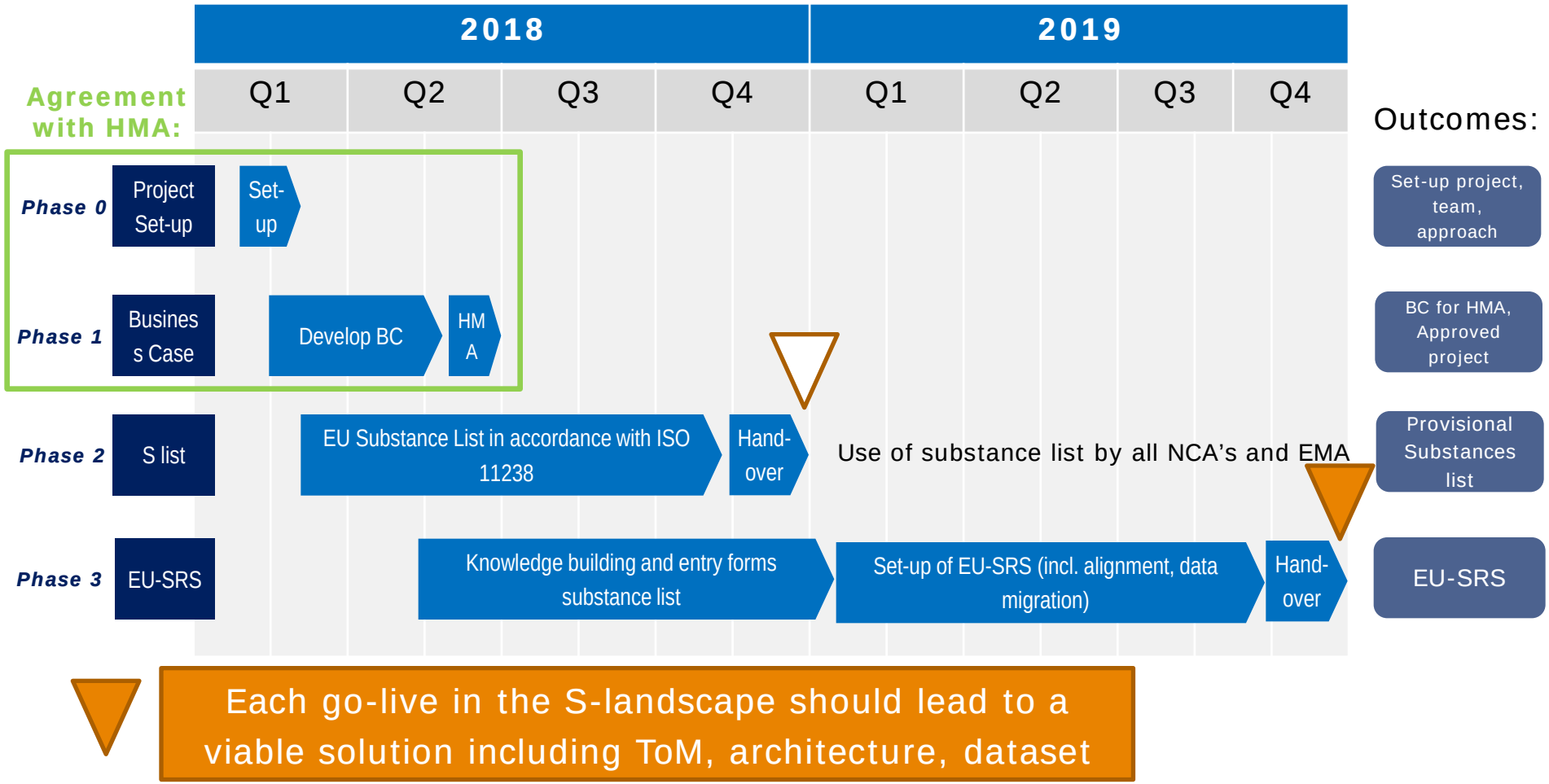
Phase 2: SMS suitable substance list

- By end 2018 to be completed for some substance types (Human & Vet)
- To support EU network identified use cases
- Detailed requirements under discussion

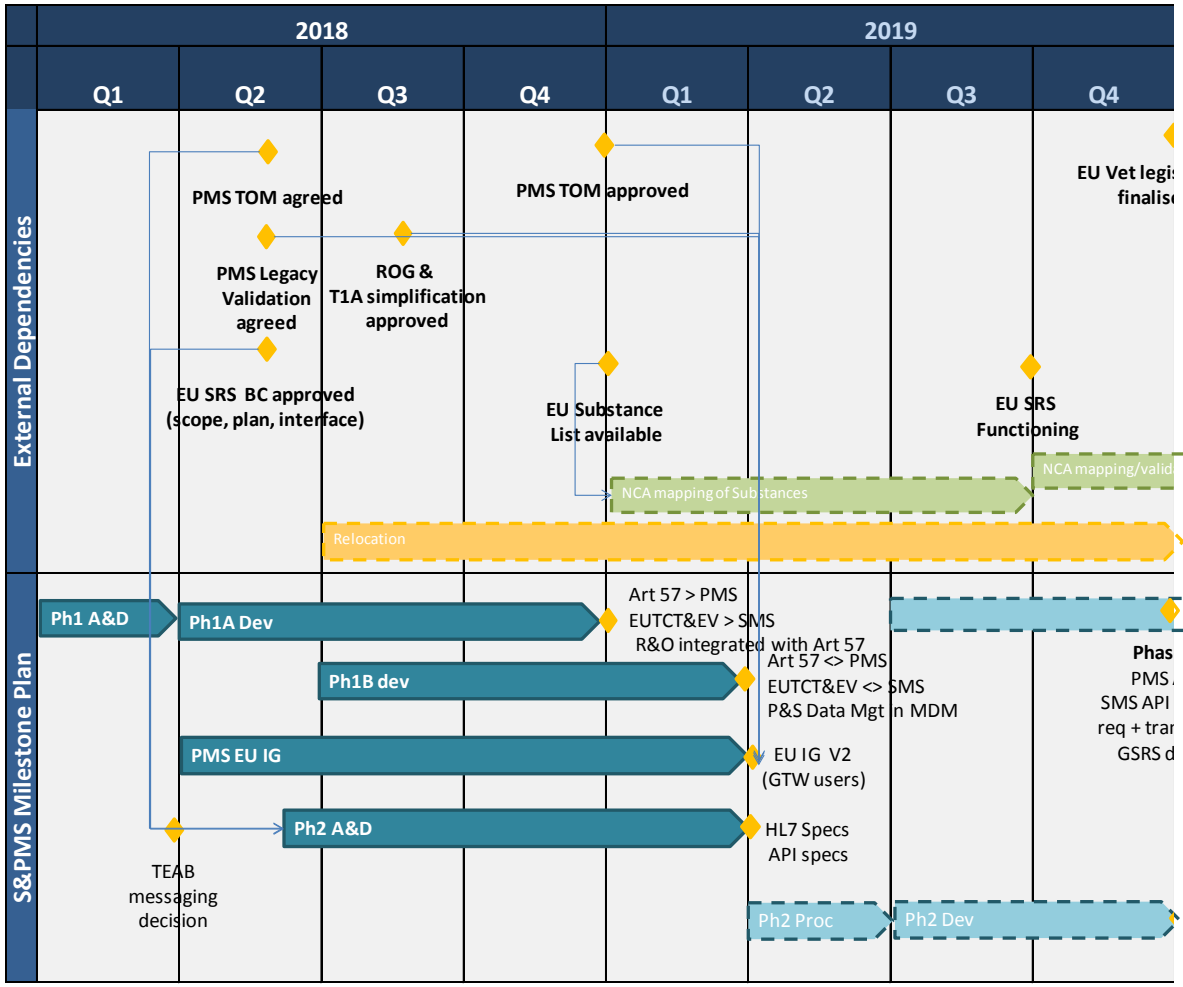
Phase 3: delivery of EU-SRS

- Only after HMA approval
- As described under plan in Business Case

Current project plan for EU-SRS



Relation to SMS plans



- **Phase 1A**
  - SMS ISO compatible/simplified hub
  - EUTCT&EV (H&V) migration into SMS
- **Phase 1B**
  - S data mgt in MDM (CRUD)
  - SMS feedback loop into EUTCT & EV – Backwards compatibility
  - Possible data load???
- **Phase 2 A&D**
  - TOM, Business process - syncronisation
  - Use cases
  - HL7 & API specs
- **Phase 2 Dev**
  - SMS API
  - SMS UI (CRs & transl)
  - EU SRS sync
  - EUTCT decommissioning

- Dependencies already in 2018
- Mitigation involves monitoring and exploring options
- If materialised may imply delays or a re-plan

Business case

"EU-SRS builds and extends the EU single source of reliable, high quality substance data at sufficient level of detail to enable.."

The use cases to be supported are shown in the next slide

Backwards compatibility	Must	Should	Could	Wont
Via EUTCT: • Clinical Trials: (EudraCT, new CT) • H Pre-submissions (Orphan, UPI, PedDRA) • H&V MAA & Var Regulatory submission (SIAMED, eAF, CESSP) • NCAs **Via Art 57:** • Pharmacovigilance: (EV H, PSUR rep.) • Referrals • Fees	• Pharmacovigilance (signal detection, analytics) – legal driver • Product (composition) registration (H&V) – PMS TOM • Consumption (Veterinary business case) – legal driver • MRL (veterinary use case) – legal driver • Cross Border ePrescription – EC/public health	• Evaluation of Risk of Shortages - EC/public health • Variations (manufacturer details change) – ROG • CEP Management - ROG • Toxicology use case (under investigation)	• GMDP Inspection Support	• ASMF Management • Batch Recall Support • Supply Chain Traceability

Use cases for substance management

For SPOR TF input

Backwards compatibility	Must	Should	Could	Wont
Via EUTCT: • Clinical Trials: (EudraCT, new CT) • H Pre-submissions (Orphan, UPI, PedDRA) • H&V MAA & Var Regulatory submission (SIAMED, eAF, CESSP, CTS) • NCAs **Via Art 57:** • Pharmacovigilance: (EV H, PSUR rep.) • Referrals • Fees	• Pharmacovigilance (signal detection, analytics) – legal driver • Product (composition) registration (H&V) – PMS TOM • Consumption (Veterinary business case) – legal driver • MRL (veterinary use case) – legal driver • Cross Border ePrescription – EC/public health	• Evaluation of Risk of Shortages - EC/public health • Variations (manufacturer details change) – ROG • CEP Management - ROG • Toxicology use case (under investigation)	• GMDP Inspection Support	• ASMF Management • Batch Recall Support • Supply Chain Traceability

Content plan for substance management

For SPOR TF input

Must (2018)	Must (2019)	Could / Wont (PoC)
• **Concepts (MRL, IMPs, legacy)?** • Substances (chemicals) – actives • SSG1 – multi-constituents (structurally diverse) - actives • SSG3 (grade) * - actives ** Not necessarily structured data, if a unique name is provided*	• Substances – adjuvants • Substances – excipients • SSG1 – multi-constituent – excipient • SSG1 – physical form* – actives • SSG2 - high level process* – actives	• SSG1 – multi-constituent – excipients • SSG1 – physical form - excipients • SSG2 – extended level process* – actives (certain classes only) • SSG2 - excipients • SSG3 – excipients • **SSG2 – manufacturer ID > will be traced at product level** • **SSG4** • **Non Pharmaceutical Substances eg Food, Cosmetics, etc**

Baseline data will be available in SMS; optimized data will follow from EU-SRS for Structurally Diverse substances (leading to increased data quality)

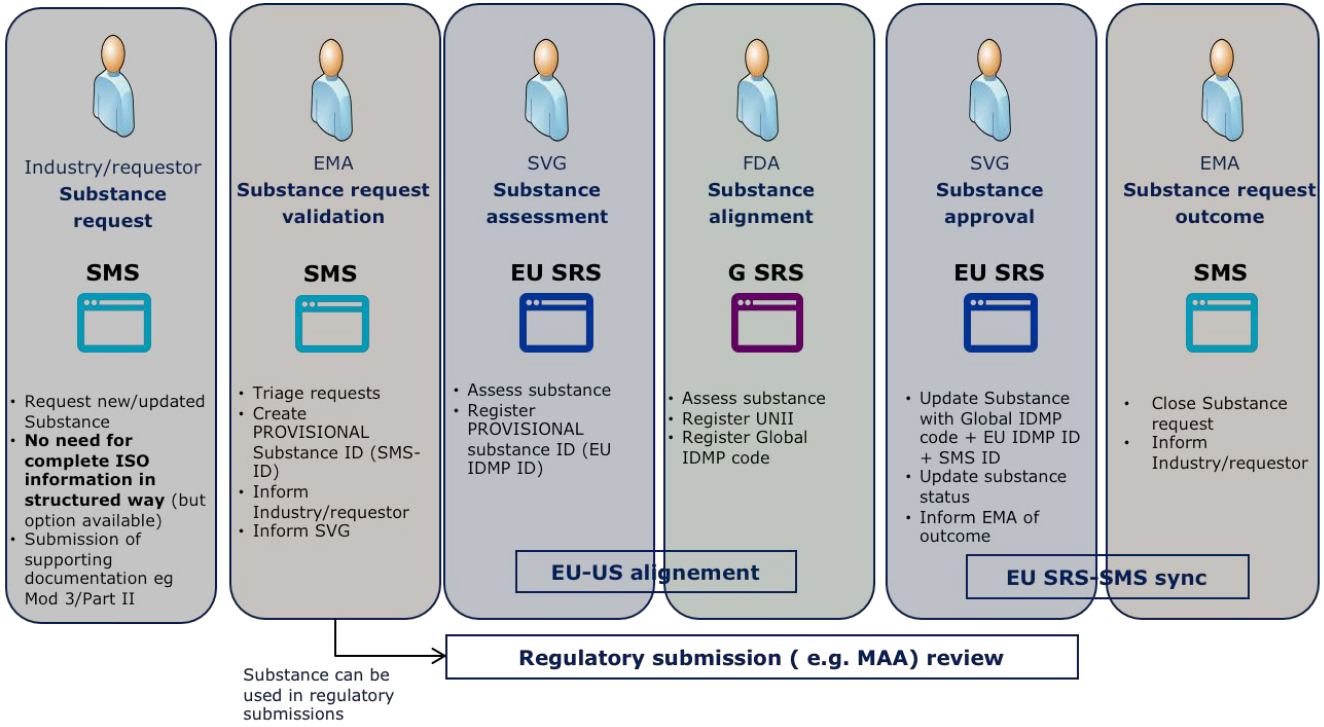
SMS, EU-SRS and G-SRS

	SMS	EU-SRS	G-SRS
Purpose	• Selection in EU regulatory processes and enables to distinguish two or more similar substances	• Scientific identification of substances	• Scientific identification of substances
Nature	• PUBLIC information. • Need for CONFIDENTIAL TBD	• PUBLIC and CONFIDENTIAL information subject to controlled access	• PUBLIC and CONFIDENTIAL information subject to controlled access
Depth	• "Simplified" substance data – reduced number of ISO IDMP fields	• Comprehensive ISO IDMP substance data – extended number of fields	• Comprehensive ISO IDMP substance data – extended number of fields
Width	• All records required for EU regulatory business cases – see content needs - TBD	• All records required for EU regulatory cases – see content needs - TBD • Potentially more records than SMS? - see content needs - TBD	• Overlap with some records also required for EU regulatory use cases • More records than EU SRS (Food, Tobacco, etc) required for US regulatory use cases

Substance Management Target Operating Model

- SPOR is the one-stop-shop for data required to support regulatory submissions so requests on Substances will be in SMS and not directly to EU SRS
- Substance registration should support the full product lifecycle (OD, SA, Pediaetrics, CT, MAA, Var)
- Substance registration should collect “available/mandated” information to support identification of the substance, this could be documents such as Investigator Brochure, CT Protocol or extracts of Module 3 (but not full Module 3!)
- Industry will be requested to provide substance codes/names in previous submissions

Substance Management TOM



SMS TOM ensures:

- Regulatory processes can start as soon as substance is Provisionally registered
- EU-US alignment
- Data is approved by SVG before conclusion of regulatory processes i.e **only trusted data is used in regulatory processes**

Substance Validation Group

- To execute substance assessment, to be recorded in EU-SRS (for specific classes)
- Intention to act as (virtual) European organization to maintain substances at this level of detail, for re-use at NCA's
- Next steps:
  - To discuss NCA and EMA tasks, SVG role, SVG organisation
    - Cost of SVG vs cost spread out across NCAs
    - Effort to maintain substances
    - Number/effort expected by May/Jun
    - Consider a model with lines of support e.g. first line EMA and second line SVG
  - Nominations/set up will be done if/once BC approved

Conclusions

Substance management will be provided through a combination of SMS and EU-SRS, where EU-SRS acts as extension for structurally diverse substances

Plans have been aligned to allow progress within SPOR and increased data quality upon full release

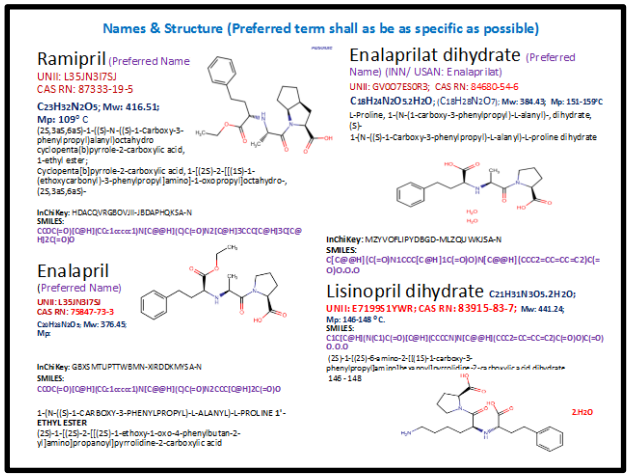
Target Operating Model is designed, discussions on Substance Validation Group are ongoing (experts will be needed, but estimates are to be completed first)

Concerns for veterinary substances have been noted and are under discussion

We work towards a clear and valuable business case for the HMA in June!

Extra slides

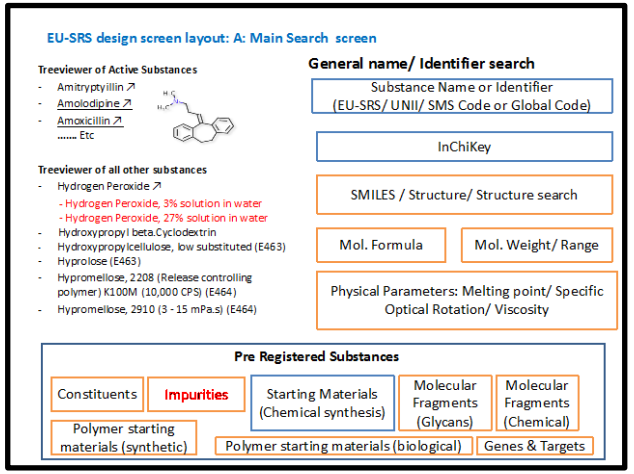
Supporting materials on how to approach structurally diverse substances are available



Creation of functional cases by Herman Diederik to:

- Clarify details required to allow identification
- Illustrate value of substance identification in specific cases
- Show possible lay-out to collect / show / review the substance information (mock-ups)

These details describe the way of processing such substance classes and determine the design for EU-SRS



EU-SRS Steering Committee

Chair: Alexis Nolte (EMA)

Senior EMA IT representative: Stefan Blixen-Finecke (EMA)

Senior MEB IT representative: Joris Kampmeijer (MEB)

Senior Scientific representative: Herman Diederik (MEB)

Representatives from participating National Competent Authorities (one per NCA): to be determined

Representatives from US FDA as a observer: to be determined

EU G-SRS project manager: Frits Stulp (MEB)

Specific Substance situation for Veterinary products

Concerns have been expressed:

- Insufficient vet involvement
- To ensure proportionate approach
  - data gathering is risk based and driven by use cases
  - do not increase regulatory hurdles
- Excessive details:
  - May confuse users/prescribers
  - May reduce space in labels
- EU-US alignment
  - Status? Does it cover VMP?
  - Industry consent to share data?
- Assumptions
  - Data from Part II just before MAA submission (no CT)
  - Changes to naming conventions do not imply changes to SmPC, leaflets etc

These concerns will be addressed in the coming period