MedDRA was developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Committee, which is composed of the six ICH parties (EU, EFPIA, MHLW, JPMA, FDA, PhRMA), the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, Health Canada, and the WHO (as Observer).
**Disclaimer and Copyright Notice**

- This presentation is protected by copyright and may, with the exception of the MedDRA and ICH logos, be used, reproduced, incorporated into other works, adapted, modified, translated or distributed under a public license provided that ICH's copyright in the presentation is acknowledged at all times. In case of any adaption, modification or translation of the presentation, reasonable steps must be taken to clearly label, demarcate or otherwise identify that changes were made to or based on the original presentation. Any impression that the adaption, modification or translation of the original presentation is endorsed or sponsored by the ICH must be avoided.

- The presentation is provided "as is" without warranty of any kind. In no event shall the ICH or the authors of the original presentation be liable for any claim, damages or other liability arising from the use of the presentation.

- The above-mentioned permissions do not apply to content supplied by third parties. Therefore, for documents where the copyright vests in a third party, permission for reproduction must be obtained from this copyright holder.

**Course Overview**

- Review the MedDRA Data Retrieval and Presentation: Points to Consider document
- Review use of MedDRA for developing queries
- Discuss features of Standardised MedDRA Queries (SMQs) including:
  - Background
  - Data characteristics
  - Using SMQs
  - Browser demonstration
- Discuss the creation and use of customized searches
- Conclude with a question and answer session
- Appendix - MedDRA’s scope, structure, and characteristics/Browsers
MedDRA Data Retrieval and Presentation: Points to Consider

- Provides data retrieval and presentation options for industry or regulatory purposes
- Most effective when used in conjunction with MedDRA Term Selection: PTC document
- Recommended to be used as basis for individual organization’s own data retrieval conventions
MedDRA Data Retrieval and Presentation: PTC (cont)

- Developed by a working group of the ICH Management Committee
- Updated twice yearly with each MedDRA release
- Available on MedDRA and JMO websites
  - English and Japanese
  - Word (“clean” and “redlined”), PDF, HTML formats
  - “Redlined” document identifies changes made from previous to current release of document

ICH M1 Points to Consider Working Group (PtC WG)

- Regulators and industry from EU, US, and Japan
  - Health Canada
  - MSSO
  - JMO
  - WHO (Observer)

New members 2017/2018
- MFDS, Republic of Korea
- ANVISA, Brazil
- CFDA, China

Meeting 13-15 November 2017, Geneva, Switzerland
Data Retrieval PTC

Points Addressed

• General Principles
  – Quality of Source Data
  – Documentation of Data Retrieval and Presentation Practices
  – Do Not Alter MedDRA
  – Organisation-Specific Data Characteristics
  – Characteristics of MedDRA that Impact Data Retrieval and Analysis
  – MedDRA Versioning

• General Queries and Retrieval
• Standardised MedDRA Queries
• Customised Searches

MedDRA Versioning

• MedDRA is updated twice a year
  – 1 March X.0 release (all levels)
  – 1 September X.1 release (LLT and PT levels only)
• Version used in data retrieval and presentation should be documented
• Resources:
  – “What’s New” document
  – Version report
  – MedDRA Version Analysis Tool (MVAT)
• Terms used for queries should be in same version as data being queried
MedDRA Version Analysis Tool (MVAT)

- Web-based (https://tools.meddra.org/mvat)
- Free to all users
- Features
  - Version Report Generator (produces exportable report comparing any two versions)
  - Data Impact Report (identifies changes to a specific set of MedDRA terms or codes uploaded to MVAT)
  - Search Term Change (identifies changes to a single MedDRA term or code)
- User interface and report output available in all MedDRA languages

Developing Queries Using MedDRA
What is a Query?

Clinical Trial Database
Safety Database

Query Strategy Tips

• Define the condition
• Develop inclusion/exclusion criteria
• Good browser is key component
• Search “non multi-axial” and “other/support” SOCs
• Search a term’s “neighbors”, including secondary locations
• Use grouping terms where applicable
• Avoid using LLTs (Exception: species information at LLT level in SOC *Infections and infestations*)
• Store for future use
• Review for impact of new MedDRA versions
Complete the Circle
(Connect the DOTSSS!)

- **Diagnosis/disease terms**
- **Operations**
  (Surgical and medical procedures)
- **Tests**
  (Investigations)
- **Signs & symptoms**
- **Support SOCs (Other...)**
- **Social circumstances**

---

Standardised MedDRA Queries
(SMQs)
Standardised MedDRA Queries (SMQs)

- Collaboration between CIOMS (Council for International Organizations of Medical Sciences) and ICH (MSSO)
- Groupings of terms from one or more MedDRA SOCs related to medical condition or area of interest
- Terms relate to signs/symptoms, diagnoses, syndromes, physical findings, laboratory and other test data, etc.
- Intended to aid in case identification

SMQ Benefits and Limitations

- Benefits
  - Application across multiple therapeutic areas
  - Validated reusable search logic
  - Standardized communication of safety information
  - Consistent data retrieval
  - Maintenance by MSSO/JMO
- Limitations
  - Do not cover all medical topics or safety issues
  - Will evolve and undergo further refinement even though they have been tested during development
SMQs in Production - Examples

- As of Version 21.0, a total of 103 level 1 SMQs in production
  - Agranulocytosis
  - Anaphylactic reaction
  - Cerebrovascular disorders
  - Convulsions
  - Depression and suicide/self-injury
  - Hepatic disorders
  - Hypersensitivity
  - Ischaemic heart disease
  - Lack of efficacy/effect
  - Medication errors
  - Osteonecrosis
  - Peripheral neuropathy
  - Pregnancy and neonatal topics
  - Pseudomembranous colitis
  - Rhabdomyolysis/myopathy
  - Severe cutaneous adverse reactions
  - Systemic lupus erythematosus

SMQ Development Summary

- Pre-release testing by CIOMS Working Group members
  - Typically, at least one company and one regulator database
  - Cases retrieved reviewed for relevance
  - Fine-tuning of SMQ may require several iterations
  - Reviewed and approved by CIOMS WG
- Production Phase: continue to be fine-tuned through the MSSO maintenance process
SMQ Data Characteristics

- MedDRA term inclusion
- SMQ naming convention
- Broad/narrow
- Algorithms
- Hierarchy
- SMQ status/term status within an SMQ
- Term versioning in an SMQ
- Text data included in SMQ

MedDRA Term Inclusion

- SMQs are constructed at MedDRA PT level
- LLTs that are subordinate to an included PT are also included
SMQ Naming Convention

• SMQ titles have “(SMQ)” appended to the end to ensure there is no name conflict with existing MedDRA terms
• E.g., “Agranulocytosis (SMQ)”
• Each SMQ has a unique 8-digit code starting with “2”

Narrow and Broad Searches

• “Narrow” scope – specificity (cases highly likely to be condition of interest)
• “Broad” scope – sensitivity (all possible cases)
• “Broad search” = All broad + all narrow terms
Text Data Included in SMQ

- Description field
  - Additional information about each SMQ (from SMQ Introductory Guide)
- Source field
  - Medical references used in development/maintenance
- Development note
  - Pertinent notes for proper use
  - Description of algorithm (if applicable), and definition of categories

Narrow vs. Broad Example

SMQ Lactic acidosis

**Definition**

Lactic acidosis is a form of high anion gap metabolic acidosis. Intracellular contractility may be depressed, but contractility can be normal because of catecholamine release. Peripheral arterial vasodilatation and central vasoconstriction can be present. Central nervous system function is depressed, with headache, lethargy, stupor, and, in some cases, even coma. Glucose intolerance may occur. Characterized by an increase in plasma L-lactate. Acidosis is seldom significant unless blood lactate exceeds 5 mmol/L. Clinical presentation in type B lactic acidosis: Symptoms: Hyperventilation or dyspnea, stupor or coma, vomiting, drowsiness, and abdominal pain. Onset of symptoms and signs is usually rapid accompanied by deterioration in the level of consciousness.

**Source**


**Note**

Testing in two regulatory databases confirmed that the term “acidosis” identified cases, but this may be a phenomenon of the database characteristics (coding of variables to terms of an older terminology or other coding conventions).

<table>
<thead>
<tr>
<th>Narrow Terms</th>
<th>Broad Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood lactic acid increased</td>
<td>Acid base balance abnormal</td>
</tr>
<tr>
<td>Hyperlactacidemia</td>
<td>Acidsis</td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>Anion gap abnormal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Narrow Terms</th>
<th>Broad Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pH abnormal</td>
<td>Blood acidosis</td>
</tr>
<tr>
<td>Blood bicarbonate abnormal</td>
<td>Blood pH decreased</td>
</tr>
<tr>
<td>Blood bicarbonate decreased</td>
<td>Coma acidotic</td>
</tr>
<tr>
<td>Blood gases abnormal</td>
<td>Kussmaul respiration</td>
</tr>
<tr>
<td>Blood lactic acid abnormal</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Blood PCO&lt;sub&gt;2&lt;/sub&gt; abnormal</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Blood PCO&lt;sub&gt;2&lt;/sub&gt; decreased</td>
<td>PCO&lt;sub&gt;2&lt;/sub&gt; abnormal</td>
</tr>
<tr>
<td>Urine lactic acid increased</td>
<td>PCO&lt;sub&gt;2&lt;/sub&gt; increased</td>
</tr>
</tbody>
</table>
Algorithmic SMQs

• Some SMQs are designed to utilize algorithms
• Better case identification among broad search terms may result if cases are selected by a defined combination of selected terms

Algorithmic SMQ Example

• Anaphylactic reaction (SMQ):
  – A case with any of the following PTs:
    • Anaphylactic reaction
    • Anaphylactic shock
    • Anaphylactic transfusion reaction
    • Anaphylactoid reaction
    • Anaphylactoid shock
    • Circulatory collapse
    • Dialysis membrane reaction
    • Kounis syndrome
    • Procedural shock
    • Shock
    • Shock symptom
    • Type I hypersensitivity

  (Narrow search terms = Category A)
Algorithmic SMQ Example (cont)

<table>
<thead>
<tr>
<th>Category B – Upper airway/Respiratory</th>
<th>Category C – Angioedema/ Urticaria, etc.</th>
<th>Category D – Cardiovascular/ Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute respiratory failure</td>
<td>Allergic oedema</td>
<td>Blood pressure decreased</td>
</tr>
<tr>
<td>Asthma</td>
<td>Angioedema</td>
<td>Blood pressure diastolic decreased</td>
</tr>
<tr>
<td>Bronchial oedema</td>
<td>Erythema</td>
<td>Blood pressure systolic decreased</td>
</tr>
</tbody>
</table>

- Case = A (Narrow terms)
- Or Term from Category B **and** term from Category C
- Or Term from either Category B or Category C **plus** Term from Category D

Hierarchical SMQs

- Some SMQs may develop as set of queries related to one another in a hierarchical relationship
- Not related to MedDRA standard hierarchy
- One or more subordinate SMQs combined to create a superordinate, more inclusive SMQ
Hierarchical SMQ Example

Haematopoietic cytopenias

- Haematopoietic cytopenias affecting more than one type of blood cell
- Haematopoietic erythropenia
- Haematopoietic leukopenia
- Haematopoietic thrombocytopenia

SMQ Status/Term Status

- Each SMQ has a status (Active/Inactive)
- Similar in concept to MedDRA currency
- Terms assigned to an SMQ also have a status flag
  - Once a term is added to an SMQ, it will always be included in the SMQ but the status may be inactive
• It is recommended that organizations use the SMQs with data coded with the same version of MedDRA
  – Match the MedDRA version of the SMQ with the MedDRA version of the coded data
  – Mismatches of SMQ and MedDRA coded data could produce unexpected results

• Example of PT added to SMQs in MedDRA Version 19.0:
  – PT *End stage renal disease* in SMQ *Chronic kidney disease*

• Using version 18.1 SMQs which do not contain these PTs would fail to identify cases coded to these terms in a database using MedDRA Version 19.0
How to “Run” SMQs

- IT perspective of SMQs = stored queries
- Code at LLT level; most organizations store coded data as LLTs
- SMQ ASCII files include PTs and LLTs
- Load SMQs into a query tool; run query against coded MedDRA terms in safety or clinical trial database for “Hits”
- Use SMQ options, if applicable
  - Narrow/broad search
  - Algorithms
  - Hierarchy
How to “Run” SMQs (cont)

Using an SMQ (Acute renal failure)
SMQ Applications

• Clinical trials
  – Where safety profile is not fully established, use multiple SMQs on routine basis as screening tool
  – Selected SMQs to evaluate previously identified issue (pre-clinical data or class effect)

• Post-marketing
  – Selected SMQs to retrieve cases for suspected or known safety issue
  – Signal detection (multiple SMQs employed)
  – Single case alerts
  – Periodic reporting (aggregate cases for safety and other issues, e.g., lack of efficacy)

Use of SMQs at FDA

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
Use of SMQs at FDA (cont)

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA

<table>
<thead>
<tr>
<th>Study</th>
<th>Use of SMQs at FDA (cont)</th>
<th>Use of SMQs at FDA (cont)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
<tr>
<td>Study</td>
<td>Use of SMQs at FDA (cont)</td>
<td>Use of SMQs at FDA (cont)</td>
</tr>
</tbody>
</table>
Use of SMQs at FDA – Reviewing Prescribing Information

- Proposed Prescribing Information:
- Warnings & Precautions:
  - Dizziness/Somnolence
  - Withdrawal of Antiepileptic Drugs
  - Suicidal Behavior and Ideation (class labeling)

<table>
<thead>
<tr>
<th>SMQ (Narrow Search)</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Hostility/aggression</td>
<td>4.4</td>
</tr>
<tr>
<td>(2) Vestibular disorders</td>
<td>4.258</td>
</tr>
<tr>
<td>(1) Hearing and vestibular disorders</td>
<td>4.088</td>
</tr>
<tr>
<td>(1) Hyponatraemia/SIADH</td>
<td>3.832</td>
</tr>
<tr>
<td>(2) Hearing impairment</td>
<td>3.832</td>
</tr>
<tr>
<td>(1) Dyslipidaemia *</td>
<td>2.555</td>
</tr>
<tr>
<td>(1) Biliary disorders</td>
<td>2.135</td>
</tr>
<tr>
<td>(2) Functional, inflammatory and gallstone related biliary disorders</td>
<td>2.135</td>
</tr>
</tbody>
</table>

Final Prescribing Information
- Boxed Warning:
  - Serious Psychiatric and Behavioral Reactions
- Warnings & Precautions:
  - Falls
  - Dizziness & somnolence
  - Withdrawal of Antiepileptic Drugs
  - Suicidal Behavior and Ideation (class labeling)

Acknowledgement: Dr. Christopher Breder, Office of New Drugs, CDER, FDA

EMA: Signal Detection Analysis

- ICSR coding at LLT level, analysis at PT level (medical concept):
  ✓ It may be important to conduct analysis at higher level of hierarchy: SOC, HLG, HLT
    • When doing so, impact of axial and non-multi-axial SOCs needs to be taken into account: relevant PTs in more than 1 SOC
  ✓ It may be important to conduct analysis at SMQ level to maximise likelihood that all terms related to a specific medical condition of interest are identified

- Challenge: strike the correct balance
  ✓ Too narrowly focused search (specificity): exclude events of potential relevance
  ✓ Too broad search (sensitivity): difficult to identify a trend or signal that may require further analysis (incl. case review)

Acknowledgement: Dr. Aniello Santoro, EMA
Signal of Angioedema - PT vs. SMQ

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>SOCs</th>
<th>IILTs</th>
<th>HILTs</th>
<th>SMQ Broad</th>
<th>SMQ Narrow</th>
<th>PTs</th>
<th>LTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug A Skin</td>
<td>Angioedema And Urticae</td>
<td>Angioedema</td>
<td>Angioedema</td>
<td>Angioedema</td>
<td>Angioedema</td>
<td>Angioedema</td>
<td>Angioedema</td>
</tr>
</tbody>
</table>

**SMQ Angioedema (Narrow search)**

<table>
<thead>
<tr>
<th>PT</th>
<th>N. ICSR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angioedema</td>
<td>9</td>
</tr>
<tr>
<td>Eye swelling</td>
<td>1</td>
</tr>
<tr>
<td>Face oedema</td>
<td>1</td>
</tr>
<tr>
<td>Laryngeal oedema</td>
<td>1</td>
</tr>
<tr>
<td>Oedema mouth</td>
<td>1</td>
</tr>
<tr>
<td>Pharyngeal oedema</td>
<td>4</td>
</tr>
<tr>
<td>Swelling face</td>
<td>10</td>
</tr>
<tr>
<td>Swollen tongue</td>
<td>6</td>
</tr>
<tr>
<td>Urticaria</td>
<td>4</td>
</tr>
</tbody>
</table>

Acknowledgement: Dr. Aniello Santoro, EMA

Customized Searches
Customized Searches – Modified SMQs

- Do not modify SMQ unless there is a compelling reason – makes it non-standard
- “Modified MedDRA query based on an SMQ”
  - To be used to refer to an SMQ that has been modified
  - All modifications must be documented
  - Version updates and maintenance are responsibility of organization that created it

Modified SMQs

- Adding PTs
- Excluding PTs
- Changing scope of SMQ term (narrow to broad or vice versa)
- SMQ *Lack of efficacy/effect* often modified based on particular product
Customized Searches – 
*Ad Hoc Queries*

- Need medical knowledge
- Need knowledge of structure and characteristics of MedDRA and of your data
- Refer to the *MedDRA Data Retrieval and Presentation: Points to Consider* document for query construction tips
- Save query for future use; maintenance needed for MedDRA version changes
- Consider submitting *ad hoc* query to MSSO via change request for possible development as an SMQ

---

**Summary**

In this course, we:
- Reviewed the MedDRA Data Retrieval and Presentation: Points to Consider document
- Reviewed use of MedDRA for developing queries
- Discussed Standardised MedDRA Queries (SMQs)
- Discussed the creation and use of customized searches
MSSO Contacts

- Website
  - www.meddra.org
- Email
  - mssohelp@meddra.org
- Frequently Asked Questions
  - www.meddra.org/faq

Question and Answer Session
Appendix – MedDRA’s Scope, Structure, and Characteristics/Browsers

MedDRA Definition

MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.
Scope of MedDRA

OUT

IN

Medical conditions
Indications
Investigations (tests, results)
Medical and surgical procedures
Medical, social, family history
Medication errors
Product quality issues
Device-related issues
Product use issues
Pharmacogenetic terms
Toxicologic issues
Standardized queries

Patient demographic terms
Clinical trial study design terms
Frequency qualifiers
Numerical values for results
Severity descriptors
Not an equipment, device, diagnostic product dictionary

MedDRA Structure

System Organ Class (SOC) (27)
High Level Group Term (HLGT) (337)
High Level Term (HLT) (1,737)
Preferred Term (PT) (23,088)
Lowest Level Term (LLT) (78,808)
A Multi-Axial Terminology

• Multi-axial = the representation of a medical concept in multiple SOCs
  – Allows grouping by different classifications
  – Allows retrieval and presentation via different data sets

• All PTs assigned a primary SOC
  – Determines which SOC will represent a PT during cumulative data outputs
  – Prevents “double counting”
  – Supports standardized data presentation
  – Pre-defined allocations should not be changed by users

SOC = Respiratory, thoracic and mediastinal disorders (Secondary SOC)
  HLT = Viral upper respiratory tract infections
  HLGT = Respiratory tract infections

SOC = Infections and infestations (Primary SOC)
  HLT = Influenza viral infections
  HLGT = Viral infectious disorders

PT = Influenza
MSSO’s MedDRA Browsers

• MedDRA Desktop Browser (MDB)
  – Download MDB and release files from MedDRA website

• MedDRA Web-Based Browser (WBB)
  – https://tools.meddra.org/wbb/

• Features
  – Both require MedDRA ID and password
  – View/search MedDRA and SMQs
  – Support for all MedDRA languages
  – Language specific interface
  – Ability to export search results and Research Bin to local file system