Standardised MedDRA Queries (SMQs)
MedDRA was developed under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Board, which is composed of the six ICH parties (EU, EFPIA, MHLW, J PMA, FDA, PhRMA), the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, the Health Canada, and the WHO (as Observer).
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Background of SMQ Development
CIOMS and SMQs

- CIOMS (Council for International Organizations of Medical Sciences): An international, non-governmental, non-profit organization established jointly by World Health Organization (WHO) and United Nations Educational, Scientific and Cultural Organization (UNESCO)
- CIOMS and ICH have established terms of reference for cooperative development of SMQs
- Maintenance of SMQs is the joint responsibility of the user community (through MSSO Change Request process) and the MSSO
SMQ Definition
Definition of SMQ

- Result of cooperative effort between CI OMS and ICH (MSSO)
- Groupings of terms from one or more MedDRA System Organ Classes (SOCs) related to defined medical condition or area of interest
- Included terms may relate to signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data, etc., related to medical condition or area of interest
- Intended to aid in case identification
SMQs Development Status
SMQs in Production - Examples

- As of Version 15.1, a total of 87 in production

- Agranulocytosis
- Anaphylactic reaction
- Cerebrovascular disorders
- Convulsions
- Depression and suicide/self-injury
- Hepatic disorders
- Ischaemic heart disease
- Lack of efficacy/effect
- Peripheral neuropathy
- Pregnancy and neonatal topics
- Pseudomembranous colitis
- Rhabdomyolysis/myopathy
- Severe cutaneous adverse reactions
- Systemic lupus erythematosus
SMQ Production and Development List

- Refer to MSSO Web site for current status of SMQs in production and development

http://www.meddramsso.com/subscriber_smq.asp
SMQ Data Characteristics
MedDRA Term Inclusion

- SMQs are constructed at MedDRA PT level
- LLTs that are subordinate to an included PT are also included
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
Narrow vs. Broad Example

*Lactic acidosis (SMQ)*

**Definition**
Lactic acidosis is a form of high anion gap metabolic acidosis. Intrinsic cardiac contractility may be depressed, but inotropic function 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. Acidoses 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 list is adequate; in one regulatory database, the term “acidosis” identified cases, but this may be a phenomenon of the database characteristics (coding of verbatim to terms of an older terminology or other coding conventions).
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
    - First use syndrome
    - Kounis syndrome
    - Shock
    - 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
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
SMQ Testing and Production Maintenance
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 Production Maintenance

- Essentially a change request process
- Final disposition is not time limited
- MSSO reviews all new terms in new release for inclusion in existing SMQs
- MSSO reviews existing terms for impact of demotions, moves, etc.
- All SMQ change requests reviewed by CI OMS WG after 18-24 months in production
SMQ Production Maintenance (cont)

- SMQ change requests undergo the same process as other MedDRA change requests
  - SMQ change requests are considered simple change requests
  - SMQ change requests are part of the 100 allotted change requests for each core subscriber
SMQ Applications
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)

• Postmarketing
  - 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)
Summary

- Background of SMQ development
- SMQ definition
- SMQ development status
- SMQ data characteristics
- SMQ testing and maintenance
- SMQ applications
MSSO Contacts

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