



44TH
Annual Meeting



Boston 2008

Practical Applications of SMQs in an Industry Pharmacovigilance Group

Bobbie Michaelis

Senior Director, Global
Pharmacovigilance Operations
Wyeth Research

Wyeth
Research

Learning Objectives

- Understand the design concepts of SMQs
- Know the Volume 9A recommendations regarding SMQs
- Experience the Wyeth SMQ journey
 - Learn how Wyeth currently uses SMQs
 - Learn Wyeth's goals for SMQs in the future



What Are Standardised MedDRA Queries (SMQs)?

- Groupings of MedDRA terms
 - At the Preferred Term (PT) level
- Relate to a defined medical condition or area of interest
- Intended to aid in the identification and retrieval of potentially relevant individual case safety reports



SMQs in Production - Examples

- As of Version 11.0, a total of 58 in production (Many other SMQs in development)
- Adverse pregnancy outcome/reproductive toxicity (incl neonatal disorders)
- Agranulocytosis
- Anaphylactic reaction
- Cerebrovascular disorders
- Convulsions
- Depression and suicide/self-injury
- Hepatic disorders
- Ischaemic heart disease
- Lack of efficacy/effect
- Peripheral neuropathy
- Pseudomembranous colitis
- Rhabdomyolysis/myopathy
- Severe cutaneous adverse reactions
- Systemic lupus erythematosus



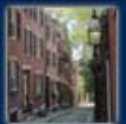
SMQ Development Summary

- 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 Design Concepts

- Three main designs
 - Narrow and Broad
 - Algorithm
 - Hierarchy



Narrow and Broad Searches

- Narrow and broad
 - “Narrow” scope - specificity. Identify cases that are highly likely to represent the condition of interest
 - “Broad” scope - sensitivity. Identify all possible cases
 - All narrow terms should be included when performing a broad search

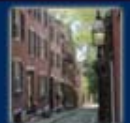


Narrow and Broad SMQ Example

- Lactic acidosis (SMQ)

Narrow Terms
Blood lactic acid increased
Hyperlactacidaemia
Lactic acidosis

Broad Terms
Acid base balance abnormal
Acidosis
Anion gap abnormal
Anion gap increased
Blood bicarbonate abnormal
Blood bicarbonate decreased
Blood gases abnormal
Blood lactic acid abnormal
Blood pH abnormal
Blood pH decreased
Coma acidotic
Kussmaul respiration
Metabolic acidosis
PCO2 abnormal
PCO2 decreased
Urine lactic acid increased



Algorithm Searches

- Some SMQs are designed to utilize algorithms
- Cases are identified by a defined combination of selected terms
 - Provides better case identification among broad search terms
 - Reduces “noise”



Algorithm Example

- *Anaphylactic reaction (SMQ):*
 - A case with any of the following PTs:
 - *Anaphylactic reaction*
 - *Anaphylactic shock*
 - *Anaphylactoid reaction*
 - *Anaphylactoid shock*
 - *Circulatory collapse*
 - *First use syndrome*
 - *Shock*
 - *Type I hypersensitivity*

(Narrow search terms = Category A)



Algorithm Example (cont.)

Category B – Upper airway/Respiratory	Category C – Angioedema/ Urticaria, etc.	Category D – Cardiovascular/Hypotension
<i>Acute respiratory failure</i>	<i>Allergic oedema</i>	<i>Blood pressure decreased</i>
<i>Asthma</i>	<i>Angioedema</i>	<i>Cardiac arrest</i>
<i>Dyspnoea</i>	<i>Erythema</i>	<i>Hypotension</i>

Case of Interest identified, if there is a PT from:

A (e.g. Anaphylactic shock) **or**

B + C (e.g. Asthma and Erythema) **or**

D and (B or C) (e.g. Hypotension and Angioedema or Hypotension and Dyspnoea)

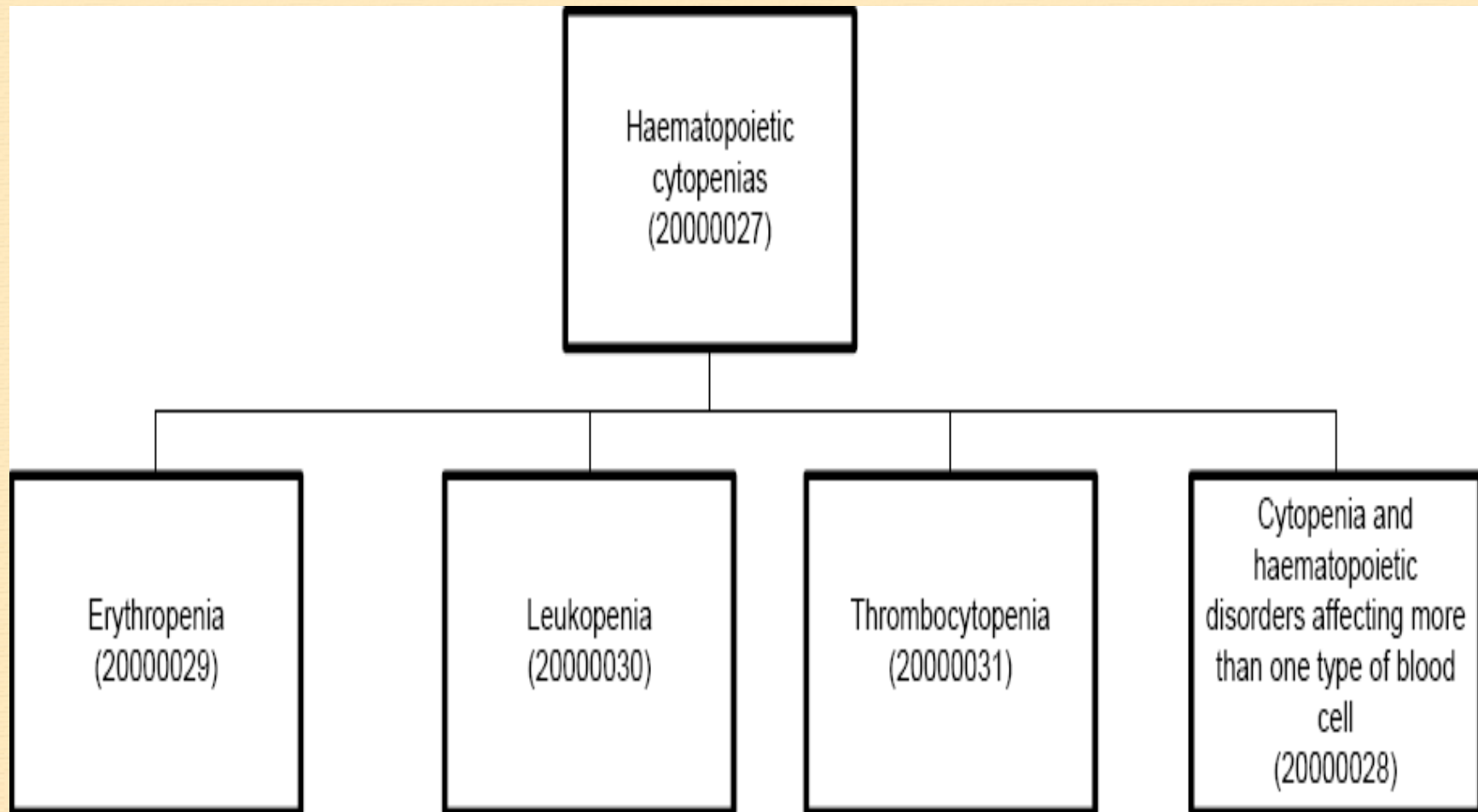


Hierarchy Searches

- Hierarchy SMQs are a set of queries that have a hierarchical relationship to each other
- One or more subordinate SMQs combined to create a superordinate, more inclusive SMQ
 - Not related to MedDRA standard hierarchy



Hierarchy Example



Volume 9A Speaks Out on SMQs

“SMQs may be used for signal detection and the use of SMQs is recommended in order to retrieve and review cases of interest where signals are identified from adverse reaction databases”



Take the Wyeth SMQ Journey



Good SMQ Practices

- Always read the *Introductory Guide for SMQs* to fully understand the scope of the SMQ
- Do not modify term content or structure of an SMQ unless there is a compelling reason
 - Altering makes the SMQ non-standard
 - If altering, document



Good SMQ Practices (cont.)

- Decide initially if using the broad or narrow search, a specific sub-search, or an algorithm and document choice
- Define adjudication rules for cases identified by an SMQ
 - Noise, especially with broad searches
- Evaluate search results against the question originally posed
 - Search output alone may not be sufficient for data assessment



MedDRA/SMQ Training Tools at Wyeth

- Introduction to MedDRA training
- MedDRA Browser training
- MedDRA Coding Conventions
- Coding workshops and tutorials
- MedDRA Data Retrieval and Presentation: Points to Consider
- Strategic Approach to Safety Queries training
- Signal Detection training
- SOPs
- One-on-one mentoring from Subject Matter Experts



Software SMQ Tools at Wyeth

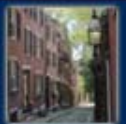
- QuEST (Query Evaluation and Surveillance Tool)
 - Pharmacovigilance (PV) staff performs ad hoc queries of safety database
 - PV staff completes a robust training program prior using tool
 - Generates reports, graphs, charts; exports to Excel
 - Validated program/QM procedures
- BRIO
 - Same as above, but only specially trained Information Management staff can perform searches



Other SMQ Tools at Wyeth

- GSSEL MedDRA Committee
- GSSEL MedDRA web page

GSSEL = Global Safety Surveillance & Epidemiology and Labeling




GSSEL MedDRA web page


MedDRA

MedDRA Training

For MedDRA training click on "[Training & Education](#)" in the left navigation bar or login to EDMS and click the training folder.


MedDRA Browser


 [MedDRA Browser User Manual](#)
Version 2.0

 [MedDRA Desktop Browser Exercises \(using MedDRA version 10.0\)](#)
Try the exercises after completing MedDRA Desktop Browser training (Click on "Training & Education" on left navigation pane)

 [MedDRA Desktop Browser Exercises with Answer Key \(using MedDRA version 10.0\)](#)
Use this to check answers after completing the MedDRA Desktop Browser Exercises, above

MedDRA MSSO and ICH Documents

 [MedDRA MSSO Web Page](#)
Maintenance and Support Services Organization (MSSO) for MedDRA

 [MedDRA Points to Consider: Current Documents](#)
MedDRA Points to Consider: Current Documents

Contact the MedDRA Committee


[GSSE MedDRA Committee@wyeth.com](mailto:GSSE_MedDRA_Committee@wyeth.com)

[GSSEL Form 3012](#)
MedDRA Change Request Form

MedDRA Dictionary

 [Coding Conventions](#)
GSSEL RG 9203


 [Impact Of On-Going MedDRA Updates](#)
PowerPoint presentation

 [Introductory Guide MedDRA Version 10.1](#)
September 2007

 [Introductory Guide MedDRA Version 11.0](#)
March 2008

 [What's New MedDRA Version 11.0](#)
March 2008

 [MedDRA Reports](#)
Click here for all updated MedDRA reports.

 [MedDRA Version Availability Dates](#)
Updated 05-Mar-2008

 [Overview of the COSTART to MedDRA Conversion](#)
Coding Symbols for Thesaurus Adverse Reaction Terms (COSTART) to Medical Dictionary for Regulatory Activities (MedDRA) Conversion

MedDRA SMQs

 [FAQ for MedDRA SMQs](#)

 [Gender Specific \(Male, Female\) Adverse Event Terms MedDRA Version 11.0](#)

 [Introductory Guide for Standardized MedDRA Queries- MedDRA Version 11.0](#)
Guide to SMQs

 [Pediatric Adverse Event Terms MedDRA Version 11.0](#)

 [Standard MedDRA Query Spreadsheet Version 11.0](#)
SMQ hierarchy



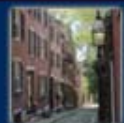
How Wyeth's PV Group Uses SMQs

- Surveyed Pharmacovigilance (PV) Group regarding:
 - Understanding of SMQs
 - Obstacles to using SMQs
 - Use of SMQs in PV activities
 - How SMQs are applied to searches
- Surveyed PV physicians and scientists
 - 74% responded (20/27)



Results: Understanding SMQs

Level of understanding	None (%)	A little familiarity (%)	Basic (%)	Intermediate (%)	Expert (%)
I understand what SMQs are	0	5	45	40	10
I understand the structure of SMQs	0	10	55	25	10
I understand the purpose of SMQs	0	0	40	50	10



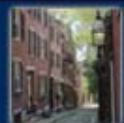
Results: Obstacles to Using SMQs

Obstacles to Using SMQs	Yes (%)	No (%)	N/A (%)	No response (%)
I know where to find SMQs	95	5		
I would use SMQs more often if better supported by existing technology	75	10		15
I would use SMQs more often if I better understood them	35		65	



Results: How are SMQs Applied?

How do you apply SMQs?	Never (%)	Almost Never (%)	Sometimes (%)	Often (%)	Always (%)	No response (%)
How often do you use the SMQ "as-is"	8	17	25	42	8	0
How often do you use only the narrow search	8	25	25	17	8	17
How often do you use the narrow and broad search	0	17	17	42	8	17
How often do you use the algorithm	42	17	17	8	0	17
How often do you modify the SMQ, by deleting terms	50	25	17	8	0	0
How often do you modify the SMQ, by adding terms	17	17	67	0	0	0
How often do you use an SMQ as a reference tool to develop your own custom search?	8	8	75	8	0	0



Results: Use of SMQs in PV Activities

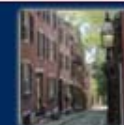
SMQs are used for the following PV Activities:

- Regulatory queries
- PSUR analysis
- Signal evaluation
- White papers
- Alliance Partner queries
- Healthcare professional queries
- Analysis of similar events for IND Safety Reports
- Other



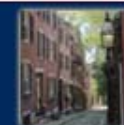
Examples

- PSUR analysis
 - Review of arrhythmias - used Cardiac arrhythmias SMQ (superordinate hierarchy)
 - Review of lack of efficacy - used Lack of efficacy/effect (SMQ), plus 2 additional PTs
- Regulatory query for product under review
 - Evaluate risk of interstitial lung disease - used Interstitial lung disease SMQ (narrow search)



Examples

- Regulatory Query: Compare serious allergic reactions when product is administered once weekly compared to twice weekly in divided doses
- Used narrow terms from Anaphylactic reaction SMQ, Oropharyngeal allergic conditions SMQ and Angioedema SMQs, and selected PTs
 - Deleted Circulatory collapse and Shock because product is listed for fatal sepsis
 - Fully documented search strategy and terms used/not used



Opportunities

- Increase understanding of SMQs
 - More training/workshops/leverage experience of experts
- Improve technology
 - New software/optimize use of existing software
- Define when SMQs are required
- Standardize how SMQs are applied



Next Steps in the Journey

- Wyeth will develop and document a standard search criteria using SMQs to be used by all Medical PV staff by early fall
- More training of staff on SMQs
- Training on the new standard search policy



In Summary

- To Effectively use SMQs
 - Understand the SMQ design concepts
 - Refer to the Introductory Guide for SMQs before using an SMQ
 - Have easy to use software tools
 - Follow best practices in regards to standardization and documentation and have adjudication rules for case identification
 - Petition the MSSO to add or delete PTs to SMQs, as needed and, if appropriate, request new SMQs



Thank you !

