Introduction to MedDRA

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Deputy Director, MedDRA MSSO
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Agenda

• Introduction of MedDRA
• Introduction of MedDRA Coding
• Introduction of MedDRA data retrieval and presentation
• Introduction of Standardised MedDRA Queries (SMQs)
Introduction of MedDRA
What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities
MedDRA’s Purpose

• Facilitate the exchange of clinical information through standardization
• Important tool for product evaluation, monitoring, communication, electronic records exchange, and oversight
• Supports coding (data entry) and retrieval and analysis of clinical information about human medical products including pharmaceuticals, biologics, vaccines, and drug-device combination products
MedDRA and the MSSO

- International support and development of terminology
- Foster use of MedDRA through communications and educational offerings
- "Custodians", not owners, of the terminology
- JMO (partner organization for Japanese-language MedDRA)
- Governed by a Management Board (industry, regulators, multi-national, other interested parties)
Regulatory Status

• US FDA, MedDRA is used in
  – FAERS (drugs and biologics)
  – VAERS (vaccines)
  – CAERS (foods, dietary supplements, cosmetics)

• EU EMA
  – Mandate the use of MedDRA
  – MedDRA is used in EudraVigilance database
    • Clinical trial SUSARs (Suspected Unexpected Serious Adverse Reactions)
    • Post-authorization Individual Case Safety Reports (ICSRs)
    • Requires current version of MedDRA or the one previous to it
Regulatory Status

- **Japanese Ministry of Health, Labour and Welfare (MHLW)**
  - Mandatory use of MedDRA in electronic reporting

- **Canada**
  - MedDRA is used in Canada Vigilance database
  - MedDRA is recommended/preferred terminology for adverse reaction reporting and Product Monograph (labeling)
  - Electronic reporting via Gateway requires current version of MedDRA
Scope of MedDRA

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

**OUT**
- Frequency qualifiers
- Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
- Not a drug dictionary
- Patient demographic terms
- Clinical trial study design terms
System Organ Classes

- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- Infections and infestations
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (incl cysts and polyps)
- Nervous system disorders
- Pregnancy, puerperium and perinatal conditions
- Product issues
- Psychiatric disorders
- Renal and urinary disorders
- Reproductive system and breast disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Social circumstances
- Surgical and medical procedures
- Vascular disorders
MedDRA Structure

System Organ Class (SOC) (27)

High Level Group Term (HLGT) (337)

High Level Term (HLT) (1,738)

Preferred Term (PT) (22,499)

Lowest Level Term (LLT) (77,248)
MedDRA Structure (cont)

- **SOC** = Cardiac disorders
- **HLGT** = Cardiac arrhythmias
- **HLT** = Cardiac conduction disorders
- **PT** = Atrioventricular block

**LLT**
- Atrioventricular block (NOS)
- Atrioventricular block
- LLT (Non-current) Other heart block

Heart block atrioventricular

Not all LLTs shown
Non-Current Terms

- Flagged at the LLT level in MedDRA
- Not recommended for continued use
- Retained to preserve historical data for retrieval and analysis
- Terms that are vague, ambiguous, out-dated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules
MedDRA Codes

• Each MedDRA term assigned an 8-digit numeric code starting with “1”
• The code is non-expressive
• Codes can fulfill a data field in various electronic submission types (e.g., E2B)
• New terms are assigned sequentially
**A Multi-Axial Terminology (cont)**

**SOC = Respiratory, thoracic and mediastinal disorders (Secondary SOC)**

**HLGT = Respiratory tract infections**

**HLT = Viral upper respiratory tract infections**

**PT = Influenza**

**SOC = Infections and infestations (Primary SOC)**

**HLGT = Viral infectious disorders**

**HLT = Influenza viral infections**
If a PT links to more than one of the exceptions, the following priority will be used to determine primary SOC:

1st: Congenital, familial and genetic disorders
2nd: Neoplasms benign, malignant and unspecified (incl cysts and polyps)
3rd: Infections and infestations
4th: Primary site of manifestation
PTs in the following SOCs only appear in that particular SOC and not in others, i.e., they are not multi-axial

- Investigations
- Surgical and medical procedures
- Social circumstances
MedDRA Web-Based Browser Demonstration
Introduction of MedDRA Coding
• MedDRA Term Selection: Points to Consider (MTS:PTC) Document

MedDRA® TERM SELECTION:
POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.11
Based on MedDRA Version 19.0

1 March 2016
ICH MedDRA Coding Guide

• Detailed coding instructions

SECTION 3 – TERM SELECTION POINTS

3.1 – Definitive and Provisional Diagnoses with or without Signs and Symptoms
3.2 – Death and Other Patient Outcomes
3.3 – Suicide and Self-Harm
3.4 – Conflicting/Ambiguous/Vague Information
3.5 – Combination Terms
3.6 – Age vs. Event Specificity
3.7 – Body Site vs. Event Specificity
3.8 – Location-Specific vs. Microorganism-Specific Infection
3.9 – Modification of Pre-existing Conditions
3.10 – Exposures during Pregnancy and Breast Feeding
3.11 – Congenital Terms
3.12 – Neoplasms
3.13 – Medical and Surgical Procedures
3.14 – Investigations

3.15 – Medication Errors, Accidental Exposures and Occupational Exposures
3.16 – Misuse, Abuse and Addiction
3.17 – Transmission of Infectious Agent via Product
3.18 – Overdose, Toxicity and Poisoning
3.19 – Device-related Terms
3.20 – Drug Interactions
3.21 – No Adverse Effect and “Normal” Terms
3.22 – Unexpected Therapeutic Effect
3.23 – Modification of Effect
3.24 – Social Circumstances
3.25 – Medical and Social History
3.26 – Indication for Product Use
3.27 – Off Label Use
3.28 – Product Quality Issues
Always Select a Lowest Level Term
Select Only Current LLTs

• Lowest Level Term that most accurately reflects the reported verbatim information should be selected

• Degree of specificity may be challenging
  – Example: “Abscess on face” → select “Facial abscess,” not simply “Abscess”

• Select current LLTs only
  – Non-current terms for legacy conversion/historical purposes
Manual Coding vs Autocoding - Example 1

- Verbatim: “fall in hemoglobin”
- Manual coding
  - LLT “Hemoglobin decreased”: a test result
- Auto-encoding
  - LLT Fall
  - LLT Hemoglobin: a test name, not a test result
Manual Coding vs Autocoding - Example 2

• Verbatim: “…can lead to overdose and death”

• Manual coding
  – LLT Overdose
  – LLT Death

• Auto-encoding
  – LLT Lead -> PT Blood lead: a test name, not a test result
  – LLT Overdose
  – LLT Death
Manual Coding vs Autocoding - Example 3

- Verbatim: “high risk of severe birth defects…”
- Manual coding
  - LLT Birth defects
- Auto-encoding
  - LLT High (non-current) -> PT Euphoric mood (SOC Psychiatric disorders)
  - LLT Birth defects
Manual Coding vs Autocoding - Example 4

• Verbatim: “Allergic to CAT scan”
• Manual coding
  – LLT Contrast media allergy
• Auto-encoding
  – LLT Allergic to cats -> PT Allergy to animal
Quality Control and Quality Assurance

• Check for deviation from coding guide
• Check for emerging drifts/biases
  – Look for suspicious SOC, e.g., unusual number of terms in Psychiatric SOC for a product that has no known psychiatric effect
• Detect autoencoder pitfalls
  – Look for patterns of wrongly coded verbatim texts, e.g. test name without result
• Performed by a qualified individual
  – Medical knowledge
  – MedDRA knowledge
  – Coding knowledge
• Machine learning by building a knowledge base
  – Synonym list

<table>
<thead>
<tr>
<th>Verbatim</th>
<th>LLT</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Throbbing above temple</td>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Aching all over head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulsing pain in head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscular pain in legs</td>
<td>Myalgia of lower extremities</td>
<td>LLT Myalgia of lower extremities is a better choice than LLT Muscular pain since it captures both the event and body site</td>
</tr>
</tbody>
</table>

– Built-in process to prompt for manual coding when encountering challenging verbatim
Introduction of MedDRA Data Retrieval and Presentation
Search For Trends and Signals

• Goal of collecting data is to search for trends and signals by aggregating similar data

• How can MedDRA help?
  – Hierarchy
    • PT
    • HLT
    • HLGT
    • SOC
  – Standardised MedDRA Queries (SMQs)
Search For Trends and Signals (cont)

• Hierarchy

PT Arrhythmia

HLGT Cardiac arrhythmias

1 PT

~100 PTs

SOC

HLGT

HLT

PT

LLT

Granularity

Signal Strength
Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
MedDRA Data Retrieval and Presentation: Points to Consider

- MedDRA Data Retrieval and Presentation: Points to Consider Document

MedDRA® DATA RETRIEVAL AND PRESENTATION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users on Data Output

Release 3.11
Based on MedDRA Version 19.0

1 March 2016
MedDRA Data Retrieval and Presentation: Points to Consider

- Detailed retrieval and presentation instructions

Section 2. General Principles
  2.1 Quality of Source Data
  2.2 Documentation of Data Retrieval and Presentation Practices
  2.3 Do Not Alter MedDRA
  2.4 Organisation-Specific Data Characteristics
  2.5 Characteristics of MedDRA that Impact Data Retrieval and Analysis
  2.6 MedDRA Versioning

Section 3 General Queries and Retrieval
  3.1 General Principles
  3.2 Overall Presentation of Safety Profiles

Section 4 Standardised MedDRA Queries

Section 5 Customised Searches
  5.1 Modified MedDRA Query Based on an SMQ
  5.2 Customised Queries
• Primary links
  – Overall Presentation of Safety Profiles: safety data in all SOCs
• Primary links
  – Viewing data in multiple SOCs
    • Organ and system specific SOCs (17)
    • Disorder SOCs (22)
    • Disorder SOCs plus SOC Injury, poisoning and procedural complications (23)
When Use Primary

When Use Secondary (cont)

- Primary and secondary links
  - Providing a more comprehensive view of the data by taking the advantage of MedDRA’s multi-axiality
  - Used in focused searches

<table>
<thead>
<tr>
<th>SOC Endocrine disorders</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HLGT Thyroid gland disorders</td>
<td></td>
</tr>
<tr>
<td>HLT Acute and chronic thyroiditis</td>
<td></td>
</tr>
<tr>
<td>PT Autoimmune thyroiditis</td>
<td>Primary</td>
</tr>
<tr>
<td>PT Thyroiditis</td>
<td>Primary</td>
</tr>
<tr>
<td>PT Thyroiditis acute</td>
<td>Primary</td>
</tr>
<tr>
<td>PT Thyroiditis chronic</td>
<td>Primary</td>
</tr>
<tr>
<td>PT Thyroiditis fibrous chronic</td>
<td>Primary</td>
</tr>
<tr>
<td>PT Thyroiditis subacute</td>
<td>Primary</td>
</tr>
<tr>
<td>PT Atrophic thyroiditis</td>
<td>Secondary (primary to SOC immune system disorders)</td>
</tr>
<tr>
<td>PT Infectious thyroiditis</td>
<td>Secondary (primary to SOC Infections and infestations)</td>
</tr>
<tr>
<td>PT Thyroglossal cyst infection</td>
<td>Secondary (primary to SOC Infections and infestations)</td>
</tr>
<tr>
<td>PT Thyroid echinococcosis</td>
<td>Secondary (primary to SOC Infections and infestations)</td>
</tr>
<tr>
<td>PT Thyroid gland abscess</td>
<td>Secondary (primary to SOC Infections and infestations)</td>
</tr>
<tr>
<td>PT Thyroid tuberculosis</td>
<td>Secondary (primary to SOC Infections and infestations)</td>
</tr>
<tr>
<td>PT Radiation thyroiditis</td>
<td>Secondary (primary to SOC Injury, poisoning and procedural complications)</td>
</tr>
<tr>
<td>PT Hashimoto's encephalopathy</td>
<td>Secondary (primary to SOC Nervous system disorders)</td>
</tr>
</tbody>
</table>
Non-Disorder Data

- SOC Investigations
- SOC Surgical and medical procedures
- SOC Product issues
- SOC Social circumstances
Introduction of Standardised MedDRA Queries (SMQs)
Standardised MedDRA Queries (SMQs)

- Result of cooperative effort between CIOMS (Council for International Organizations of Medical Sciences) 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
SMQ Development and Oversight

- CIOMS SMQ Working Group
  - Senior scientists (as members or observers) from several drug regulatory authorities and other organizations
  - Senior scientists from many pharmaceutical companies
  - One physician from MSSO

- ICH Advisory Panel
  - Representatives from industry and regulators from the three ICH regions, MHRA, Health Canada and WHO (as an observer)
SMQ Description
Acute renal failure (ARF) is characterized by a relatively rapid decline in renal function that leads to the accumulation of water, crystalloid solutes, and nitrogenous metabolites in the body. Other clinical features include: increase in serum creatinine and urea nitrogen levels (azotemia) greater than 0.5 and 10 mg per deciliter, respectively; oliguria; and changes in the rate of urine flow. ARF may present with a de novo onset in individuals whose baseline renal function was within normal limits. Additionally, ARF may consist of acute exacerbation of pre-existing chronic renal insufficiency.

SMQ Source

SMQ Note
## SMQ Term list

<table>
<thead>
<tr>
<th>Narrow Terms</th>
<th>Broad Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute kidney injury</td>
<td>Albuminuria</td>
</tr>
<tr>
<td>Acute phosphate nephropathy</td>
<td>Oedema due to renal disease</td>
</tr>
<tr>
<td>Acute prerenal failure</td>
<td>Blood creatinine abnormal</td>
</tr>
<tr>
<td>Anuria</td>
<td>Blood creatinine increased</td>
</tr>
<tr>
<td>Azotaemia</td>
<td>Blood urea abnormal</td>
</tr>
<tr>
<td>Continuous haemodiafiltration</td>
<td>Blood urea increased</td>
</tr>
<tr>
<td>Dialysis</td>
<td>Blood urea nitrogen/creatinine ratio increased</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>Creatinine renal clearance abnormal</td>
</tr>
<tr>
<td>Haemofiltration</td>
<td>Creatinine renal clearance decreased</td>
</tr>
<tr>
<td>Hyponatriuria</td>
<td>Creatinine urine abnormal</td>
</tr>
<tr>
<td>Neonatal anuria</td>
<td>Creatinine urine decreased</td>
</tr>
<tr>
<td>Nephropathy toxic</td>
<td>Crystal nephropathy</td>
</tr>
<tr>
<td>Oliguria</td>
<td>Fractional excretion of sodium</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>Glomerular filtration rate abnormal</td>
</tr>
<tr>
<td>Prerenal failure</td>
<td>Glomerular filtration rate decreased</td>
</tr>
<tr>
<td>Renal failure</td>
<td>Hypercreatininaemia</td>
</tr>
<tr>
<td>Renal failure neonatal</td>
<td>Intradialytic parenteral nutrition</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>Kidney injury molecule-1</td>
</tr>
<tr>
<td>Renal impairment neonatal</td>
<td>Nephritis</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SMQ Acute pancreatitis – with Algorithm

• SMQ topic definition, source, note

SMQ Description
Drug-induced pancreatitis is usually an acute condition. If clinically suspected, it should always be confirmed by biochemical investigations - Definition of acute pancreatitis: o An inflammatory disease of the pancreas characterized by upper abdominal pain and vomiting; in severe cases - abdominal guarding, rigidity, rebound tenderness and diminution or loss of bowel sounds o Almost always accompanied by increased pancreatic enzymes - amylase and lipase - in the blood and urine o Other signs/findings are icterus, increased alkaline phosphatase and/or bilirubin, ileus, ascites, hyperglycemia, hypocalcemia and leukocytosis o Cullen's sign is sometimes associated with severe necrotizing pancreatitis - Severe attacks may lead to shock with renal and pulmonary insufficiency, which may be fatal.

SMQ Source

SMQ Note
To apply algorithm - A report is considered a relevant case for further review if: 1) it includes a term from Category A (Narrow terms) OR 2) it includes at least one term from Category B (the list of laboratory values) and at least one term from Category C (the list of signs and symptoms)
## SMQ Acute pancreatitis – with Algorithm

### SMQ Term list

<table>
<thead>
<tr>
<th>Narrow Terms</th>
<th>Broad Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cullen's sign</td>
<td>Amylase abnormal</td>
</tr>
<tr>
<td>Grey Turner's sign</td>
<td>Amylase creatinine clearance ratio abnormal</td>
</tr>
<tr>
<td>Haemorrhagic necrotic pancreatitis</td>
<td>Amylase increased</td>
</tr>
<tr>
<td>Hereditary pancreatitis</td>
<td>Bilirubin conjugated abnormal</td>
</tr>
<tr>
<td>Ischaemic pancreatitis</td>
<td>Blood bilirubin increased</td>
</tr>
<tr>
<td>Oedematous pancreatitis</td>
<td>Blood trypsin increased</td>
</tr>
<tr>
<td>Pancreatic abscess</td>
<td>Hyperamylasaemia</td>
</tr>
<tr>
<td>Pancreatic haemorrhage</td>
<td>Hyperbilirubinaemia</td>
</tr>
<tr>
<td>Pancreatic necrosis</td>
<td>Hyperlipasaemia</td>
</tr>
<tr>
<td>Pancreatic phlegmon</td>
<td>Lipase abnormal</td>
</tr>
<tr>
<td>Pancreatic pseudocyst</td>
<td>Lipase increased</td>
</tr>
<tr>
<td>Pancreatic pseudocyst drainage</td>
<td>Lipase urine increased</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Pancreatic enzyme abnormality</td>
</tr>
<tr>
<td>Pancreatitis acute</td>
<td>Pancreatic enzymes abnormal</td>
</tr>
<tr>
<td>Pancreatitis haemorrhagic</td>
<td>Pancreatic enzymes increased</td>
</tr>
<tr>
<td>Pancreatitis necrotising</td>
<td>Ultrasound pancreas abnormal</td>
</tr>
<tr>
<td>Pancreatitis relapsing</td>
<td>B Abdominal compartment syndrome</td>
</tr>
<tr>
<td>Pancreatorenalsyndrome</td>
<td>B Abdominal distension</td>
</tr>
<tr>
<td>C Abdominal pain</td>
<td>B Abdominal pain</td>
</tr>
<tr>
<td>B Abdominal pain upper</td>
<td>B Abdominal rebound tenderness</td>
</tr>
<tr>
<td>C Abdominal rigidity</td>
<td>B Abdominal tenderness</td>
</tr>
<tr>
<td>C Abdominal tenderness</td>
<td>B Acute abdomen</td>
</tr>
<tr>
<td>C Ascites</td>
<td>B Fat necrosis</td>
</tr>
<tr>
<td>C Gastrointestinal pain</td>
<td>B Gastrointestinal sounds abnormal</td>
</tr>
<tr>
<td>C Haemorrhagic ascites</td>
<td>B Ileus paralytic</td>
</tr>
<tr>
<td>C Ileus paralytic</td>
<td>B Intra-abdominal pressure increased</td>
</tr>
<tr>
<td>C Jaundice</td>
<td>B Nausea</td>
</tr>
<tr>
<td>C Pancreatic duct rupture</td>
<td>C Pancreatic duct rupture</td>
</tr>
<tr>
<td>C Peripancreatic fluid collection</td>
<td>C Peripancreatic fluid collection</td>
</tr>
<tr>
<td>C Vomiting</td>
<td>C Vomiting</td>
</tr>
<tr>
<td>C Vomiting projectile</td>
<td>C Vomiting projectile</td>
</tr>
</tbody>
</table>
• **Next step is case review** – a manual process
  – Confirm positive cases
  – Filter out negative cases

• **By a qualified individual**
  – Medical knowledge
  – MedDRA knowledge
  – Drug safety knowledge
**Use of SMQs at FDA**

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

<table>
<thead>
<tr>
<th>SMQ name</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia (SMQ)</td>
<td>19 (4.44%)</td>
<td>48 (11.03%)</td>
<td>67 (7.74%)</td>
<td></td>
</tr>
<tr>
<td>Depression and suicide/self-injury (SMQ)</td>
<td>17 (3.97%)</td>
<td>22 (5.06%)</td>
<td>39 (4.50%)</td>
<td></td>
</tr>
<tr>
<td>Peripheral neuropathy (SMQ)</td>
<td>16 (3.74%)</td>
<td>19 (4.37%)</td>
<td>35 (4.04%)</td>
<td></td>
</tr>
<tr>
<td>Malignancies (SMQ)</td>
<td>11 (2.57%)</td>
<td>13 (2.99%)</td>
<td>24 (2.77%)</td>
<td></td>
</tr>
<tr>
<td>Malignant or unspecified tumours (SMQ)</td>
<td>11 (2.57%)</td>
<td>13 (2.99%)</td>
<td>24 (2.77%)</td>
<td></td>
</tr>
<tr>
<td>Haematopoietic cytopenias (SMQ)</td>
<td>12 (2.90%)</td>
<td>10 (2.30%)</td>
<td>22 (2.54%)</td>
<td></td>
</tr>
<tr>
<td>Leukopenia (SMQ)</td>
<td>11 (2.57%)</td>
<td>9 (2.07%)</td>
<td>20 (2.31%)</td>
<td></td>
</tr>
<tr>
<td>Asthma/bronchospasm (SMQ)</td>
<td>2 (0.47%)</td>
<td>6 (1.38%)</td>
<td>8 (0.92%)</td>
<td></td>
</tr>
<tr>
<td>Angioedema (SMQ)</td>
<td>2 (0.47%)</td>
<td>4 (0.92%)</td>
<td>6 (0.69%)</td>
<td></td>
</tr>
<tr>
<td>Acute pancreatitis (SMQ)</td>
<td>1 (0.23%)</td>
<td>4 (0.92%)</td>
<td>5 (0.58%)</td>
<td></td>
</tr>
<tr>
<td>Convulsions (SMQ)</td>
<td>3 (0.70%)</td>
<td>3 (0.69%)</td>
<td>6 (0.69%)</td>
<td></td>
</tr>
<tr>
<td>Ischaemic heart disease (SMQ)</td>
<td>0 (0.00%)</td>
<td>3 (0.69%)</td>
<td>3 (0.35%)</td>
<td></td>
</tr>
<tr>
<td>Acute renal failure (SMQ)</td>
<td>0 (0.00%)</td>
<td>2 (0.46%)</td>
<td>2 (0.23%)</td>
<td></td>
</tr>
<tr>
<td>Interstitial lung disease (SMQ)</td>
<td>0 (0.00%)</td>
<td>2 (0.46%)</td>
<td>2 (0.23%)</td>
<td></td>
</tr>
<tr>
<td>Embolic and thrombotic events, arterial (SMQ)</td>
<td>1 (0.23%)</td>
<td>2 (0.46%)</td>
<td>3 (0.35%)</td>
<td></td>
</tr>
<tr>
<td>Embolic and thrombotic events (SMQ)</td>
<td>3 (0.70%)</td>
<td>2 (0.46%)</td>
<td>5 (0.58%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension (SMQ)</td>
<td>0 (0.00%)</td>
<td>3 (0.69%)</td>
<td>3 (0.35%)</td>
<td></td>
</tr>
</tbody>
</table>
Use of SMQs at FDA (cont)

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

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Data Retrieval Exercise

- FlowChart

  Safety topic: Hepatotoxicity

  Develop MedDRA Search Strategy

  Focused Search/Customized Query MedDRA Groupings with 2nd links

  SMQs or Modified SMQs

  List of MedDRA PTs relevant to Hepatotoxicity

  Retrieve Events/Cases

  Review and Confirm Events/Cases

  Statistical Analysis

Medical & MedDRA Expert

Statistician /IT Expert
Hepatotoxicity: MedDRA Query Development

- Focused search/ customized query: DOTSSS

Diagram:
- Diagnosis/disease terms
- Operations (Surgical and medical procedures)
- Tests (Investigations)
- Support SOCs (Other...)
- Signs & symptoms
- Social circumstances
Hepatotoxicity: MedDRA Query Development (cont)

- Focused search/ customized query
- SOC or MedDRA grouping with 2\textsuperscript{nd} links

- And other SOCs...
- Interested in drug-induced?
Hepatotoxicity – SMQs

- Applied SMQs or modified SMQs

- Hepatic disorders (SMQ)
  - Congenital, familial, neonatal and genetic disorders of the liver (SMQ)
  - Drug related hepatic disorders - comprehensive search (SMQ)
    - Cholestasis and jaundice of hepatic origin (SMQ)
    - Drug related hepatic disorders - severe events only (SMQ)
      - Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions (SMQ)
      - Hepatitis, non-infectious (SMQ)
  - Liver neoplasms, benign (incl cysts and polyps) (SMQ)
  - Liver neoplasms, malignant and unspecified (SMQ)
    - Liver malignant tumours (SMQ)
    - Liver tumours of unspecified malignancy (SMQ)
  - Liver related investigations, signs and symptoms (SMQ)
  - Liver-related coagulation and bleeding disturbances (SMQ)
  - Hepatic disorders specifically reported as alcohol-related (SMQ)
  - Liver infections (SMQ)
  - Pregnancy-related hepatic disorders (SMQ)
Questions?