

Linda Jeng, M.D., Ph.D.



Associate Director, Biomedical Informatics and Regulatory Review Science (BIRRS) (acting)
FDA/CDER/Office of New Drugs/Office of Drug Evaluation Science

Office of New Drugs Custom Medical Queries (OCMQs)* for Safety Signal Detection in Clinical Trial Data

*Formerly known as FDA Medical Queries (FMQs)

- ▶ The views and opinions expressed in this presentation are those of the presenter and do not represent official policy or position of the FDA.
- ▶ I have no relevant financial or non-financial relationships to disclose.

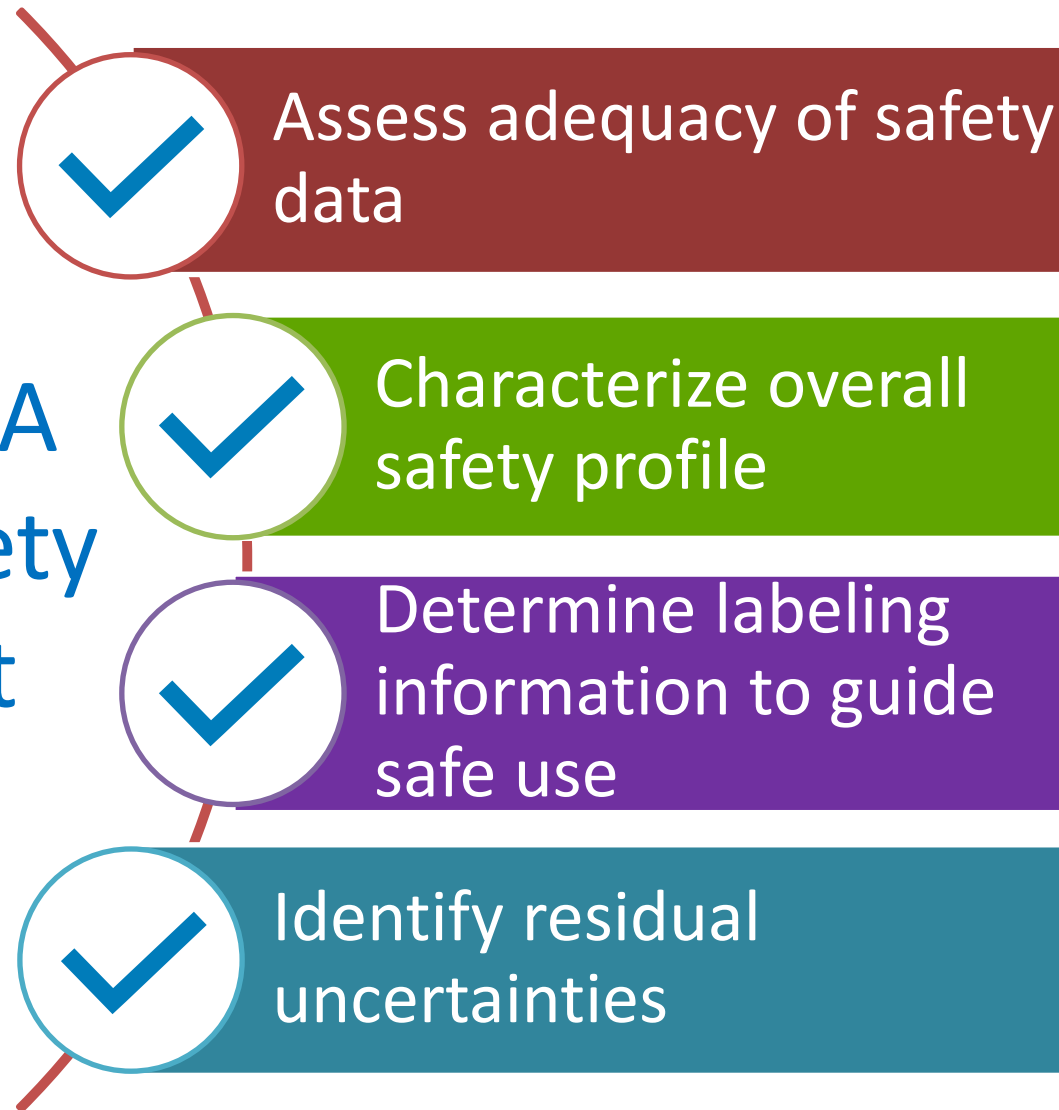
Overview

OND Custom Medical Queries
(OCMQs) Background

OCMQ Manual of Policies and
Procedures (MAPP)

Frequently Asked Questions
(FAQs)

Goals of FDA Clinical Safety Assessment



Pre-market Safety Analysis

- OCMQs
- Standard Tables and Figures

Challenge of Safety Analysis

Identification of safety signals

- Verbatim terms are coded to standard terms from the Medical Dictionary for Regulatory Activities (MedDRA®)
- Specificity can be counterproductive
- Related adverse events (AEs) should be grouped together

Inconsistent Standard Groupings



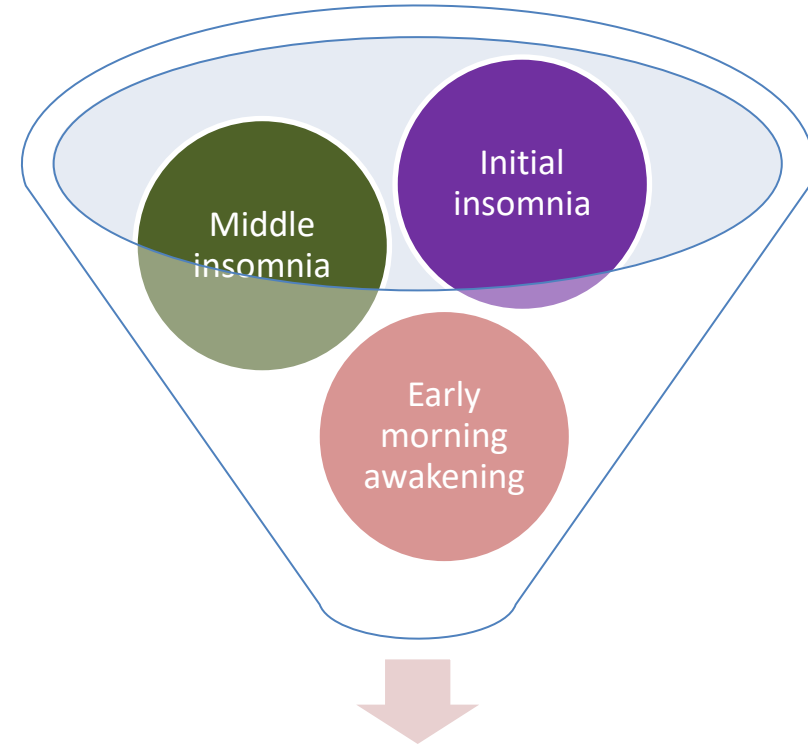
Ungrouped
related PTs



Potential
missed safety
signals

What are OCMQs?

- ▶ Standardized groupings of related terms
- ▶ Designed for premarket drug safety evaluation
- ▶ Focused on commonly labeled adverse reactions



OCMQ Version 4.1 – Released 4/29/2026

- | | | | |
|------------------------------------|----------------------------------|-----------------------------------|-------------------------------------|
| 1. Abdominal Pain | 27. Diabetic Ketoacidosis | 53. Hypotension | 79. Pyrexia |
| 2. Abnormal Uterine Bleeding | 28. Diarrhea | 54. Insomnia | 80. Rash |
| 3. Acute Coronary Syndrome | 29. Dizziness | 55. Irritability | 81. Renal & Urinary Tract Infection |
| 4. Acute Kidney Injury | 30. Dry Mouth | 56. Leukopenia | 82. Respiratory Depression |
| 5. Alopecia | 31. Dysgeusia | 57. Lipid Disorder | 83. Respiratory Failure |
| 6. Amenorrhea | 32. Dyspepsia | 58. Local Administration Reaction | 84. Seizure |
| 7. Anaphylactic Reaction | 33. Dyspnea | 59. Malignancy | 85. Self-Harm |
| 8. Anemia | 34. Erectile Dysfunction | 60. Mania | 86. Sexual Dysfunction |
| 9. Angioedema | 35. Erythema | 61. Muscle Injury | 87. Somnolence |
| 10. Anxiety | 36. Excessive Menstrual Bleeding | 62. Myalgia | 88. Stroke and TIA |
| 11. Arrhythmia | 37. Fall | 63. Myocardial Infarction | 89. Study Agent Abuse Potential |
| 12. Arthralgia | 38. Fatigue | 64. Myocardial Ischemia | 90. Syncope |
| 13. Arthritis | 39. Fracture | 65. Nasopharyngitis | 91. Systemic Hypertension |
| 14. Back Pain | 40. Fungal Infection | 66. Nausea | 92. Tachycardia |
| 15. Bacterial Infection | 41. Glaucoma | 67. Opportunistic Infection | 93. Tendinopathy |
| 16. Bacterial Vaginosis | 42. Gout | 68. Osteoporosis | 94. Thrombocytopenia |
| 17. Bronchospasm | 43. Gynecomastia | 69. Palpitations | 95. Thrombosis |
| 18. Cachexia | 44. Headache | 70. Pancreatitis | 96. Thrombosis Arterial |
| 19. Cardiac Conduction Disturbance | 45. Heart Failure | 71. Parasomnia | 97. Thrombosis Venous |
| 20. Cholecystitis | 46. Hemorrhage | 72. Paresthesia | 98. Tremor |
| 21. Confusional State | 47. Hepatic Failure | 73. Peripheral Edema | 99. Urinary Retention |
| 22. Constipation | 48. Hepatic Injury | 74. Pneumonia | 100. Urticaria |
| 23. Cough | 49. Hyperglycemia | 75. Pneumonitis | 101. Vertigo |
| 24. Decreased Appetite | 50. Hyperprolactinemia | 76. Pruritus | 102. Viral Infection |
| 25. Decreased Menstrual Bleeding | 51. Hypersensitivity | 77. Psychosis | 103. Volume Depletion |
| 26. Depression | 52. Hypoglycemia | 78. Purulent Material | 104. Vomiting |

Why OCMQs?



- ▶ Clinically meaningful groupings designed for premarket setting
- ▶ Consistent approach to safety signal detection
- ▶ Inconsistencies in clinical trial data submitted to the FDA
 - Variable coding to MedDRA preferred terms (PTs)
 - AEs may manifest in different, but related ways

OCMQ Development



Phase 1

- Natural language processing of 38,000+ drug labels (1960-2017)

Phase 2

- Collaboration with OND Divisions and subject matter experts (SMEs)

Phase 3

- Development of algorithmic groupings

OCMQ: Narrow vs. Broad Queries

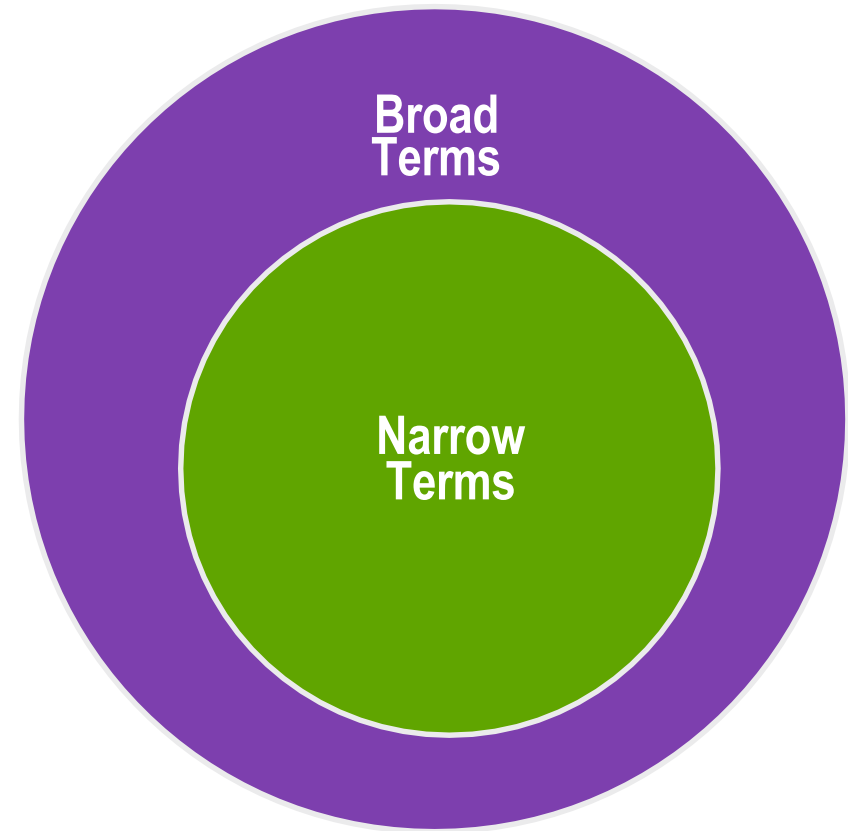


► **Narrow OCMQs**

- High degree of specificity
- Ensure a high confidence that the OCMQ occurred

► **Broad OCMQs**

- Aim to enhance the detection sensitivity of the OCMQ
- Greater sensitivity, but lower specificity
- Includes all narrow terms



Algorithmic OCMQs



- ▶ Drug-Induced Muscle Injury, Hypoglycemia, Hyperglycemia, and Hypersensitivity
- ▶ **Algorithmic OCMQs**
 - Use multiple datasets to leverage more of the available information
 - Adverse event datasets
 - Laboratory datasets
 - Concomitant meds datasets
 - Medical history datasets
 - Temporal relationships

Example Mock Algorithm:

1. PT + PT
2. Lab value >ULN
3. PT + Con Med within 3 days
4. PT + Medical History

Algorithmic OCMQ Example:

Drug-Induced Muscle Injury

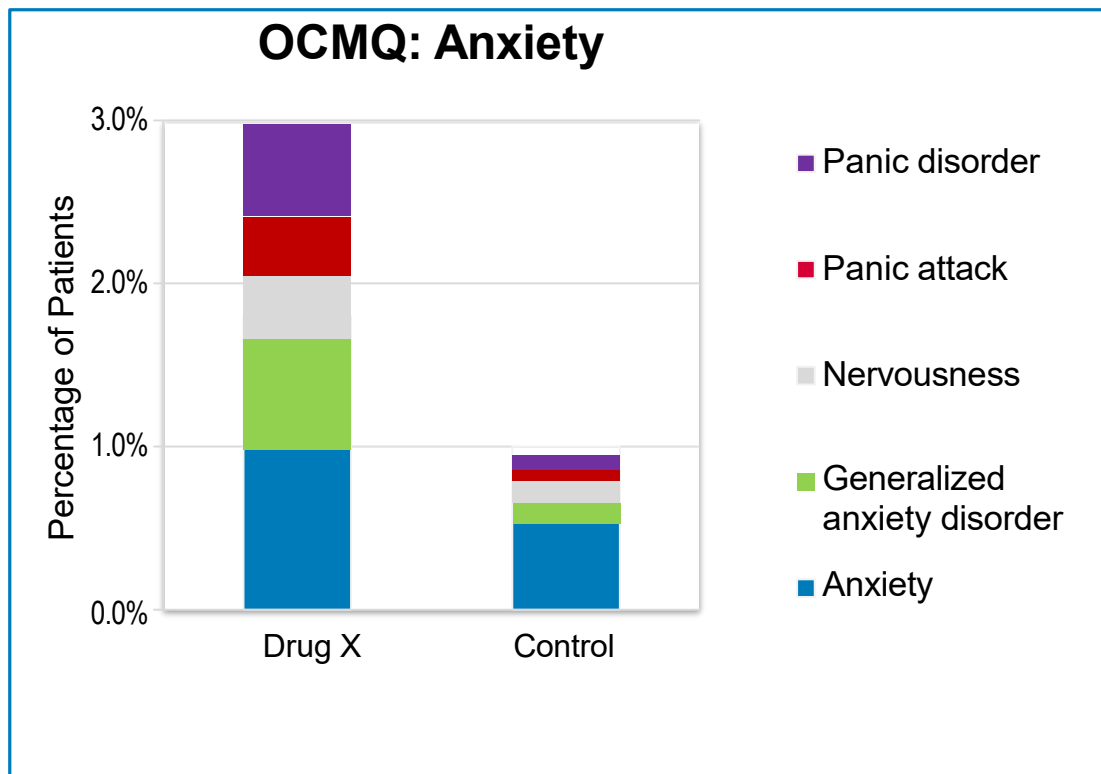
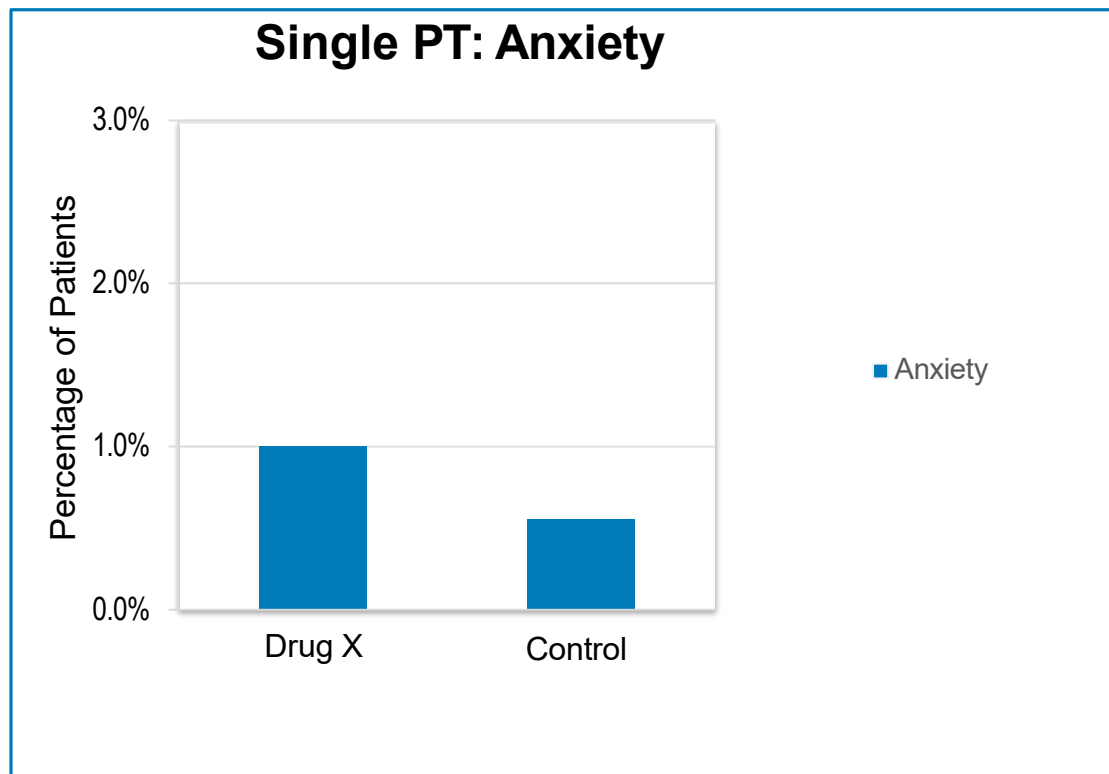
- Subjects qualify for the algorithm if they meet any of the following criteria:
1. Any Muscle Injury OCMQ Narrow term
 2. Urine myoglobin >ULN
 3. CPK >5 x ULN **AND NO**:
 - CPK >ULN at baseline OR
 - CPK-MB/CPK >0.05 with start date within 3 days
 4. [PT Myalgia + PT Muscular weakness + (PT Myoglobin urine present OR PT Chromaturia)] with start date within 7 days of each other

Abbreviations: ULN= Upper limit of normal, CPK = creatine phosphokinase

Single PT Analysis versus OCMQ



- ▶ “Anxiety” safety signal may only become apparent when all variations of anxiety are included.



► Examples:

- Standardised MedDRA Queries (SMQs)
- Sponsor custom medical queries (CMQs)
- Individual reviewer custom queries

NOTE: OCMQs are not intended to replace review of individual reported AE terms, MedDRA System Organ Classes, or other available and appropriate groupings of AE terms.

OCMQs attempt to capture all instances of an AE, even if PT indicates a “non-drug-related” cause:

OCMQ Pancreatitis

(Does Contain)



SMQ Acute Pancreatitis

(Does Not Contain)



Alcoholic pancreatitis
Autoimmune pancreatitis
Obstructive pancreatitis
Pancreatitis viral

MAPP

6025.8



POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Good Review Practices: OND Custom Medical Queries

Table of Contents

PURPOSE	1
BACKGROUND	2
POLICY	2
RESPONSIBILITIES	3
PROCEDURES	3
REFERENCE	5
DEFINITIONS	5
EFFECTIVE DATE	5
CHANGE CONTROL TABLE	6
ATTACHMENT 1: Ground Rules for Creating OND Custom Medical Queries (V.3.2)	7

PURPOSE

- This Manual of Policies and Procedures (MAPP) and its attachments describe good review practices (GRPs) for the Office of New Drugs (OND) within the Center for Drug Evaluation and Research (CDER) when developing and updating OND Custom Medical Queries (OCMQs)¹ and use of OCMQs during review of new drug applications (NDAs), biologics license applications (BLAs), and supplemental NDAs and BLAs.

Purpose of OCMQs



Provide standard groupings of adverse event terms



Help identify potential safety issues

Manual of Policies and Procedures



MAPP 6025.8

- ▶ Establishes Good Review Practices for OCMQs
- ▶ Standardizes the approach across OND
 - New molecular entity NDAs, original 351(a) BLAs, and relevant supplements
- ▶ Defines responsibilities for OCMQ maintenance and implementation
- ▶ Clarifies that use of OCMQs by applicants is voluntary

OCMQ Ground Rules: Narrow Queries



Near-synonyms of the OCMQ

- “*Abdominal discomfort*” in OCMQ
Abdominal Pain

Subgroups of the OCMQ

- “*Anaemia megaloblastic*” in OCMQ
Anemia

Specify an etiology for the OCMQ

- “*Uraemic pruritus*” in OCMQ
Pruritus

Ensure the occurrence of the OCMQ

- “*Aortic rupture*” in OCMQ
Hemorrhage

OCMQ Ground Rules: Broad Queries



May result in the OCMQ

- *“Osteopenia”* in OCMQ Osteoporosis

Provide test results reasonably suggestive of an OCMQ

- *“Blood glucose abnormal”* in OCMQ Hyperglycemia

Reasonably suggestive, but not required by the OCMQ

- *“Bronchospasm”* in OCMQ Hypersensitivity

Indicate a “carrier” status of infection for the OCMQ

- *“Bacterial disease carrier”* in OCMQ Bacterial Infection

OCMQ Ground Rules: Exclusions



Terms that are too vague are excluded from OCMQs

- ▶ Neither a required component nor reasonably specific for the OCMQ
 - “Nausea” not be included in OCMQ Migraine
- ▶ Names of laboratory, radiologic, or other diagnostic tests without a result
 - “Clostridium test”

NOTE: *Unless the test would only be performed in the presence of the OCMQ concept and the term otherwise qualifies*

OCMQ Ground Rules: Additional Exclusions



Additional AEs for conditions that are extremely rare and difficult to categorize are excluded from OCMQs

- ▶ AEs that identify congenital, familial, or genetic disorders
- ▶ AEs that identify pregnancy, puerperium and perinatal conditions

NOTE: *Consider using the relevant MedDRA System Organ Class to cover these AEs during safety analysis.*

OCMQ Generation and Maintenance



**Established Ground Rules
to maintain consistency
in application of medical
judgement**



**Annual updates following
the main MedDRA
annual release**

Where to Find OCMQs?



▶ <https://www.fda.gov/drugs/development-resources/office-new-drugs-custom-medical-queries-ocmqs>

The screenshot shows the FDA website header with the logo and 'U.S. FOOD & DRUG ADMINISTRATION'. Below the header is a breadcrumb trail: Home / Drugs / Development & Approval Process | Drugs / Development Resources / Office of New Drugs Custom Medical Queries (OCMQs). The main heading is 'Office of New Drugs Custom Medical Queries (OCMQs)'. On the left is a sidebar with 'Development Resources' and links to 'Advancing Real-World Evidence Program' and 'Antibacterial Drug Development Task Force'. The main content area has a 'Background' section.

Development Resources

- [Advancing Real-World Evidence Program](#)
- [Antibacterial Drug Development Task Force](#)

Background

Office of New Drugs (OND) Custom Medical Queries (OCMQs), formerly known as FDA Medical Queries (FMQs), are standardized groupings of similar adverse event (AE) terms¹ intended to assist with the identification of potential safety issues during the review of AE safety data. While other AE groupings already exist, (e.g., Standardised MedDRA Queries (SMQs)), OCMQs are clinically meaningful groupings used by OND staff for premarket safety evaluation. The use of OCMQs promotes a consistent safety signal detection strategy across OND Divisions.

When will new OCMQ updates be released?



We anticipate annual updates to incorporate new MedDRA PTs following annual major releases. However, review of new terms is dependent on Agency resources.

What MedDRA terms are included in OCMQ v4.0?



OCMQ v4.0 incorporates terms up through MedDRA v27.0.

Do NDA/BLA applicants have to use OCMQs?



No, use of OCMQs in NDAs and BLAs is voluntary for applicants.

Who should I contact with questions about OCMQs?



ONDBiomedicalinformatics@fda.
hhs.gov

Where can I find the most recent version of the OCMQs?



https://www.fda.gov/drugs/development-resources/office-new-drugs-custom-medical-queries-ocmqs?utm_medium=email&utm_source=govdelivery

OCMQ FAQs (6)



► Why do OCMQs include terms that are not MedDRA PTs?

Terms included in the OCMQs came from over 5000 clinical trials, MedDRA, existing queries, and FDA Adverse Event Reporting System (FAERS). To be comprehensive and inclusive, OCMQs contain terms from the MedDRA hierarchy and other terms that have been submitted in the safety data of marketing applications, including misspelled terms identified in clinical trial datasets, based on manual review of combined datasets from more than 5000 clinical trials. Note that not all terms included in the OCMQs are MedDRA PTs and not all MedDRA PTs are included in the OCMQs. If a term was a PT in an earlier MedDRA version and is now considered a lower-level term (LLT), the term will continue to be included in the OCMQs.

Main OCMQ Takeaways

- ▶ Support safety signal detection through standardized groupings
- ▶ Cover common and medically important adverse reactions
- ▶ Used for NME NDAs and original BLAs
- ▶ Complement, but do not replace review of individual terms

Knowledge Question



► OCMQs include two main categories of terms. What does the "Narrow" category indicate about the occurrence of the medical condition?

A. High level of confidence

B. Reasonably suggestive

C. Possible presence

D. Low probability

