Introduction to MedDRA Labeling Grouping (MLG): A Standardized Approach to Grouping Adverse Reactions in Product Safety Labels

Members, Advisors and Observers who Contributed to the Expert Working Group (EWG) on Medical Dictionary for Regulatory Agency (MedDRA) Labeling Groupings (MLG) (2019-2023)

Name	Organization
Silvia BADER-WEDER	Roche
Sonja BRAJOVIC	U.S. Food and Drug Administration (FDA)
Andrea BROWN	Gilead
Brian DILLMAN †	Eli Lilly
Diane FARKAS	Sanofi Aventis
William GREGORY	Pfizer **
Ilona GROßE-MICHAELIS	Bayer/ retired **
Tomohiko HARA	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
Tomohiro HATTA	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
Judith JONES †	Pharmalex
Kanae KOBAYASHI	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
Sue LE ROUX	CIOMS
Lynn MACDONALD	Health Canada/ retired **
Christiane MICHEL	Novartis
Yutaka NAGAO	MedDRA Japanese Maintenance Organization (JMO)
Tomoko NARITA	MedDRA Japanese Maintenance Organization (JMO)

Name	Organization
Members, advisors and observers who contributed to the MLG EWG (continued)	
Norbert PAESCHKE	Federal Institute for Drugs and Medical Devices (BfArM), Germany **
Catherine PENFORNIS	Sanofi Aventis
Scott PROESTEL	U.S. Food and Drug Administration (FDA) *
Lembit RÄGO	CIOMS
Radhika RAO	Abbvie
Jill ROBINSON	Amgen
Aniello SANTORO	European Medicines Agency (EMA)
Debbra SCOTTI	Pfizer
Alima TAPSOBA	Health Canada
Laurence TRINH-LA	Gilead
Omi WATANABE	Pharmaceuticals and Medical Devices Agency (PMDA), Japan

* Currently at Medpace, Inc.

** Retired

CIOMS MLG EWG Members (2019)

Introduction of the Speakers/Panelists

Ilona Grosse-Michaelis
Bayer/Retired

Radhika M Rao
AbbVie

Silvia Bader-Weder
Roche

Scott Proestel
Formerly FDA / Currently at Medpace

Aniello Santoro
EMA

CIOMS – Introduction (https://cioms.ch/)

Council for
International
Organizations of
Medical
Sciences (41 member organizations)

Founded in 1949 by WHO and UNESCO

In official relations with WHO

UNESCO associated partner

ICH Observer since 2016

Mission Statement

CIOMS mission is to advance public health through guidance on health research including ethics, medical product development and safety

Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenters and should not be attributed to any organization, including those with which the presenters are employed or affiliated.

Agenda

- Background
- MLG Characteristics and MLG Objective
- MLG Principles and MLG Conventions
- Benefits of MLGs and Unexplored Potential Applications
- Labeling considerations with Illustration
- MLG Examples
- Comparison of SMQ and MLG
- MLG Limitations
- Conclusion and Future Considerations

Panel Discussion

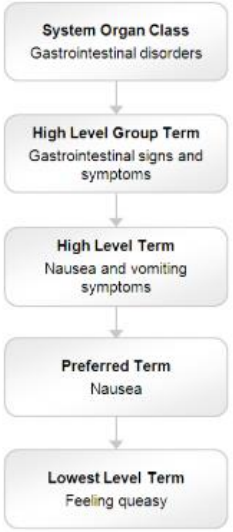
Aniello Santoro

EMA

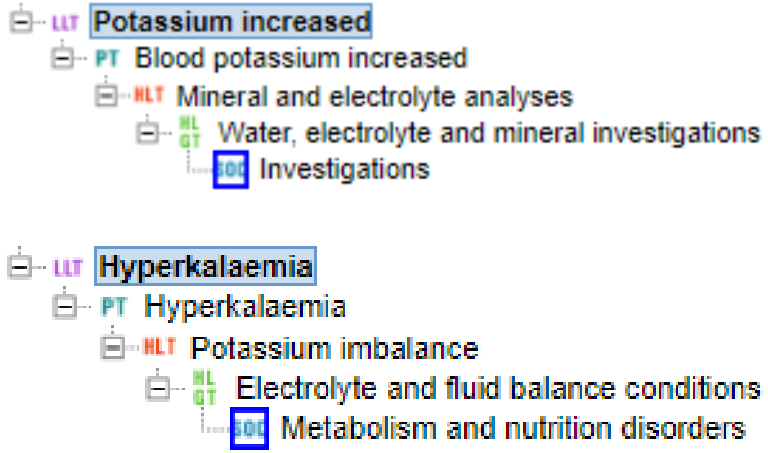
Background

Medical Dictionary for Regulatory Activities:

- Used to present adverse drug reactions (ADRs) in product labels
- Hierarchical: 5 levels
- Highly granular: distinct Preferred Terms (PTs) available (in different sections of MedDRA) to represent highly similar medical concepts:
  - useful for precise **coding** of ADRs
  - can **hinder the clarity of communication** of the safety profile in a product label, if no appropriate grouping



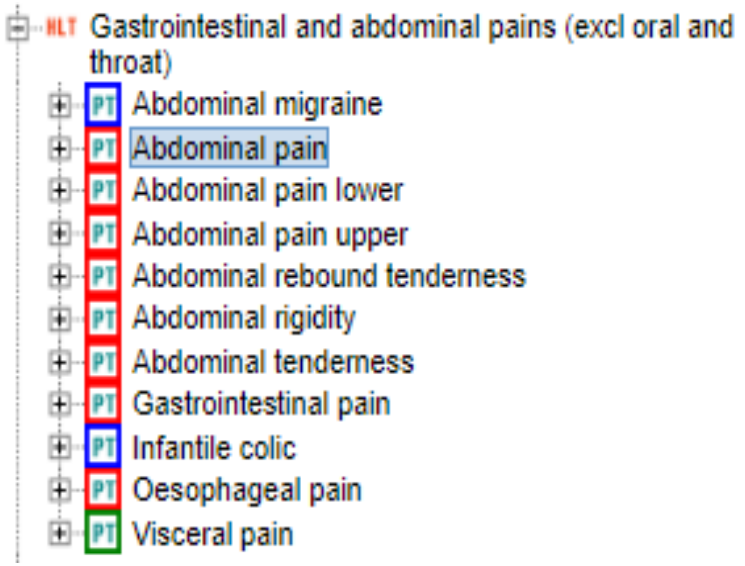
> 25K PTs in v. 24.1



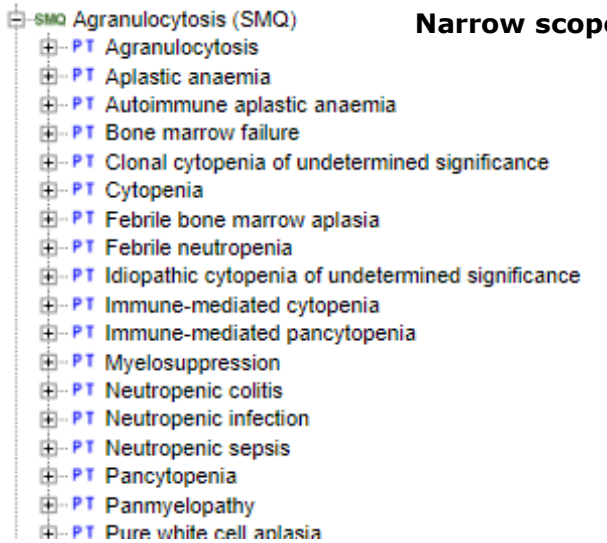
Background (continued)

MedDRA allows for grouping of PTs:

- within hierarchy, e.g. High Level Term groups various PTs



- outside the hierarchy, e.g. Standardised MedDRA Queries (SMQs)



Neither is designed with the objective to communicate safety information in product labels

Regulatory Guidance


EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

Revision 2

NOTICE TO APPLICANTS

A GUIDELINE ON

SUMMARY OF PRODUCT CHARACTERISTICS

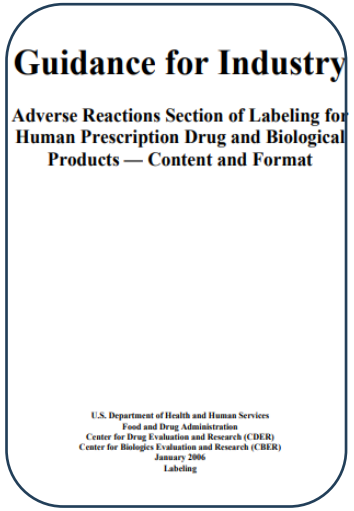
(SmPC)

September 2009

This guideline will be included in The Rules Governing Medicinal Products in the European Union Volume 2C Notice to Applicants

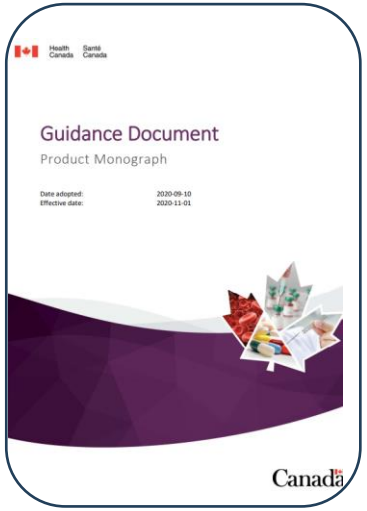
- MedDRA should be used to present ADRs in label
- Reactions reported under different terms should be grouped as a single adverse reaction, if they represent the same phenomenon (e.g. sedation, somnolence, drowsiness)
- Important to avoid diluting or obscuring the true effect
- It may be appropriate to use **ad-hoc grouping** of terms or to adapt MedDRA group terms if the established MedDRA group terms are not appropriate

https://health.ec.europa.eu/document/download/6a043dea-7d0f-4252-947b-cef58f53d37e_en


Guidance for Industry

Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products — Content and Format

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
January 2006
Labeling


Health Canada / Santé Canada

Guidance Document

Product Monograph

Date adopted: 2020-09-10
Effective date: 2020-11-01

Canada

- Similar recommendation for grouping different terms that represent the same phenomenon

https://www.fda.gov/media/72139/download

https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/pdf/prodpharma/applic-demande/guide-ld/monograph/pm-guid-ld-mp-eng.pdf

The Gap

- Previously no guidance on how to make those groupings of clinically related concepts, when neither MedDRA hierarchy nor SMQs are adequate for communication within labels
- Risk of disharmony (in the absence of guidance) among labels
- CIOMS MLG EWG remit was to provide guidance on how to group nearly synonymous MedDRA terms representing an adverse reaction for communication within labels

Journey of CIOMS MLG EWG

CIOMS WG on MedDRA SMQs proposed new CIOMS group to explore MLGs for use in product label

MedDRA Management Committee supported feasibility assessment, development of principles and conventions to support the creation of MLGs in a harmonized fashion

Draft report and engagement activities

2018 — 2019 — Mar 2024

Concept paper and one-pager on possible development and use of MLGs

CIOMS MLG EWG established.
Goal: develop principles and conventions to support creation of MLGs in a harmonized fashion (establish an internationally agreed approach to their creation)
The actual creation of MLGs might be undertaken in a future phase, if supported


Final v2.0
01 May 2018

Concept Paper

Principles for Simplification of Biopharmaceutical Produc
MedDRA® Terms for Unique Medical Concepts: a proposal

14 May 2018

Executive Summary

An Expert Working Group (EWG) coordinated by the Council fo
Sciences (CIOMS) is proposed to develop principles and pragmc
consistency and understandability of medical concepts, e.g. sus
biopharmaceutical product safety labeling. The granularity anc
Regulatory Activities (MedDRA) provide opportunities for preci
MedDRA terms. However, the high granularity of MedDRA cou
labeled SARs and, thus, are important to communicate to healt
hierarchy provides groupings of related and meaningful medic
inadequate to clearly communicate unique clinical concepts tha
MedDRA terms. To simplify communication of such concepts th

Principles for Simplification of Biopharmaceutical Product Safety Labeling by Grouping Similar MedDRA® Terms for Unique Medical Concepts

Summary: Driven by business needs and based on regulatory guidance[1-4], the communication of suspected adverse reactions in labeling should be presented as unique medical concepts, rather than always as individual MedDRA Preferred Terms (PT). This would enhance understandability of the concerned clinical concepts by the health care community. MLGs would also facilitate calculation of frequencies of suspected adverse reactions from clinical trial data and for comparison of frequencies between products (and, perhaps, indications, populations, or posology).

Although the established Medical Dictionary for Regulatory Activities (MedDRA) hierarchy provides groupings of related and meaningful medical concepts, these groupings can be of a broader scope, beyond the medical concepts intended for the label. Other types of groupings may also be needed to appropriately cluster individual MedDRA terms that convey the same clinical concept, thus supporting clearer communication. To this effect, several organizations have already independently created their own groups of medically related terms.

It is proposed that globally harmonized principles, points to consider, and pragmatic recommendations for development of MedDRA Labeling Groupings (MLGs) be developed by a Council for International Organizations of Medical Sciences (CIOMS) working group. The desired outcome is an international approach which would be available for voluntary consideration.

Goal achieved + few examples of proposed MLGs created for illustrative purposes only

Engagement Activities

	Title of presentation
18th Annual ISoP Meeting (13Nov18)	*•MLGs: A Harmonised Approach to Safety Communication* *•MLGs: Examples from a Pharmaceutical company*
DIA Global Annual meeting (25Jun19)	*•MLGs: A New CIOMS Initiative* *•MLGs: Practical Examples Underscore Feasibility*
DIA-NIFDS PV workshop, virtual (18Nov20)	*•Rationale for Grouping Near-Synonymous MedDRA Terms* *•Practical Aspects of Grouping Near-Synonymous MedDRA Terms*
FDA SACB meeting, virtual (17Sep21)	*•CIOMS MLGs*
PERI Global Labeling & Regulatory Symposium, virtual (18Oct23)	*•CIOMS MLGs*

Therapeutic Innovation & Regulatory Science (2022) 57:1–6
https://doi.org/10.1007/s43441-022-00393-1

COMMENTARY

MedDRA Labeling Groupings to Improve Safety Communication in Product Labels

Ilona Große-Michaelis, MD, PhD[1] · Scott Proestel, MD[2] · Radhika M. Rao, MD MPH[3] · Brian S. Dillman, MD[4] · Silvia Bader-Weder, MD[5] · Lynn Macdonald, BSP[6] · William Gregory, MD, PhD[7]

Received: 7 September 2021 / Accepted: 14 March 2022 / Published online: 8 August 2022

Abstract
The granularity and structure of the International Council for Harmonisation's (ICH) Medical Dictionary for Regulatory Activities (MedDRA) are useful for precise coding of adverse events (AEs) for data analysis. In product labeling for healthcare practitioners, however, the granularity of MedDRA Preferred Terms (PTs) can obscure the communication of adverse reactions (ARs). Driven by a focus on patient safety, business needs, and regulatory guidance, many sponsors and regulators have begun to develop institution-specific approaches to clustering similar AR terms in medical product prescribing information on a product-by-product basis. However, there are no agreed upon conventions that describe which AR terms may be appropriate to group together. In order to improve safety communication to patients and healthcare providers, there is an urgent need for a harmonized international approach to the creation and use of groups of MedDRA PTs which we refer to as "MedDRA Labeling Groupings (MLGs)" in medical product prescribing information. Given its long-standing contributions towards the design of Standardised MedDRA Queries (SMQs), the Council for International Organizations of Medical Sciences (CIOMS) convened an Expert Working Group (EWG) with involvement of multiple major stakeholders to produce a consensus document on principles and points to consider in the development of MLGs. The CIOMS MLG EWG identified variations in grouping of MedDRA PTs in product labels, and in the current document, proposes a strategy for improving the communication of drug safety labeling. It is envisaged that the use of these consensus recommendations would be voluntary and applied to product labels in a manner that is consistent with existing regulatory frameworks.

DIA: Drug Information Association
DIA-NIFDS: National Institute of Food and Drug Safety Evaluation
ISoP: International Society of Pharmacovigilance
PERI: Pharmaceutical Education and Research Institute, Inc.
PV: Pharmacovigilance
SACB: Safety Analytics Control Board

Where did we start from?

- Are terms that represent the same phenomenon actually grouped in labels?
- How are they grouped (when they are)?

Analysis of Product Labels in the US and EU

Very **heterogeneous** picture, with a few challenges identified:

- Groupings are **not created** when they could have (highly similar Terms representing the same adverse reaction are listed separately)
- Groupings are used, but their **content is not documented** in label
- Groupings are used, content documented but terms included have:
  - very **broad scope**
  - **different severity**
  - **different etiology**
- Groupings for the same product may have **different content** in the label in use in **different jurisdictions**

Examples of Labels

ADR	Drug	Grouping created	Terms in Table	Grouped terms listed in footnote	Challenges
Gastrointestinal perforation	A	No	Gastrointestinal perforation, Large intestinal perforation, Intestinal perforation	n/a	No grouping created but various Terms representing gastrointestinal perforation are individually presented in the table
Rash	B	Yes	Rash	None. The note says that Rash includes multiple adverse reactions	Group exists, but content not indicated
Abdominal pain	C	Yes	Abdominal pain	Abdominal pain, Abdominal pain lower, Abdominal pain upper, **Abdominal rigidity**, Abdominal tenderness, **Acute abdomen**, Esophageal pain	Variable severity and prognosis
Neutropenia	D	Yes	Neutropenia	**Agranulocytosis**, Febrile neutropenia, Neutropenia, Neutrophil count decreased.	Variable severity and prognosis
Depression	E	Yes	Depression	Depressed mood, Depression, **Suicidal ideation,** and **Completed suicide**	Variable severity and prognosis

A-E represent different drugs, whose identity has been anonymised

Examples of Labels (continued)

ADR	Drug	Grouping created	Terms in Table	Grouped terms listed in footnote	Challenges
Edema	F	Yes	Edema	**Face edema**, Generalized edema, Local swelling, Localized edema, Edema, Edema peripheral, **Periorbital edema**	Different etiology (**allergic** and cardiac)
Neuropathy	G	Yes	Neuropathy	Burning sensation, Dysaesthesia, Formication, Gait disturbance, Hyperaesthesia, Hypoaesthesia, Hypotonia, Motor dysfunction, Muscle atrophy, Muscular weakness, Neuralgia, Neuritis, Neuropathy peripheral, Neurotoxicity, Paraesthesia, Peripheral motorneuropathy, Peripheral sensorimotor neuropathy, Peripheral sensory neuropathy, Peroneal nerve palsy, Polyneuropathy, Sensory disturbance, Skin burning sensation (**label in one jurisdiction**) Gait disturbance, Hypoesthesia, Muscular weakness, Neuralgia, Neuropathy peripheral, Paresthesia, Peripheral sensory neuropathy, Polyneuropathy, Sensory disturbance (**label in another jurisdiction**)	Very broad scope of terms included, **variable content across jurisdictions**

F-G represent different drugs whose identity has been anonymised

Outcome of Analysis and Next Steps

- There is **need for guidance** to promote harmonisation in the representation of ADRs within product labels

- CIOMS MLG EWG undertook task to provide this guidance by defining principles and conventions to support the creation of MLGs

- Work of the MLG CIOMS EWG **does not have any impact on the existing regulatory framework**: product labels remain the result of the negotiation between the Applicant and Regulators

- MLGs are only intended as a supportive tool (**voluntary use**)

Radhika M Rao, MD MPH

AbbVie

MLG Characteristics and Objective

Characteristics:

- Definition: MLGs are **groupings of near-synonymous MedDRA PTs that convey substantially similar clinical concepts**
- An MLG can represent a medical diagnosis or describe specific clinical signs and symptoms, but will generally not group all potential signs and symptoms under a medical diagnosis unless the PTs for these categories are near-synonymous
- Due to similar etiology and homogeneity of the PTs, the scope of the MLG medical concept is quite narrow

Objective:

- Provide an accurate and consistent presentation of adverse reactions within product safety labels (PSL) for clear communication to health care providers
- Avoid diluting or obscuring the true effect of the safety information, as described in relevant regulatory guidances

Principles for the Development and Use of MLGs

1. MedDRA PTs that convey **substantially** similar **clinical concepts** should be combined into MLGs when presented in product safety labeling

2. The process of grouping of PTs into MLGs should not result in the loss of **clinically meaningful safety information**

3. The use of MLGs, while recommended, should be **voluntary**

4. The content of MLGs, when used publicly, should be specified in order to ensure **transparency**

5. The use of MLGs is intended to foster international harmonization in a manner **consistent with existing regulatory frameworks**

6. MLGs should be made **easily accessible** and widely available to ensure transparency and **consistency**

MLG Conventions

1. MLGs are based on MedDRA terminology and are comprised of **MedDRA PTs**

2. The medical **concept** of the MLG should be clearly defined
   MLGs represent defined clinical conditions like diagnoses or specific clinical signs or symptoms or test results
   If an MLG represents a diagnosis, PT content usually does not reflect signs or symptoms of the ADR
   Typically, an MLG does not include complications of an ADR

3. PTs that specify or imply different **etiologies** should not be combined in the same MLG (e.g., should not combine “Haemolytic anaemia” with “Anaemia”)

4. PTs included should be **age-agnostic,** specific age groups should not be included (e.g., “neonatal”)

5. PTs that indicate different **clinical importance** should not be grouped together, e.g.:
   - PT *Abdominal pain* / PT *Abdominal rigidity*
   - PT *Migraine* / PT *Headache*
   - PT *Renal impairment* / PT *Renal failure*
   - PT *Haematoma* / PT *Subarachnoid haemorrhage*
   - PT *Angina pectoris* / PT *Myocardial infarction*

MLG Conventions contd.

6. The clinical concept reflected by the PTs should not be different from the **concept implied by the MLG name**

7. PTs that indicate nonspecific laboratory results such as “abnormal” may be included in an MLG only if the **lab abnormality is clinically meaningful in only one direction**, e.g., PT *Blood glucose abnormal* should not be included in the MLG *Hyperglycemia* because both increase and decrease of blood glucose are clinically meaningful
However, PT *Blood creatinine abnormal* could be included in an MLG *Renal insufficiency* because decreased blood creatinine is generally not clinically meaningful

8. MLGs, when created, should be in the most **current MedDRA version**

9. The MedDRA version of the MLG and the **MedDRA version of the respective data** should always be identical

Ilona Grosse-Michaelis, MD
Bayer/Retired

Benefits of MLGs and Unexplored Potential Applications

- MLGs aim to enhance the communication of the true safety profile of medicinal products, thus benefiting health care professionals
  - Avoid diluting or obscuring the true effect of the safety information

- Wherever MedDRA PTs are utilized to describe clinically meaningful safety information, grouping the MedDRA PTs could be helpful

- MLGs may have limited potential applications beyond product safety labeling, such as other safety documents with product-related information, (Investigator's Brochure, Company Core Data Sheet, and package leaflet), signal detection and other evaluation of clinical study safety data,
  - If MLGs are used in safety documents in addition to the safety section of the Product Safety Label, consistent Adverse Reaction representation in regard to MLG grouping is important
  - **However, these potential additional applications are not the objective of the MLGs**

- **The existing regulatory framework should be followed**

MLG Illustration: Part of Section 4.8 of SmPC for Product X

Frequency	Adverse reactions
SOC *Gastrointestinal disorder*	
Very common	*Nausea*
Common	*Abdominal pain* *

*Options of presenting an example MLG are illustrated below:

Option 1
Footnotes include only terms for which adverse events were reported

Abdominal pain* includes the **reported *terms Abdominal pain, Abdominal pain upper* and ***Gastrointestinal pain***.

Option 2
Footnotes include all terms that were grouped, stating which ones were reported

Abdominal pain* includes terms *Abdominal pain, Abdominal pain lower, Abdominal pain upper, Abdominal tenderness, Epigastric discomfort,* and *Gastrointestinal pain*. Only the terms ***Abdominal pain, Abdominal pain upper* and ***Gastrointestinal pain*** **have been reported**.

Silvia Bader-Weder, MD
Roche

Examples of MLG Development

Proposed MLG *Hyperkalemia*

Included PTs^:

- PT *Blood potassium increased*[1]
- PT *Hyperkalaemia*[2]

[1] SOC *Investigations**
[2] SOC *Metabolism and nutrition disorders**

Comments:

- The PTs belong to different MedDRA SOCs but are seen as describing the same medical concept
- Although they are a sign/symptom and a diagnosis, they are grouped together because they are near-synonymous PTs

Excluded PTs^:

- PT *Blood potassium abnormal*[1]
- PT *Pseudohyperkalaemia*[2]

[1] SOC *Investigations**
[2] SOC *Metabolism and nutrition disorders**

Comments:

- PT *Blood potassium abnormal* is clinically meaningful in both directions of laboratory abnormality and hence excluded
  PTs that indicate nonspecific laboratory results may be included in MLG only if lab abnormality is clinically meaningful in only one direction
- PT *Pseudohyperkalaemia* represents a false elevation in potassium that reflects a different medical concept than Hyperkalemia

* The System Organ Class (SOC) information is provided only for this proposed MLG example for illustrative purposes.
^Throughout the slides, unless indicated otherwise, the MedDRA versions used are MedDRA versions 24.0 and 24.1.

Examples of MLG Development (continued)

Proposed MLG *Abdominal Pain*

Included PTs:

- PT *Abdominal discomfort*
- PT *Abdominal pain*
- PT *Abdominal pain lower*
- PT *Abdominal pain upper*
- PT *Abdominal tenderness*
- PT *Epigastric discomfort*
- PT *Gastrointestinal pain*

Comments:

- Abdominal pain known to be poorly localized by patients and location of pain can change over time

Excluded PTs:

- PT *Abdominal migraine*
- PT *Abdominal rebound tenderness*
- PT *Abdominal rigidity*
- PT *Acute abdomen*
- PT *Enteric neuropathy*
- PT *Intestinal spasm*
- PT *Oesophageal pain*
- PT *Perihepatic discomfort*
- PT *Spleen pain*

Comments:

- PT *Abdominal rebound tenderness* (sign of peritonitis) and *PT Abdominal rigidity* were seen as more clinically important than abdominal pain, based on greater severity
- PT *Oesophageal pain* was seen as questionable for localization of abdominal pain

Comparison of SMQs and MLGs with an Example

Characteristics	Standardised MedDRA Queries (SMQ)	Proposed MedDRA Labeling Groupings (MLG)
Purpose	Safety signal detection in MedDRA-coded adverse event data sets	Safety communication in product safety label
Status	International MedDRA Preferred Term (PT) groupings exist	To be established
Content	Consist of MedDRA PTs that reflect a range or different aspects of a medical concept (heterogeneous concept)	Consist of MedDRA PTs that are nearly synonymous (homogeneous concept)
	Typically contain many more PTs than MLGs, given the lower threshold for similarity	Typically contain less number of PTs than SMQs given the higher threshold for similarity
	May contain a combination of MedDRA PTs related to a medical concept presenting: – signs and symptoms, and – diagnosis, and – diagnostic and therapeutic measurements	Contain MedDRA PTs related to a medical concept presenting: – signs or symptoms only, or – diagnosis only, or – diagnostic measurements only, or – therapeutic measurements only
Output when used for data retrieval	More sensitive than MLGs, but less specific	Too specific, not very sensitive

Example	SMQ *Acute renal failure* (narrow scope)*	Proposed MLG *Acute kidney injury*
	Consists of the following 19 PTs from MedDRA v24.0:	Consists of the following 2 PTs from MedDRA v24.0:
	PT *Acute kidney injury* PT *Acute phosphate nephropathy* PT *Anuria* PT *Azotaemia* PT *Continuous haemodiafiltration* PT *Dialysis* PT *Foetal renal impairment* PT *Haemodialysis* PT *Haemofiltration* PT *Neonatal anuria* PT *Nephropathy toxic* PT *Oliguria* PT *Peritoneal dialysis* PT *Prerenal failure* PT *Renal failure* PT *Renal failure neonatal* PT *Renal impairment* PT *Renal impairment neonatal* PT *Subacute kidney injury*	PT *Acute kidney injury* PT *Subacute kidney injury*

* SMQ *Acute renal failure* (broad search) consists of 51 PTs (including 19 PTs of narrow scope)

Scott Proestel, MD
Formerly FDA / Currently at Medpace

MLG LIMITATIONS

- Not all medical concepts may be amenable to MLGs (i.e., the concept may be better characterized in other ways)
- There may not be PTs available for grouping based on the current MedDRA version for all the medical concepts
- Lack of consistency across labels may be challenging, particularly as MLG use would be voluntary

Example: Hypersensitivity

Some concepts may encompass various clinical entities, and those in turn may have different manifestations and severity
An example is the umbrella concept “Hypersensitivity” characterized by various types of exaggerated immunological responses to stimuli ranging from urticaria to anaphylaxis
The MLG principles would require exclusion of these more specific terms, and therefore presenting a Hypersensitivity MLG might be quite misleading as the term suggest that all hypersensitivity AEs are being included

A *Hypersensitivity* MLG would likely include the near synonym PT *Drug hypersensitivity*, but not the PTs *Urticaria* or *Anaphylactic reaction*, since those represent different manifestations and degrees of severity
Therefore, such an MLG would not reflect all hypersensitivity despite the broad nature of its name, which could lead to confusion

CONCLUSIONS

- The CIOMS MLG EWG has:
  - Developed principles to be used to create MLGs
  - Identified the scope and applications for MLGs
  - Developed MLG conventions to support the creation of MLGs

- We believe that:
  - MLGs will improve communication in product safety labeling
  - MLGs will need to be communicated to stakeholders
  - Consistency across product safety labels would be promoted if MLGs were centrally created and available to all MedDRA users
  - Consistent application of MLGs across labels will be a challenge, particularly as their use will be voluntary

CONCLUSIONS (continued)

- Important issues will need to be addressed prior to MLG implementation:
  - Establishing MLG ownership and maintenance (due to MedDRA and medical practice changes)
  - Determining how to present MLGs consistently
  - Deciding how to display custom PT groupings

- While implementation of MLGs poses important challenges, we believe an open and deliberate process guided by MLG principles will provide a significant advance over the current situation of each institution taking its own approach

Glossary

- ADR/AR: Adverse Drug Reaction/Adverse Reaction
- CIOMS: Council of International Organization of Medical Sciences
- DIA: Drug Information Association
- DIA-NIFDS: National Institute of Food and Drug Safety Evaluation
- EMA: European Medicines Agency
- EWG: Expert Working Group
- EU: European Union
- FDA: Food and Drug Administration
- ISoP: International Society of Pharmacovigilance
- JMO: Japanese Maintenance Organization
- MLG: MedDRA Labeling Grouping
- MedDRA: Medical Dictionary for Regulatory Agency
- PERI: Pharmaceutical Education and Research Institute, Inc.
- PMDA: Pharmaceutical and Medical Devices Agency
- PT: Preferred Term
- PSL: Product Safety Label
- PV: Pharmacovigilance
- SACB: Safety Analytics Control Board
- SMQ: Standardized MedDRA Query
- SmPC: Summary of Product Characteristics
- SOC: System Organ Class
- US/U.S.: The United States


CIOMS
Thank you for your attention

Panel Discussion

Introduction of the Speakers/Panelists

Ilona Grosse-Michaelis
Bayer/Retired

Radhika M Rao
AbbVie

Silvia Bader-Weder
Roche

Scott Proestel
Formerly FDA / Currently at Medpace

Aniello Santoro
EMA