MedDRA Important Medical Events (IME) in the EU

Patricia Mozzicato, MD
MedDRA MSSO

www.diahome.org

Topics Covered

- MedDRA refresher
- Background of IME list
- Considerations in maintaining MedDRA-based term lists
  - Inclusion/exclusion criteria
  - Version updates
  - Examples from draft IME list
- IME list survey

MedDRA Refresher

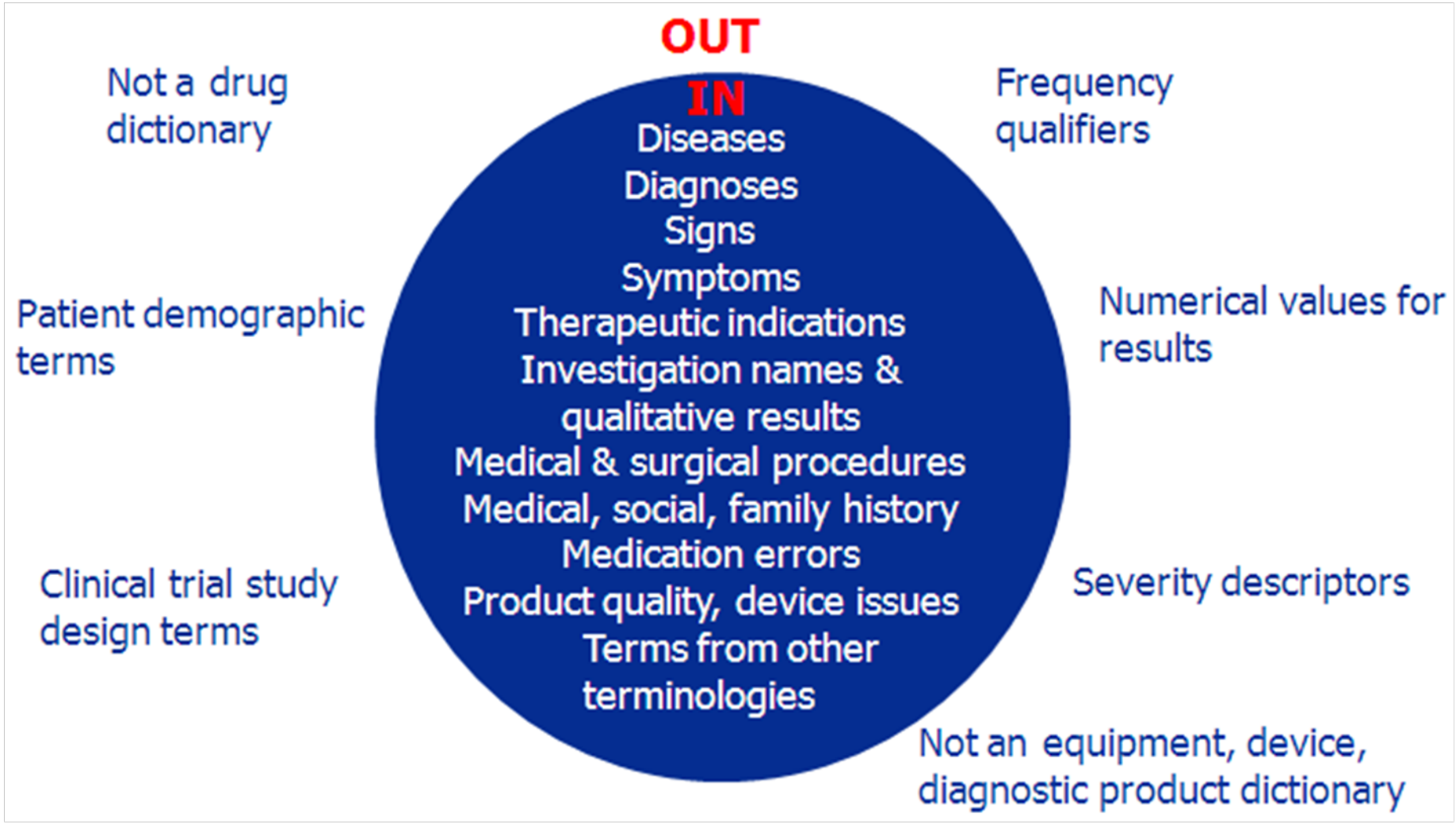
MedDRA Definition

MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.

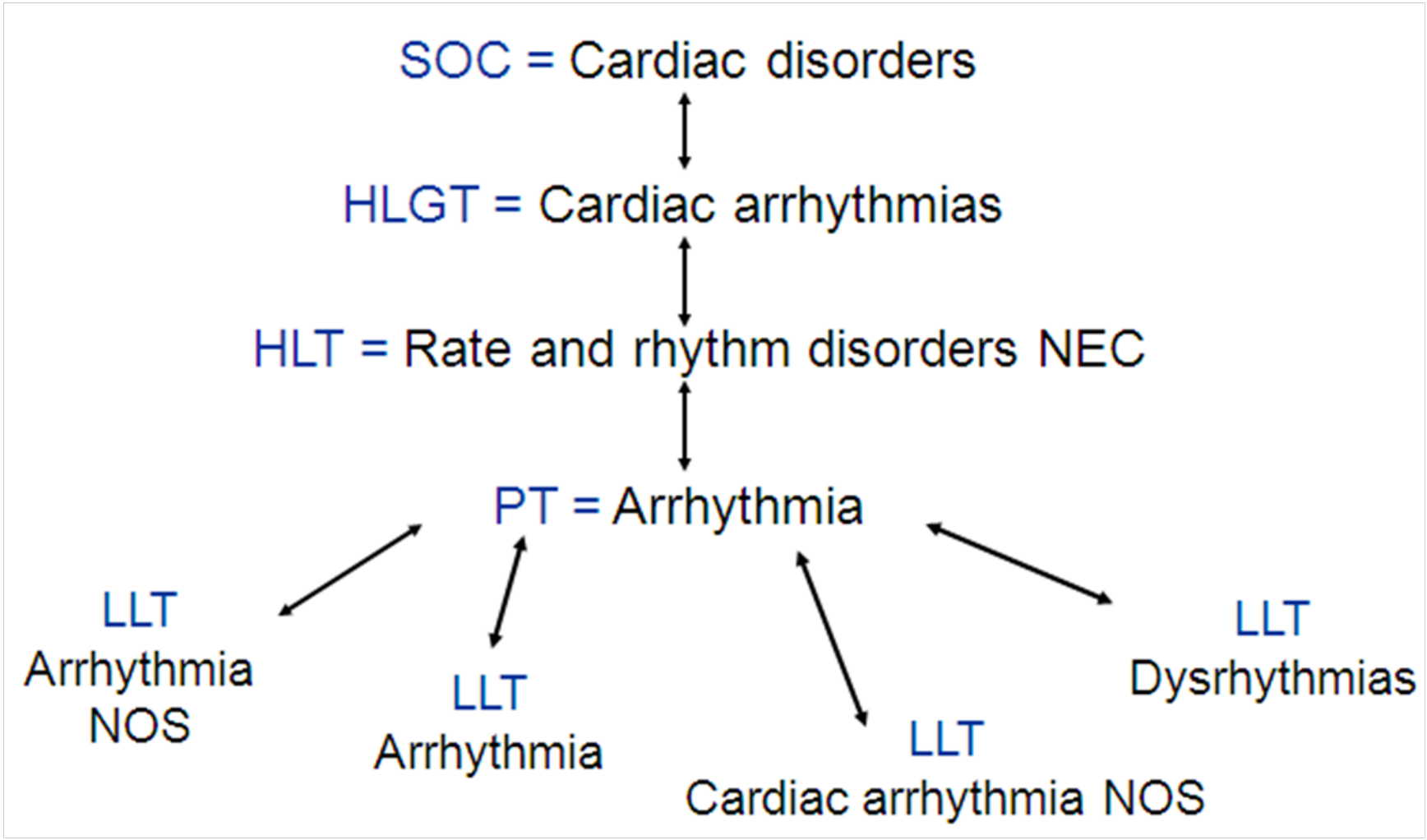
Regulatory Status of MedDRA in EU

- Clinical trials
  - SUSARs (Suspected Unexpected Serious Adverse Reactions)
- Volume 9A
  - Individual Case Safety Reports (ICSRs)
  - Adverse reactions in PSUR
  - Standardised MedDRA Queries (SMQs) recommended for signal detection
- Interface between EudraVigilance and EU Risk Management Plan – indications, risks, interactions
- Summary of Product Characteristics guideline

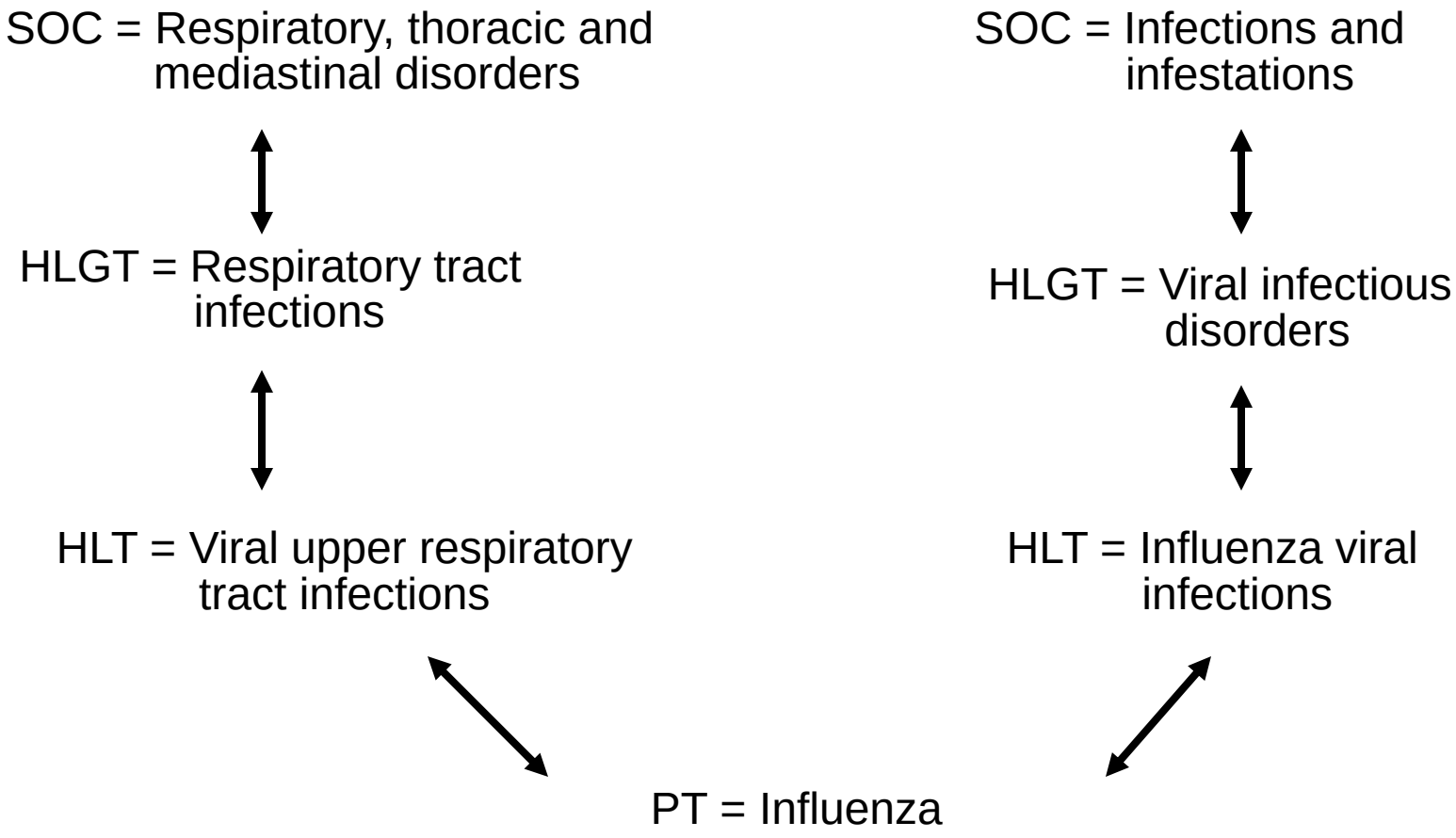
Scope of MedDRA



MedDRA's Structure



Multi-Axiality



Multi-Axiality (cont)

- For multi-axial terms, one SOC is **primary**
- Primary SOC rules for:
  - SOC *Congenital, familial and genetic disorders*
  - SOC *Infections and infestations*
  - SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
- Three SOCs are not multi-axial:
  - SOC *Investigations*
  - SOC *Social circumstances*
  - SOC *Surgical and medical procedures*

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)

Background of IME List

Purpose of IME List

- Facilitate:
  - Classification of suspected adverse reactions
  - Aggregate data analysis
  - Case assessment for pharmacovigilance activities
- Intended for **guidance purposes only**
  - Not mandatory requirement for regulatory reporting
  - Option to use it for other purposes

Initial Development of IME List

- Development by EV-EWG started in May 2007
- Identified MedDRA Preferred Terms (PTs) that are medically important regardless of presence of other regulatory seriousness criteria
- Based on an MHRA list

Initial Development of IME List (cont)

- **All terms** in three SOCs initially INCLUDED:
  - SOC *Congenital, familial and genetic disorders*
  - SOC *Infections and infestations*
  - SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
- **All terms** in two SOCs initially EXCLUDED:
  - SOC *Social circumstances*
  - SOC *Surgical and medical procedures*
- Remaining terms in 21 SOCs were assessed by volunteers with medical background

Inclusion of PTs on IME List

- Divided terms for inclusion into:
  - “Core serious” (CS) – always serious
  - “Extended serious” (ES) – serious in some circumstances only
- Teams of 4 – 6 volunteers reviewed the terms:
  - If majority agreed, term added
  - If “tie”, the more conservative assessment was taken (e.g., if 3 for CS and 3 for ES, term became CS)

Maintaining MedDRA-based Term Lists

MSSO and MedDRA Term Lists

- Term lists maintained by MedDRA MSSO
  - Gender-Specific Adverse Events
  - Pediatric Adverse events
  - Standardised MedDRA Queries (SMQs)

Considerations for Maintaining Term Lists

- Understand **purpose** of list
  - What is the intended use of the list?
  - Are there other ways the list may be used?
- Understand **scope** of list
  - What are the inclusion/exclusion criteria?

Maintenance of IME List

- List received for review in MedDRA v12.0; approx. 9000 PTs
- To update list to MedDRA v12.1, first inclusion/exclusion criteria needed to be developed
- Draft incl/excl criteria:
  - Overall
  - SOC-specific

Maintenance of IME List (cont)

- Inclusion/exclusion criteria based on **ICH definition of an IME**

"…may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above."

Examples: Inclusion/Exclusion Criteria

- Overall
  - Included
    - Generally, all infarct/infarction terms (e.g., PT *Renal infarct*)
    - Terms for failure or insufficiency of life-sustaining organ systems (PT *Hepatic failure*)
  - Excluded
    - “Pain” and “discomfort” terms (PT *Pain of skin*)

Examples: Inclusion/Exclusion Criteria (cont)

- SOC *Cardiac disorders*:
  - Included
    - All terms for cardiac valve disorders (e.g., PT *Aortic valve stenosis*)
    - All terms for endocardial disorders (PT *Endocardial fibrosis*)
  - Excluded
    - Terms for trivial arrhythmias that do not lead to more significant consequences (PT *Extrasystoles*)

Development of CS/ES Criteria

- Core serious
  - Precisely fits definition of an IME
    - Example: PT *Stroke in evolution*
- Extended serious
  - Does not precisely fit definition
  - Sometimes rather broad concept
  - *With additional clinical information,* may be or evolve into an IME
    - Example: PT *Anaemia*

Maintenance of IME List

- Original scope of IME list changed
  - **Selected** (not all) PTs from these SOCs are included:
    - SOC *Congenital, familial and genetic disorders*
    - SOC *Infections and infestations*
    - SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
  - **Selected** PTs from these SOCs are included (had originally been excluded):
    - SOC *Social circumstances*
    - SOC *Surgical and medical procedures*

Maintenance of IME List (cont)

- Apply incl/excl criteria to **new** v12.1 PTs
- Review existing terms on list against new criteria
- Review terms *not* on list against new criteria
- Check for other PT changes (demotion to LLT, change of primary SOC)

Versioning of IME List

- EV-EWG and PhVWP have both reviewed revised term list and proposed inclusion/exclusion criteria
- List will be updated with each new MedDRA version
- Experts will review updated lists and criteria with each new version

Current Activities

- EV-EWG created a survey for those who downloaded IME list
- Survey will be available online until 26 October 2010 (EudraVigilance Web site, under “News” - http://eudravigilance.emea.europa.eu/human/index.asp)
- Takes about 15-20 mins to complete
- Data will be treated in a confidential way: summary will be shared with MSSO, MedDRA Management Board and other interested parties

Goals of Survey

- To assess:
  - Type of users who tested the IME list
  - How IME list has been tested
  - How useful IME list has been
  - How to improve IME list in the future

Thank you