



# **MedDRA Blue Ribbon Panel: Proposed Revisions to the Neoplasm SOC**

12 April 2011

EMA, London, UK



# Acknowledgments

The MSSO is grateful to



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

for hosting this Blue Ribbon Panel meeting



# Agenda

0900 – 0915 Introduction

BRP members and MSSO staff

0915 – 0945 Background of topic

0945 – 1030 “Cyst” terms – delink from  
Neoplasm SOC?

Panel discussions/recommendations;  
Observer comments

[1030 – 1045 Break]



## Agenda (cont)

1045 – 1145 Specific histologic sub-types of neoplasms

Panel discussions/recommendations;  
Observer comments

1145 – 1245 Update MedDRA with current neoplasm classifications

Panel discussions/recommendations;  
Observer comments

[1245 – 1315 Break]



# Agenda (cont)

- 1315 – 1330 Summary of Panel  
Recommendations – Final comments by  
Observers
- 1330 Meeting concludes



# Panel Members

Stewart Geary (Eisai)

Jean-Marie Heim (Bristol-Myers Squibb)

Sebastian Monzon (Roche)

Gisele Sarosy (National Cancer Institute, USA  
[ret])

Atsuo Takashima (National Cancer Center, Japan)

Kevin Blake (EMA)

Multiple FDA experts (FDA)



# Why a Blue Ribbon Panel (BRP)?

- Provides a forum for MedDRA experts to discuss and make recommendations
- When there is a need for a broad discussion on a challenging MedDRA issue
- Engage subject matter experts
- Observers (audience), submitted comments
- Goal is to develop recommendations for MedDRA Management Board to consider



# **Background of Topic – Proposed Revisions to Neoplasm SOC**



# How MedDRA Is Used

- An international multi-lingual terminology
- Standardized communications
- Applied in all phases of development cycle
- Classification for a wide range of clinical information
- Support for multiple medical product areas



# Scope of MedDRA

**OUT**

**IN**

Diseases  
Diagnoses  
Signs  
Symptoms

Therapeutic indications  
Investigation names &  
qualitative results

Medical & surgical procedures  
Medical, social, family history  
Medication errors  
Product quality, device issues  
Terms from other  
terminologies

Not a drug  
dictionary

Frequency  
qualifiers

Patient demographic  
terms

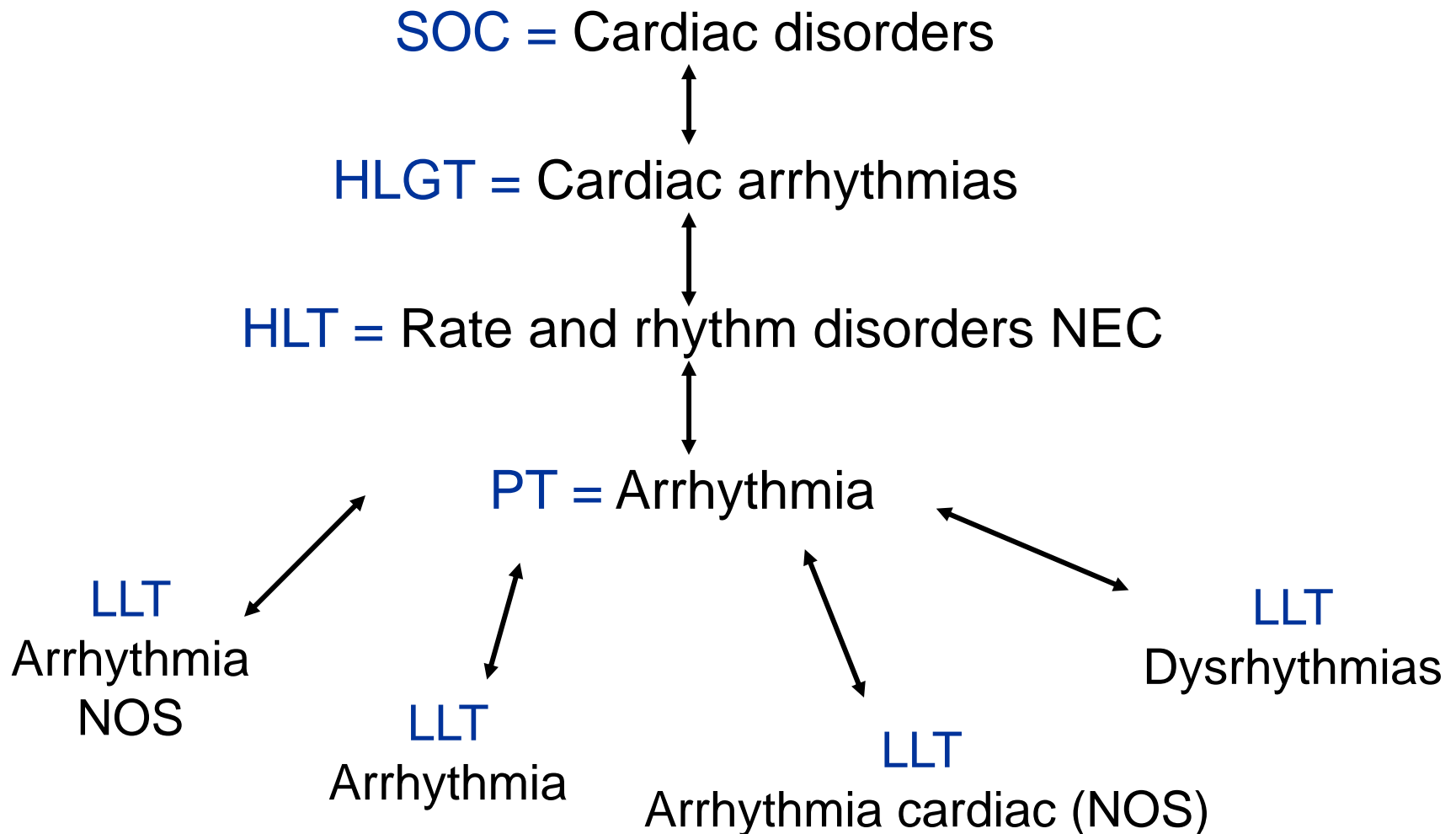
Numerical values for  
results

Clinical trial study  
design terms

Severity descriptors

Not an equipment, device,  
diagnostic product dictionary

# Organization of MedDRA





# ***SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps)***

- Characteristics:
  - Contains terms for **benign** and **malignant** neoplasms
  - Contains terms for **cysts** and **polyps**
  - Terms for benign and malignant neoplasm – this is the **primary** SOC
    - Secondary SOC is site of manifestation
  - Terms for cysts and polyps – this is the **secondary** SOC
    - Primary SOC is site of manifestation



# ***SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps) (cont)***

<b>Preferred Term</b>	<b>Primary SOC</b>	<b>Secondary SOC</b>
Benign lung neoplasm	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Respiratory, thoracic and mediastinal disorders
Chest wall cyst	Musculoskeletal and connective tissue disorders	Neoplasms benign, malignant and unspecified (incl cysts and polyps)



# Neoplasm SOC

- One of the largest MedDRA SOCs
  - Approx. 10% of all MedDRA PTs have primary or secondary link
- Growth rate parallels MedDRA's overall growth since 1999 (v2.1)



# History of Neoplasm SOC

- Initially developed from publication of US National Cancer Institute
  - Except non-Hodgkin's lymphomas (used International Lymphoma Study Group Classification)
- Basic SOC organization has not changed since 1999



## History of Neoplasm SOC (cont)

- Over the years, some users have pointed out deficiencies
- A few years ago, MSSO informally polled users:
  - Not much interest in addressing deficiencies
  - Used mainly for indications, not AE coding; not considered a priority



# MedDRA at US NCI

- Terminology serves an important role in NCI's research, clinical, and information efforts
- NCI works with many partners
  - Create and publish controlled terminology
  - Help develop and communicate information useful to scientists, clinicians, patients, and the public



## MedDRA at US NCI (cont)

- NCI Enterprise Vocabulary Services (EVS) provides services and resources
  - NCI Thesaurus
  - NCI Metathesaurus
- Facilitate standardization of terminology across the Institute and larger biomedical community



# MedDRA at US NCI (cont)

- Pathologist at NCI
  - Responsible for EVS concept modeling, defining semantic links/definitions for diseases, anatomy, cytogenetics, morphology, molecular biology, labs, etc.
  - Sources include:
    - MedDRA
    - SNOMED CT
    - ICD10; ICD9CM; ICD O
    - Others
    - Gene Ontology
    - HL7
    - CDISC
- Proposals to MSSO derived from challenges in mapping



## MedDRA at US NCI (cont)

- Cancer Therapy Evaluation Program (CTEP) uses MedDRA
  - CTCAE (Common Terminology Criteria for Adverse Events)
  - Diseases
  - Prior Therapies
  - “Other Causes” (Indications)



# What Has Changed?

- “Traditional” cancer therapeutics:
  - Local control with surgery and/or radiation, with combination chemotherapy for systemic control
  - Anti-hormonal therapies for certain malignancies (breast, prostate)
- More recently, focus on genetics of malignancy in development of therapies



# Targeted Cancer Therapy

- “The key to successful therapies is identification of critical, dysfunctional nodes in oncogenic networks whose effective inhibition will result in abrogation and/or reversal of the malignant state by apoptosis and/or differentiation. The specific targeted therapy or combination of therapies should be less toxic to normal tissue, coupled to a large therapeutic window that targets the ‘context of vulnerability’ of the tumor.”
  - Mahadevan, D. Targeted cancer therapy. eMedicine (<http://emedicine.medscape.com/article/1372666-overview>)



# Examples of Targeted Cancer Therapies

Neoplasm	Genetics	Drug
Chronic myelogenous leukemia	BCR-ABL	Imatinib
Gastrointestinal stromal tumors	C-KIT/PDGFR	Imatinib
Breast and other carcinomas	HER-2	Trastuzumab



# Specificity of Diagnosis

- “First, simply diagnosing ‘non-small-cell carcinoma’ is no longer adequate when a specific cell type can be determined. Oncologists increasingly need a specific cell type diagnosis whenever possible.”
  - William Check, PhD, *CAP Today*, June 2010



# Proposal 1: Remove “Cyst” Terms from Neoplasm SOC



# Remove “Cyst” Terms from Neoplasm SOC

- Rationale:
  - “Cyst” is an anatomic designation which only very rarely confers the quality of “neoplasia” (abnormal growth of cells)



# Remove “Cyst” Terms from Neoplasm SOC (cont)

- Mechanics:
  - Removal of secondary link of most “cyst” terms
  - Keep remaining primary links
  - Example:

	PT	Primary SOC	Secondary SOC
Currently	Bone cyst	Musculoskeletal and connective tissue disorders	Neoplasms benign, malignant and unspecified (incl cysts and polyps)
If as proposed		Musculoskeletal and connective tissue disorders	[None]



# Remove “Cyst” Terms from Neoplasm SOC (cont)

- Please consider the following:
  - Would **analysis** of data coded with terms in Neoplasm SOC be enhanced, made more difficult, or remain the same?
  - Approximately 100 “cyst” PTs in Neoplasm SOC – and approx. 140 LLTs
  - Risks vs. benefits to balance medical correctness against impact on legacy and future coded data



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Excel 97-2003 Worksh



# Remove “Cyst” Terms from Neoplasm SOC (cont)

- QUESTION 1A:
  - Does the Panel recommend making this change to the “cyst” terms in MedDRA?



# Remove “Cyst” Terms from Neoplasm SOC (cont)

- QUESTION 1B:
  - If the Panel does not recommend making this change, does it have another recommendation?
  - Or should “cyst” terms remain in their current location in Neoplasm SOC?



# Remove “Cyst” Terms from Neoplasm SOC (cont)

## User Comments



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# Discussion



# **Proposal 2: More Specific Tumor Types at PT Level**



# More Specific Tumor Types at PT Level

- Histology often correlates with prognosis
  - E.g., adenocarcinoma of lung worse prognosis than squamous cell
  - Large cell neuroendocrine lung carcinomas worse prognosis than other large cell carcinomas
- NH lymphomas – divided into B, T, NK-cell type; stage, phenotype and histology guide treatment



# More Specific Tumor Types at PT Level (cont)

- Some specificity currently at LLT, but in some cases, certain subtypes are missing
  - E.g., no term for cribriform carcinoma of breast; no term for alveolar adenoma of lung



# Genetic Terms in MedDRA

- MSSO is currently working to add relevant pharmacogenetic terms proactively to MedDRA
- Some well-recognized oncogenes, other cancer-related genetic markers
  - E.g., K-RAS, c-MYC, etc.
- Potential to augment histologic specificity of terms



# More Specific Tumor Types at PT Level (cont)

- Rationale:
  - Oncologic therapies are being targeted at specific histologic types of tumors
  - Often combined with genetics
  - Increased specificity in MedDRA would allow for aggregation and analysis of specific tumor types
  - Some specificity currently at LLT, but in some cases, certain subtypes are missing



# More Specific Tumor Types at PT Level (cont)

- Impact:
  - Could be thousands of terms, including promotion of existing LLTs
    - 1909 PTs and 8383 LLTs in the Neoplasm SOC
    - Not all LLTs and PTs may be affected
  - Adding terms for subtypes that are not in MedDRA currently
  - Related to Proposal No. 3



# More Specific Tumor Types at PT Level (cont)

- Other considerations:
  - May still need non-specific terms (e.g., PT *Breast cancer*) for reports when specific tumor type unknown
  - Currently PTs for many malignant neoplasms include stage of tumor
  - Panel is asked to consider fate of the existing “stage” PTs

# “Stage” PTs in MedDRA

- [-] **HLT** Ovarian neoplasms malignant (excl germ cell)
  - [+] **PT** Malignant ovarian cyst
  - [+] **PT** Ovarian cancer
  - [+] **PT** Ovarian cancer metastatic
  - [+] **PT** Ovarian cancer recurrent
  - [+] **PT** Ovarian epithelial cancer
  - [+] **PT** Ovarian epithelial cancer metastatic
  - [+] **PT** Ovarian epithelial cancer recurrent
  - [+] **PT** Ovarian epithelial cancer stage I
  - [+] **PT** Ovarian epithelial cancer stage II
  - [+] **PT** Ovarian epithelial cancer stage III
  - [+] **PT** Ovarian epithelial cancer stage IV
  - [+] **PT** Ovarian low malignant potential tumour
  - [+] **PT** Ovarian stromal cancer



# More Specific Tumor Types at PT Level (cont)

- Question 2A:
  - Should the MSSO add specific histologic subtypes of neoplasms to the PT level?



# More Specific Tumor Types at PT Level (cont)

- Question 2B:
  - If yes for 2A, what is the optimal approach?
    - MSSO to add terms proactively
    - Populate through Change Request process
    - Add terms in one MedDRA release or over multiple releases
    - Another approach?



# More Specific Tumor Types at PT Level (cont)

- Question 2C:
  - If yes for 2A, what should be the fate of existing “stage” terms in MedDRA (currently at the PT level)?
    - Note: “stage” terms also include “metastatic” and “recurrent” qualifiers



# More Specific Tumor Types at PT Level (cont)

- Question 2D:
  - How would increased specificity affect coding and retrieval?
    - E.g., how would one code a term describing a specific lung tumor and its EGFR status?



# More Specific Tumor Types at PT Level (cont)

## User Comments



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Word Document



# Discussion



# **Proposal 3: Update the Neoplasm SOC Tumor Classifications**



# Update Tumor Classifications

- Many tumor classification systems
  - French-American-British [FAB] classification for acute leukemia
  - World Health Organization (WHO)
    - For many – but not all – organ systems
  - ICD-O
- Evolve and change over time
  - Maintenance implications for MedDRA



# Update Tumor Classifications (cont)

- Some neoplasms currently in MedDRA are not up-to-date
  - e.g., PT/LLT *Cystosarcoma phyllodes* should be “phyllodes tumor”
- There are gaps in MedDRA
  - Many neoplasms listed in standard classifications systems are missing



# Update Tumor Classifications (cont)

- Rationale and impact
  - Similar to those for proposal No. 2
- If “gaps” of missing histologic subtypes were filled, increase in PTs could be in the 100s
- Existing out-of-date terms would need to be addressed
  - Probably be made non-current LLTs



# Update Tumor Classifications (cont)

- Considering both Proposal Nos. 2 & 3
  - If “yes” to Question 2A, then standard tumor classification systems used as basis for new terms
  - A more limited approach (if “no” on Proposal No. 2)
    - MSSO to update existing neoplasm terms to be consistent with modern neoplasm classifications



# Update Tumor Classifications (cont)

- Example: Renal cell carcinoma



Microsoft Office  
Excel Worksheet

- Example: Pancreatic exocrine carcinoma



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Excel Worksheet



# Update Tumor Classifications (cont)

- Question 3:
  - Should standard neoplasm classification systems (e.g., WHO classifications) be used as the basis for neoplasm terms in MedDRA?



# Update Tumor Classifications (cont)

## User Comments



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Word Document



# Discussion



**Thank You**