



Proactive MedDRA Maintenance Model and Proposed Revisions to the Neoplasm SOC

MedDRA MSSO User Group Meeting
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Proactive MedDRA Maintenance Model

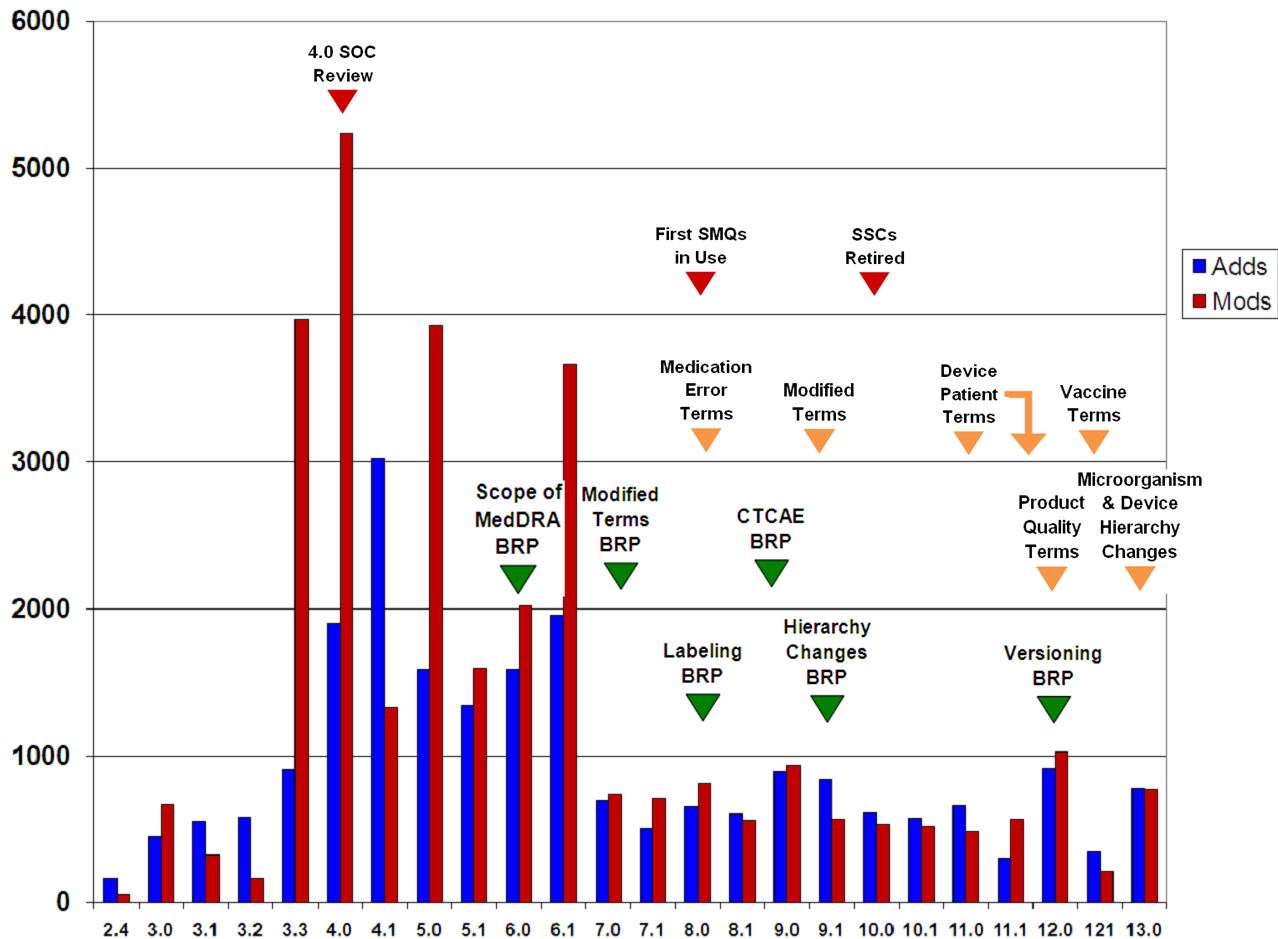


Background

- MedDRA is successful because it is user-driven
- Early days of MedDRA – filling in “gaps”
- More recently, changes of two types have become more prominent
 - Changes that increase scope (e.g., medication errors, product quality terms)
 - “Fine-tuning” of existing terms



Change Requests and MedDRA Initiatives





What is Proactive MedDRA Maintenance?

- Corrections/improvements made internally by the MSSO
 - Without need for specific subscriber Change Requests
 - May be term by term or more regional changes (consistency, etc.)
- General changes suggested by users outside the Change Request process



Submission of Ideas

- Submit your ideas to the MSSO Help Desk: msohelp@ngc.com
- Justification for submitted ideas is appreciated
- Example:
 - “Please identify all HLTs with only one PT and determine if the PT can be consolidated into other existing HLTs. Consolidating these ‘single’ PTs into existing HLTs could work to improve safety signal strength.”



Evaluation of Proposals

- MSSO will evaluate all input received
- Idea **may** be implemented in a future MedDRA version
- Things to keep in mind:
 - Not a substitute for Change Request process
 - MSSO not obligated to respond to suggestions
- Ideas posted on MSSO Web site
http://www.meddramsso.com/subscriber_proactive_maintenance.asp



Proactive MedDRA Maintenance

- MSSO will communicate with users when making major proactive changes
 - Expert Panel
 - Complex change proposals
 - Special broadcast e-mails seeking feedback
 - What's New document



Proposed Revisions to the Neoplasm SOC



Background

- *SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps)* - one of the largest SOC

MedDRA Versions							
	2.1	3.0	4.1	6.0	9.0	12.0	13.1
LLT	6299	6339	6922	7269	7662	7873	7876
PT	1338	1361	1570	1632	1629	1695	1699
HLT	200	200	198	196	196	203	203
HLGT	40	40	40	40	40	40	40
Total	7877	7940	8730	9137	9527	9811	9818



Background (cont)

- Term placement has remained largely unchanged since MedDRA v2.1
- More “stage” (clinical) than “pathology” focused
- Significant changes in malignant neoplasms therapies not reflected in MedDRA
 - Therapies for a genetic characteristic of a specific histologic tumor sub-type
- Neoplasm SOC developed when changes in therapeutic approaches were just beginning



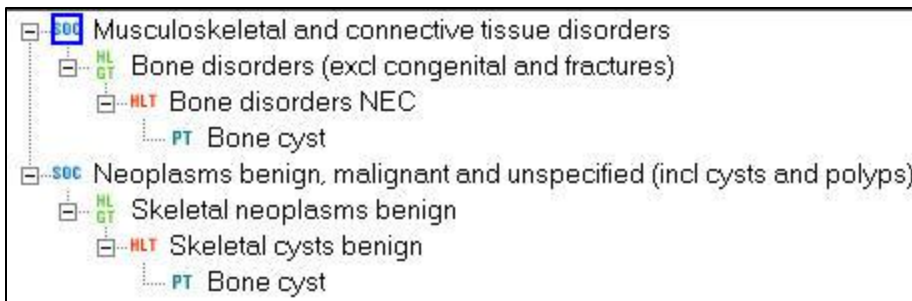
Background (cont)

- NCI physician proposed a set of revisions
 - Remove “cyst” terms
 - Increase histologic specificity (at PT level)
 - Improve neoplasm classifications
- Support from users to discuss changes in a BRP

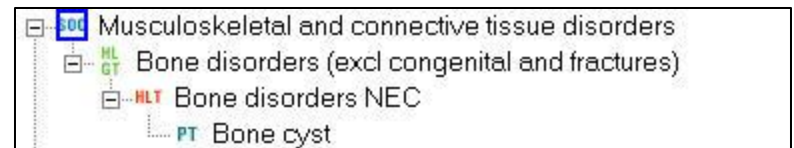
Proposal # 1

- Move “cyst” terms from Neoplasm SOC and keep them only in their “site of manifestation” SOC

Present



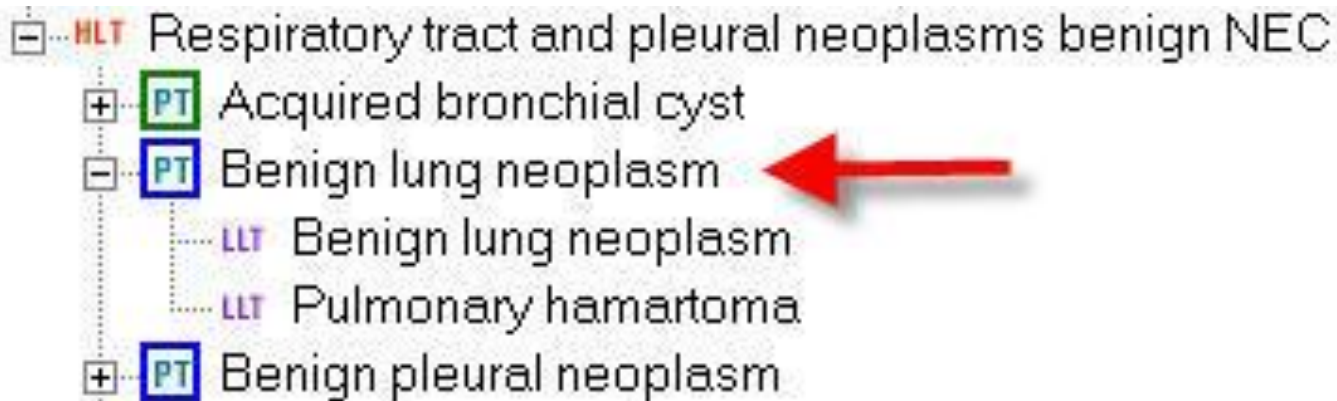
Future?



- Rationale: “cyst” is an anatomic designation which only very rarely confers the quality of “neoplasia”

Proposal # 2

- Place more specific histologic tumor types on the PT level
 - Some specific histologic subtypes at the LLT level, but others missing



Proposal # 2 (cont)

- SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps)
 - + HL Breast neoplasms benign (incl nipple)
 - + HL Breast neoplasms malignant and unspecified (incl nipple)
 - HLT Breast and nipple neoplasms malignant
 - + PT Breast cancer
 - + PT Breast cancer female
 - + PT Breast cancer in situ
 - + PT Breast cancer male
 - + PT Breast cancer metastatic
 - + PT Breast cancer recurrent
 - + PT Breast cancer stage I
 - LLT Breast adenocarcinoma stage I
 - LLT Breast cancer NOS stage I
 - LLT Breast cancer stage I
 - LLT Breast carcinoma NOS stage I
 - LLT Breast carcinoma stage I
 - LLT Carcinoma breast stage I
 - LLT Colloidal breast carcinoma stage I
 - LLT Ductal breast carcinoma stage I
 - LLT Lobular breast carcinoma stage I
 - LLT Lobular carcinoma stage I
 - LLT Medullary carcinoma of breast stage I
 - LLT Mucinous breast cancer stage I
 - LLT Mucinous ductal breast carcinoma stage I
 - LLT Tubular breast cancer stage I
 - + PT Breast cancer stage II
 - + PT Breast cancer stage III
 - + PT Breast cancer stage IV

- HLT Breast and nipple neoplasms malignant
 - + PT Breast cancer
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 - LLT Lobular carcinoma stage II
 - LLT Medullary carcinoma of breast stage II
 - LLT Mucinous breast cancer stage II
 - LLT Mucinous ductal breast carcinoma stage II
 - LLT Tubular breast cancer stage II
 - + PT Breast cancer stage III
 - + PT Breast cancer stage IV



“Broad” and “Stage” terms

- MSSO recommends that the relatively “broad” terms for neoplasms (e.g., PT Breast cancer) remain in MedDRA
 - Reported specific tumor type may not be known (e.g., breast cancer vs. medullary carcinoma)
- What should be the fate of the existing “stage” terms in MedDRA (currently at the PT level)?

Stage vs. Grade

- How should MedDRA handle stage vs. grade of tumors?
 - Many existing malignant neoplasms PTs include the tumor stage
 - Handful of terms cite the grade of a tumor

HLT	Follicle centre lymphomas, follicular grade I, II, III
PT	Follicle centre lymphoma, follicular grade I, II, III
PT	Follicle centre lymphoma, follicular grade I, II, III recurrent
PT	Follicle centre lymphoma, follicular grade I, II, III refractory
PT	Follicle centre lymphoma, follicular grade I, II, III stage I
PT	Follicle centre lymphoma, follicular grade I, II, III stage II
PT	Follicle centre lymphoma, follicular grade I, II, III stage III
PT	Follicle centre lymphoma, follicular grade I, II, III stage IV



HLT Breast and nipple neoplasms malignant

PT Breast cancer

- LLT Adenoid cystic breast carcinoma
- LLT Apocrine breast carcinoma
- LLT Breast adenocarcinoma
- LLT Breast cancer
- LLT Breast cancer aggravated
- LLT Breast cancer invasive NOS
- LLT Breast cancer NOS
- LLT Breast cancer stage unspecified
- LLT Breast carcinoma
- LLT Breast carcinoma NOS
- LLT Breast ductal cancer infiltrating
- LLT Breast ductal cancer invasive
- LLT Breast ductal carcinoma
- LLT Breast lump (malignant)
- LLT Breast tumor malignant
- LLT Breast tumour malignant
- LLT Ca breast
- LLT Carcinoma breast
- LLT Colloidal breast carcinoma
- LLT Estrogen receptor positive breast cancer
- LLT HER-2 positive breast cancer
- LLT Infiltrating ductal breast cancer
- LLT Invasive ductal breast cancer
- LLT Lobular breast carcinoma invasive
- LLT Lobular carcinoma of breast
- LLT Malignant breast neoplasm
- LLT Medullary carcinoma of breast
- LLT Mucinous breast cancer
- LLT Oestrogen receptor positive breast cancer
- LLT Papillary breast carcinoma
- LLT Tubular breast cancer



Genetics play a key role

- Oncologic therapies are being targeted at specific histologic types of tumors
- Authorised products have indications like:
 - "EGFR expressing metastatic colorectal carcinoma with non-mutated (wild-type) KRAS"



Proposal # 3

- Update the Neoplasm SOC according to standard tumor classification systems
 - WHO classification systems
- Changes to classification systems over time needs to be considered
- Terms out of date with current classifications need to be addressed
 - Probably made into non-current LLTs



WHO classification of LUNG cancer

Squamous cell carcinoma

- Papillary
- Clear cell
- Small cell
- Basaloid

Small cell carcinoma

- Combined small cell carcinoma

Adenocarcinoma

- Acinar
- Papillary
- Bronchioloalveolar carcinoma
 - Non-mucinous (Clara/pneumocyte type II)
 - Mucinous
 - Mixed mucinous and non-mucinous
- Solid adenocarcinoma with mucin
- Adenocarcinoma with mixed subtypes
- Variants
 - Well-differentiated fetal adenocarcinoma
 - Mucinous ("colloid") adenocarcinoma
 - Mucinous cystadenocarcinoma
 - Signet-ring adenocarcinoma
 - Clear cell adenocarcinoma

Large cell carcinoma

- Large cell neuroendocrine carcinoma
 - Combined large cell neuroendocrine ca.
- Basaloid carcinoma
- Lymphoepithelioma-like carcinoma
- Clear cell carcinoma
- Large cell carcinoma with rhabdoid phenotype

Adenosquamous carcinoma

- Ca. with pleomorphic, sarcomatoid elements
 - Carcinomas with spindle and/or giant cells
 - Pleomorphic carcinoma
 - Spindle cell carcinoma
 - Giant cell carcinoma
- Carcinosarcoma
- Pulmonary blastoma
- Others
- Carcinoid tumour
 - Typical carcinoid
 - Atypical carcinoid

(*) partial (malignant epithelial tumours only)



Targeted genes or proteins in lung cancer treatment

- HRAS
- BRAF
- JUN
- C-MYC
- L-MYC
- N-MYC
- 68kDa (neurofilament)
- CA 15-3
- CEA (carcino-embryonic antigen)
- Chromogranin A
- CK-20
- LSA (lipid-associated sialic acid)
- H-cadherin
- VEGF
- EGFR



How it may look like ...

SOC	HLGT	HLT	PT	LLT
				Neoplasms benign, malignant and unspecified (incl cysts and polyps)
				Respiratory and mediastinal neoplasms malignant and unspecified
				Lung neoplasms malignant
				Adenocarcinoma of lung
				Adenocarcinoma acinar of lung
				Adenocarcinoma of lung with mixed subtypes
				Adenocarcinoma papillary of lung
				Bronchioloalveolar carcinoma mucinous
				Bronchioloalveolar carcinoma nonmucinous
				Bronchioloalveolar mixed mucinous and non-mucinous or intermediate cell type
				Clear cell adenocarcinoma of lung
				Mucinous ("colloid") adenocarcinoma of lung
				Mucinous cystadenocarcinoma of lung
				Signet-ring adenocarcinoma of lung
				Solid adenocarcinoma of lung with mucin
				Well-differentiated fetal adenocarcinoma of lung
				Lung neoplasm malignant
				Lung cancer
				Lung neoplasm malignant NOS
				Small cell carcinoma of lung
				Combined small cell carcinoma of lung
				Squamous cell carcinoma of lung
				Squamous cell carcinoma basaloid of lung
				Squamous cell carcinoma clear cell of lung
				Squamous cell carcinoma papillary of lung
				Squamous cell carcinoma small cell of lung



Impact of proposals #2 and #3

- Impact to MedDRA is difficult to gauge
 - Increased degree of specificity would allow for aggregation and analysis
 - Impact could be thousands of terms
 - New terms (could be thousands)
 - Promoted LLTs
- MedDRA v14.0 Neoplasm SOC
 - 1938 PTs
 - 8441 LLTs



A possible approach ...

- Reports concerning neoplasm are subject to multiple considerations, such as the stage, histology, genetics. This may require that more than one MedDRA term be selected.
 - Invasive ductal breast cancer + Breast cancer stage III + HER-2 positive breast cancer



Proposed Revisions to Neoplasm SOC BRP

- Blue Ribbon Panel (BRP)
 - Goal: develop recommendations on an issue
 - Panel members represent ICH regions
 - Observers play important role
 - MSSO presents recommendations to Board for approval
- 12 April 2011, EMA in London, UK
- Registration is required

http://www.meddramsso.com/subscriber_events_brp.asp



Questions?