



»» TRANSFORMING PROMISING IDEAS INTO COMMERCIAL REALITY

MedDRA – Beyond that basic AE report. How SMQs and MedDRA structure can enhance reporting.

Pamela Giese

inVentiv Health Clinical, United Kingdom





The Basic AE Table

Primary System Organ Class MedDRA Preferred Term;	Treatment A N=4393 (100%)	Treatment B N=4766 (100%)
Blood and lymphatic system disorders	127 (2.89%)	117 (2.45%)
Anaemia vitamin B12 deficiency	0	0
Aplastic anaemia	0	0
Leukocytosis	7 (0.16%)	12 (0.25%)
Leukopenia	2 (0.05%)	3 (0.06%)
Lymph node calcification	1 (0.02%)	0
Lymphadenitis	1 (0.02%)	0



Problems in that Basic AE Table

- Can become huge and unwieldy
 - > Impractical to print reams of pages
 - > Reviewers resort to highlighters to find AEs of interest
- AEs are grouped by System Organ Class rather than Medical Conditions
- System Organ Class itself can contain a variety of Medical Conditions



» TRANSFORMING PROMISING IDEAS INTO COMMERCIAL REALITY

© 2014 inVentiv Health. All rights reserved.



MedDRA

- Medical Dictionary for Regulatory Activities
- Universal standard for identifying and classifying adverse events and medical history.
- Developed by the ICH (International Conference on Harmonization) and implemented first in 1999
- Currently in use by most regulatory bodies and its use is required in the USA, Europe, and Japan.



Coding is needed to harmonize terms for analysis

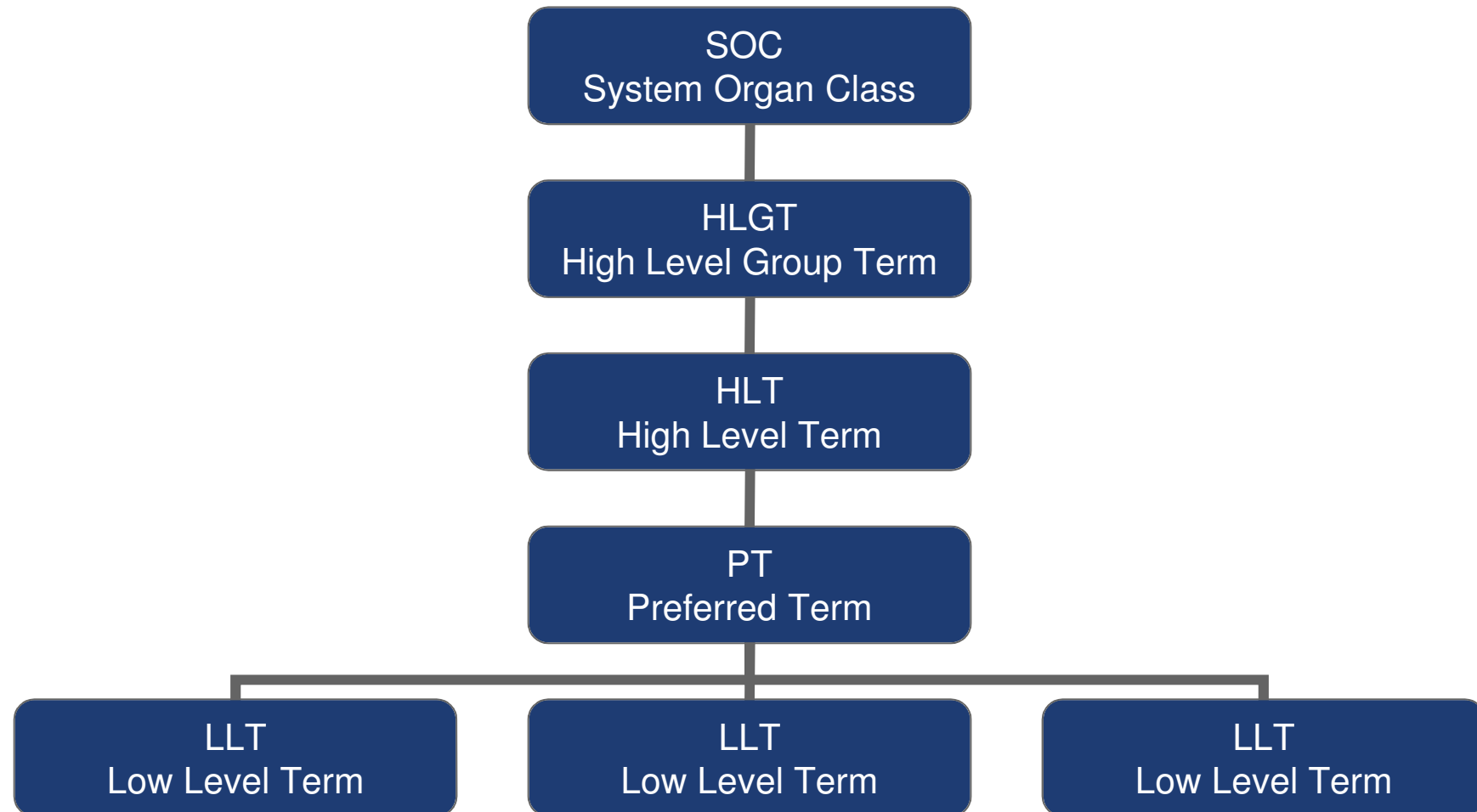
ABNORMAL LABS ALP (INCREASED)
ALP ELEVATION
ALP INCREASED
ALP elevated
ALP increase
ALP increased
ALP increased
ALP increased
CLINICALLY SIGNIFICANT
ELEVATED ALP
CLINICALLY SIGNIFICANT
ELEVATION IN ALP
ELEVATED ALP
ELEVATED ALP > 3XULN
ELEVATED ALP IN SERUM
ELEVATION OF ALP
ELEVATED LEVEL OF ALP
Elevation of ALP
FURTHER ELEVATION OF ALP
HIGH ALP
HIGH LEVEL OF ALP

Examples of original terms

ALP Increased
(LLT Term)

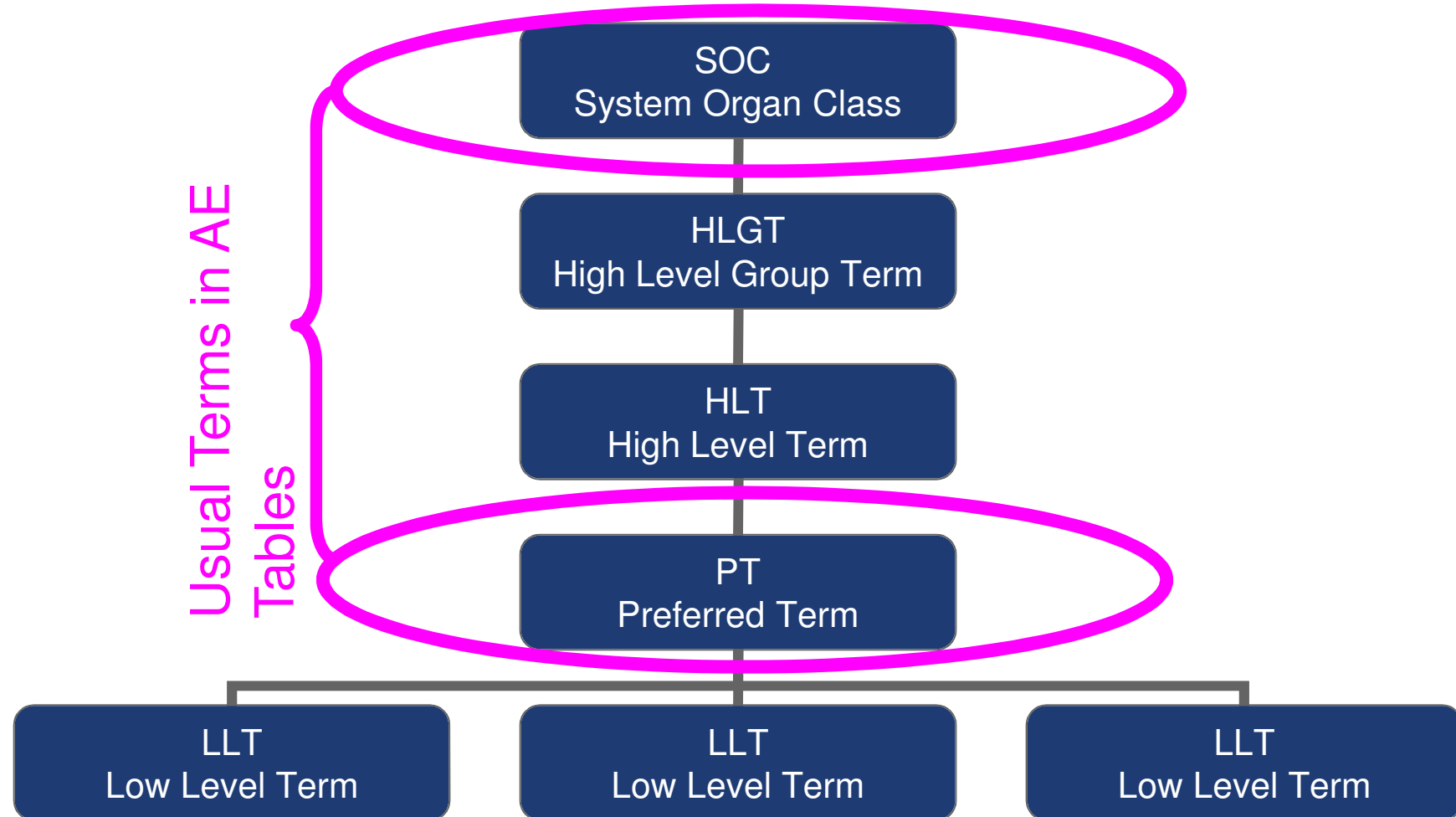


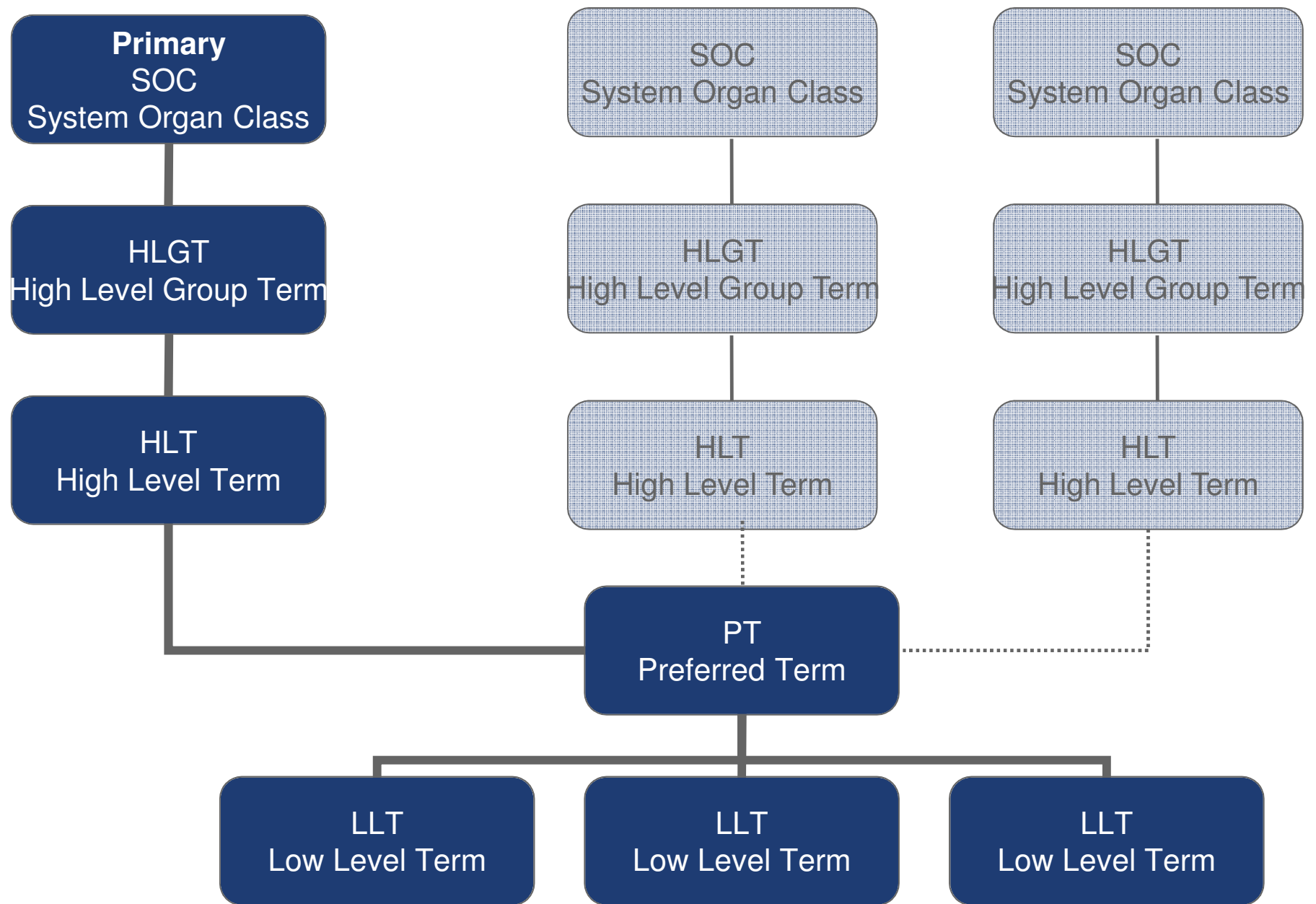
MedDRA Structure

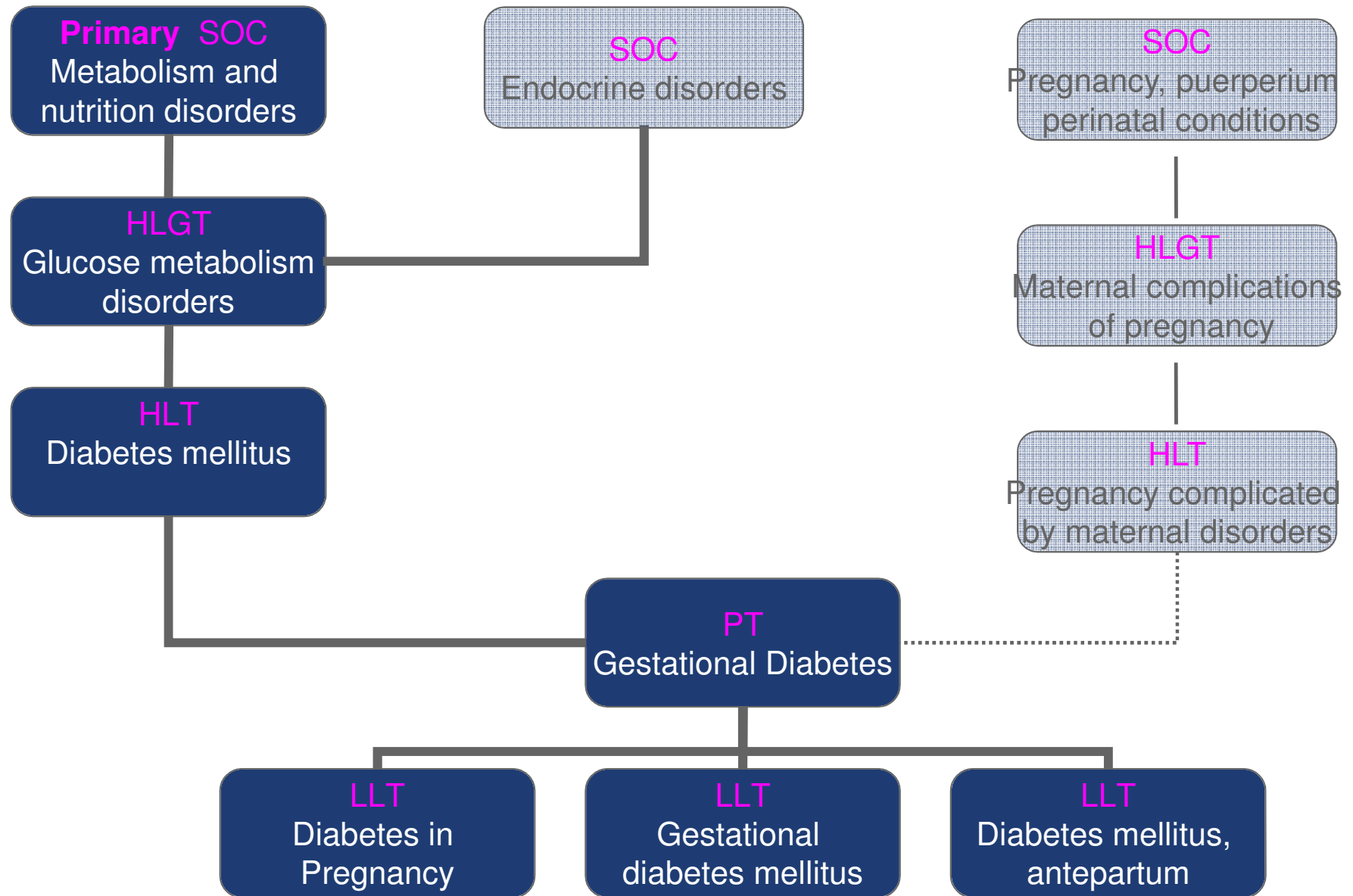




MedDRA Structure









Example –PTs within SOC

Primary	Treatment A	Treatment B
System Organ Class	N=4393 (100%)	N=4766 (100%)
MedDRA Preferred Term		
Blood and lymphatic system disorders	127 (2.89%)	117 (2.45%)
Anaemia	52 (1.18%)	50 (1.05%)
Anaemia megaloblastic	0	1 (0.02%)
Bone marrow failure	0	2 (0.04%)
Bone marrow oedema	0	1 (0.02%)
Coagulopathy	2 (0.05%)	0
Hypercoagulation	0	1 (0.02%)
Iron deficiency anaemia	9 (0.20%)	9 (0.19%)
Leukopenia	2 (0.05%)	3 (0.06%)
Lymph node calcification	1 (0.02%)	0

>> Example –PTs within SOC and High Level >> Group Term(HGLT)

Primary System Organ Class	Treatment A
High Level Group Term	N=4393 (100%)
Preferred Term	
Blood and lymphatic system disorders	127 (2.89%)
Anaemias nonhaemolytic and marrow depression	67 (1.53%)
Anaemia	52 (1.18%)
Anaemia megaloblastic	0
Bone marrow failure	0
Iron deficiency anaemia	9 (0.20%)
Coagulopathies and bleeding diatheses	15 (0.34%)
Coagulopathy	2 (0.05%)
Hypercoagulation	0
Spontaneous haematoma	1 (0.02%)

Example –PTs within SOC and High Level Term (HLT)

Primary System Organ Class	Treatment A
High Level Term	N=4393 (100%)
Preferred Term	
Blood and lymphatic system disorders	127 (2.89%)
Anaemia deficiencies	9 (0.20%)
Anaemia vitamin B12 deficiency	0
Iron deficiency anaemia	9 (0.20%)
Anaemias NEC	55 (1.25%)
Anaemia	52 (1.18%)
Microcytic anaemia	0
Normochromic normocytic anaemia	0
Bleeding tendencies	9 (0.20%)
Haemorrhagic diathesis	8 (0.18%)
Haemorrhagic disorder	0



Example –PTs within SOC, HGLT and HLT

Primary System Organ Class	Treatment A
High Level Group Term	N=4393 (100%)
High Level Term	
Preferred Term	
Blood and lymphatic system disorders	127 (2.89%)
Anaemias nonhaemolytic and marrow depression	67 (1.53%)
Anaemia deficiencies	9 (0.20%)
Anaemia vitamin B12 deficiency	0
Iron deficiency anaemia	9 (0.20%)
Anaemias NEC	55 (1.25%)
Anaemia	52 (1.18%)
Microcytic anaemia	0
Coagulopathies and bleeding diatheses	15 (0.34%)
Bleeding tendencies	9 (0.20%)
Haemorrhagic diathesis	8 (0.18%)
Haemorrhagic disorder	0



»» TRANSFORMING PROMISING IDEAS INTO COMMERCIAL REALITY

© 2014 inVentiv Health. All rights reserved.



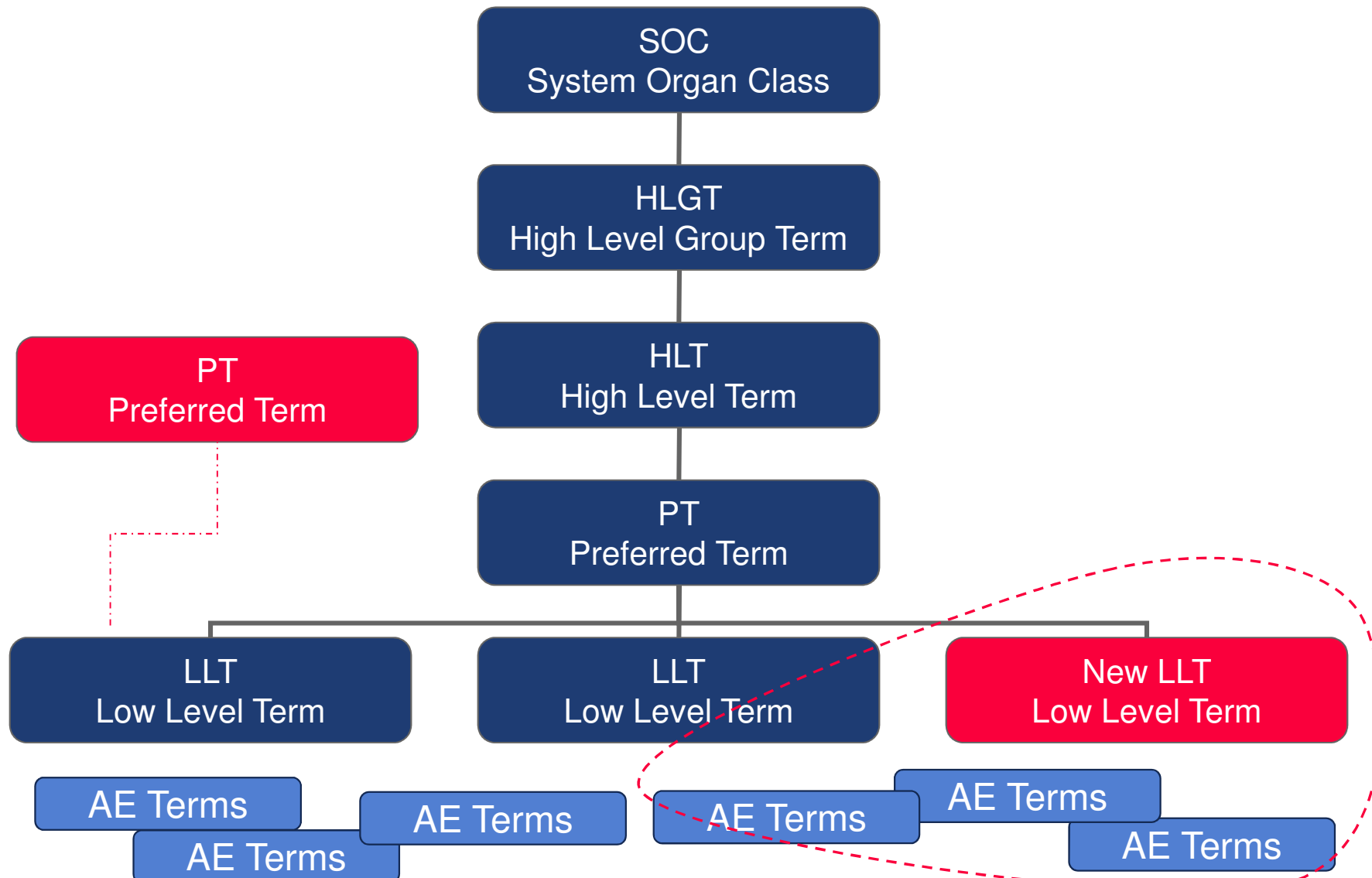
MedDRA Re-coding or Coding Updates

- MedDRA is updated every 6 months
- New codes are added
- Relationships to Primary SOC may change
- Because regulatory agencies such as EUDRA* require current use of MedDRA, long studies may need to be updated during course of study due to safety (pharmacovigilance) reporting
- Harmonization of MedDRA versions also needed in Integrated studies

*European Union Drug Regulatory Authorities



MedDRA Structure





SMQs



MedDRA Standardized Queries



inVentiv Health
clinical

»» TRANSFORMING PROMISING IDEAS INTO COMMERCIAL REALITY

© 2014 inVentiv Health. All rights reserved.



SMQ

Standardized Medical Queries

- Group AEs by Medical Condition not SOC
- Easier to identify AEs of interest
- A PT may belong to multiple SMQs (or none!)
- Useful in answering Safety/Regulatory enquiries
- SOC groups such as “Investigations” or “Infections and Infestations” contain wide variety of types of PTs



Example- Relationship of SMQs to SOC

SMQ Name	SOC Name	Count	Percent
Abdominal cavity hemorrhage	Gastrointestinal disorders	6	66.67%
Abdominal cavity hemorrhage	Investigations	1	11.11%
Abdominal cavity hemorrhage	Vascular disorders	2	22.22%
Abdominal infarction	Blood and lymphatic system disorders	1	20.00%
Abdominal infarction	Gastrointestinal disorders	3	60.00%
Abdominal infarction	Hepatobiliary disorders	1	20.00%



Example – Looking for Liver Infections

Primary SOC

Preferred Term

Treatment A

N=4393 (100%)

Infections and infestations

Genitourinary tract infection 1 (0.02%)

Gingival infection 1 (0.02%)

Graft infection 2 (0.05%)

H1N1 influenza 0

Helicobacter gastritis 1 (0.02%)

Hepatitis B 0

Hepatitis C 1 (0.02%)

Hepatitis E 1 (0.02%)

Herpes dermatitis 0

Herpes simplex 4 (0.09%)

Herpes virus infection 1 (0.02%)



SMQ: Liver Infections

SMQ	Treatment A	Treatment B	Treatment C
Preferred Term	N=4393 (100%)	N=4766 (100%)	N=5118 (100%)
Liver infections (SMQ)	2 (0.04%)	2 (0.04%)	4 (0.08%)
Hepatitis B	0	1 (0.02%)	0
Hepatitis B core antibody positive	0	1 (0.02%)	0
Hepatitis B virus test positive	0	0	1 (0.02%)
Hepatitis C	1 (0.02%)	0	1 (0.02%)
Hepatitis E	1 (0.02%)	0	1 (0.02%)
Liver abscess	0	0	1 (0.02%)



SOC source of SMQ: Liver Infections

SMQ	Treatment A	Treatment B	Treatment C
Preferred Term	N=4393 (100%)	N=4766 (100%)	N=5118 (100%)
Liver infections (SMQ)	2 (0.04%)	2 (0.04%)	4 (0.08%)
Hepatitis B	0	1 (0.02%)	0
Hepatitis B core antibody positive	0	1	0
Hepatitis B virus test positive	0	0	1 (0.02%)
Hepatitis C	1 (0.02%)	0	1 (0.02%)
Hepatitis E	1 (0.02%)	0	1 (0.02%)
Liver abscess	0	0	1 (0.02%)

Investigations

Infections and Infestations

Hepatobiliary disorders



SMQ “gotchas”

- SMQs may need medical review
- If used in a regulatory submission, SMQs need to be documented in an analysis dataset
- Because a Preferred Term can be associated with multiple SMQs, watch out for

DOUBLE COUNTING!



Resources

ICH. “MedDRA: ICH”. <http://www.ich.org/products/meddra.html>

MedDRA. “MedDRA MSSO”. <http://www.meddramsso.com>



Contact Information

Name: Pamela Giese
Enterprise: inVentiv Health Clinical
Address: 27 Logan Street
City, State ZIP: Langley Park, Durham
DH7 9YN, United Kingdom
Work Phone: +44 (0) 191 373 0550
Fax: +44 (0) 191 373 9626
E-mail: pamela.giese@inventivhealth.com
Web: <http://www.inVentivHealthclinical.com>