

Japanese Experience with MedDRA

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MedDRA

- The Medical Dictionary for Regulatory Activities (MedDRA) Terminology has been developed under the auspices of ICH.
- This new international medical terminology is particularly important in the electronic transmission of adverse event reporting, both in the pre- and post- marketing areas, as well as the coding of clinical trial data.

MedDRA

- The Terminology requires to be constantly updated and maintained and it was agreed that a Maintenance and Support Service Organisation (MSSO) would be needed to carry out this task and to distribute the terminology, on license, to users in industry and regulatory agencies.

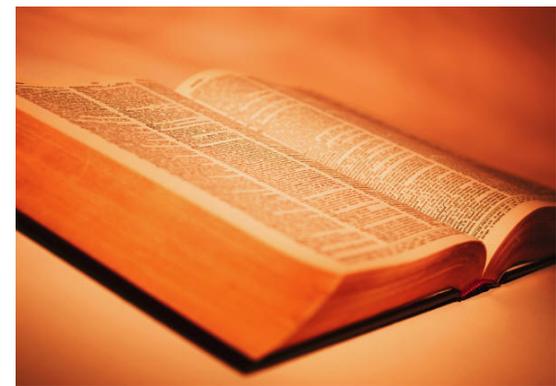
History of MedDRA

- October 1994
 - ICH recommended that MedDRA (ver.1.0) should form basis of a new medical terminology
- November 1994
 - ICH Steering Committee released a draft version (ver.1.1) of Terminology to review and evaluate
- March 1995
 - ICH Expert Working Group suggested changes as results of review
- February 1996
 - MedDRA (ver.1.5) released for review in US and Japan
- July 1997
 - ICH approval of international terminology

Implementation of MedDRA

- Implementation
 - in PMS and clinical development
 - in EU, Japan and US
- Translation for Dutch, French, Japanese etc.

Useful to exchange
ADRs between
regions



History of MedDRA/J implementation

- Before MedDRA/J
 - **J-ART (Japanese Adverse Drug Reaction Terminology) was used as terms for ADR in Japan, based on the translation of WHO-ART.**
 - Before implementation of MedDRA/J, from 1997 to 1998, the whole translation and validation were made by medical expert research group, sponsored by MHW.
- March 1999
 - The first MedDRA/J was released
- December 1999
 - Ministry of the Health and Welfare issued an official notification recommending the use of post-market ADR cases after 31 March, 2000

Transition of MedDRA/J implementation

- April 2000
 - MHLW started to receive MedDRA/J-coded ADR case reports.
 - Both J-ART terms and MedDRA/J terms became acceptable for coding ADR case reports
- September 2000
 - About **20%** of post-market ADR case reports submitted by companies to MHLW were coded with MedDRA/J terms
- October 2003
 - About **90%** of post-market ADR case reports submitted by companies to MHLW were coded with MedDRA/J terms
- From 27 October 2003, submission of company ADR reporting using MedDRA became mandatory. Nowadays, 100% of company ADR reports use MedDRA-J.

ADR Database transition of PMDA/MHLW

- Before October 2003, the old database accepted both ADRs coded by MedDRA and J-ART (WHO-ART basis)
- MedDRA terms and J-ART terms were stored inside the same database (the old database).
- Since J-ART terms were also coded with MedDRA, the old database could be retrieved in a MedDRA environment

Since 27 October 2003, all terms have been coded by MedDRA in the new database. The old database has been sustained as a legacy, however, its utility is nowadays so limited.

MedDRA vs. WHO-ART within the database before 2003

J-ART terms were also coded with MedDRA within old database

Case-ID	J-ART (code)	J-ART (term)	MedDRA (PT code)	MedDRA (term)
1	1111	YYY	100XXXXX	AAA
2	1122	ZZZ	100XXXXX	BBB
3			100XXXXX	CCC
4			100XXXXX	DDD

Case reports coded by J-ART

Case reports coded by MedDRA/J

Hierarchy	MedDRA 8.1 (Aug.2005)	WHOART (4 th Q 2003)
System Organ Class (SOC)	26	32
High Level Group Term (HLGT)	332	0
High Level Term (HLT)	1,683	171
Preferred Term (PT)	16,976	App.2,000
Lowest Level Term (LLT)	62,950	3,032

Double coding by MHLW

Expedited Reports from MAH

- Serious ADR Case Reports

- Domestic: 15 days

MedDRA/J required

- expected/unexpected death case
 - unexpected case
 - expected case of which drug was approved in the last 2 yrs
 - expected case of which drug is operating EPPV
 - unexpected ADR occurrence trends
 - case indicating health hazard by change of ADR occurrence trends

- Domestic: 30 days

MedDRA/J required

- others

- Foreign: 15 days

MedDRA/J required

- unexpected case
 - unexpected ADR occurrence trends
 - case indicating health hazard by change of ADR occurrence trends

ADRs Reporting from Healthcare Professionals

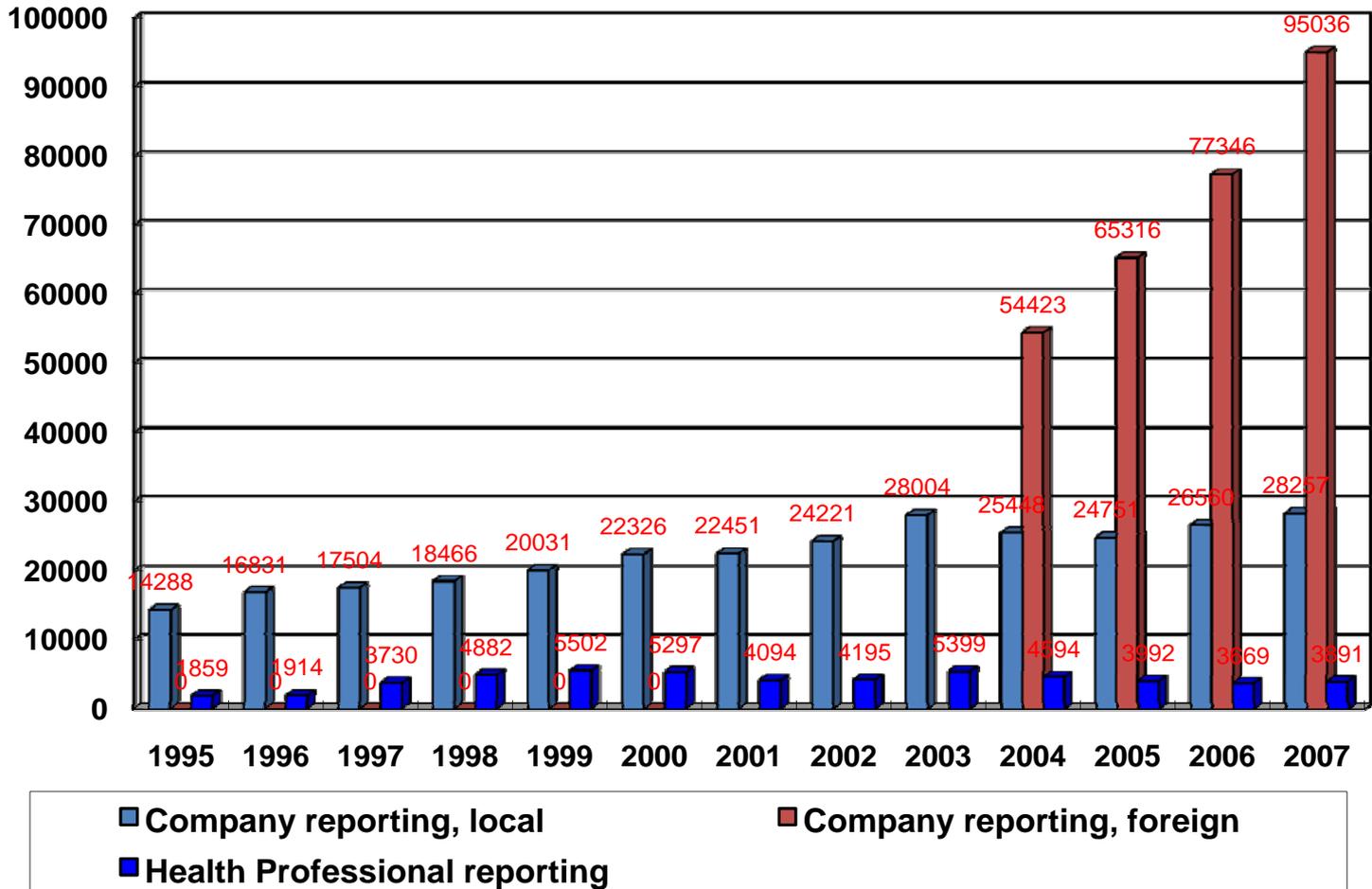
- HCPs shall report to MHLW, when
Receiving the occurrence of any diseases or
infections suspected to be caused by ADRs
and
Confirming the necessities of preventing the
occurrence or spread of hazards

MedDRA/J is not mandatory, but on receipt, PMDA codes the ADRs for database, using MedDRA.

AEs Reporting from Clinical Trial (Premarketing)

MedDRA/J required

ADR Report No.



Electronic reporting rate : 91.1% (2007)

MedDRA/J vs. MedDRA

- The same term and code of MedDRA/J corresponds to the term and code of MedDRA
- However, sometimes, a single term of Japanese translation may correspond to a few MedDRA terms, *vice versa* (NOT one to one relation)
- MedDRA/J includes Japanese originated term, such as the terms derived from J-ART code
- MedDRA/J is provided by JMO (Japanese Maintenance Organization)

Benefit of MedDRA/J

- Available world-wide
- Precise communication between regulatory authority in foreign country
- Global maintenance
- New version releases at the same time world-wide
- Provided as electronic files

Regulatory communication

- In response to the request of foreign agency to communicate, we can easily sort out PMDA's ADR database and translate them into English, using MedDRA/J to MedDRA coding.

(Example 1) Communication to other regulatory agencies

System Organ Class	Number of Adverse Events	
	H1N1 influenza vaccine	seasonal influenza vaccine (FY2006~FY2008)
Blood and lymphatic system disorders	4	15
Cardiac disorders	40	5
Ear and labyrinth disorders	7	3
Eye disorders	6	6
Gastrointestinal disorders	32	14
General disorders and administration site conditions	129	87
Hepatobiliary disorders	16	23
Immune system disorders	56	32
Infections and infestations	21	27
Injury, poisoning and procedural complications	0	1
Investigations	12	15
Metabolism and nutrition disorders	4	2
Musculoskeletal and connective tissue disorders	12	16
Neoplasmas benign, malignant and unspecified (incl cysts and polyps)	0	1
Nervous system disorders	113	153
Psychiatric disorders	2	4
Renal and urinary disorders	4	6
Respiratory, thoracic and mediastinal disorders	66	33
Skin and subcutaneous tissue disorders	30	36
Endocrine disorders	1	0
Pregnancy, puerperium and perinatal conditions	2	0
Vascular disorders	12	24
Total	569	503

(Example 2) Communication to other regulatory agencies

2010年度 (2010年4月～2011年3月)

SOC	PT	件数	
胃腸障害	イレウス	8	
	亜イレウス	2	
	悪心	1	
	胃腸出血	3	
	胃潰瘍	2	
	下部消化管出血	1	
	壊死性大腸炎	1	
	虚血性大腸炎	2	
	憩室穿孔	2	
	結腸ポリープ	1	
	十二指腸潰瘍	2	
	出血性胃潰瘍	2	
	出血性腸憩室	2	
	消化管穿孔	3	
	上部消化管出血	1	
	食道憩室炎	1	
	大腸穿孔	4	
	大腸潰瘍	2	
	腸閉塞	1	
	直腸穿孔	1	
	直腸潰瘍	2	
	腹膜炎	4	
	麻痺性イレウス	1	
	嘔吐	1	
	一般・全身障害および投与部位の状態	死亡	2
		心臓死	1
		発熱	1
	偽膜性大腸炎	1	
	虫垂炎	1	
	虫垂腫瘍	1	



FY:2010(from April 2010 to March 2011)

SOC	PT	number of cases
Gastrointestinal disorder	Ileus	8
	Subileus	2
	Nausea	1
	Gastrointestinal haemorrhage	3
	Gastric ulcer	2
	Lower gastrointestinal haemorrhage	1
	Necrotising colitis	1
	Colitis ischaemic	2
	Diverticular perforation	2
	Colonic polyp	1
	Duodenal ulcer	2
	Gastric ulcer haemorrhage	2
	Diverticulum intestinal haemorrhagic	2
	Gastrointestinal perforation	3
	Upper gastrointestinal haemorrhage	1
	Diverticulitis oesophageal	1
	Large intestine perforation	4
	Large intestinal ulcer	2
	Intestinal obstruction	1
	Rectal perforation	1
Rectal ulcer	2	
General disorders and administration site conditions	Peritonitis	4
	Ileus paralytic	1
	Vomiting	1
	Death	2
	Cardiac death	1
	Pyrexia	1
	Pseudomembranous colitis	1
	Appendicitis	1

Maintenance of Japanese Terms

- Consistency in Japanese Terms
- Japanese translation and explanation in Japanese
- Collaboration of Regulator, Users and JMO
- Management of Japanese synonyms
- Japanese disease names

Management of MedDRA/J and MedDRA

