LEADING ARTICLE

Drug Safety 1999 Feb; 20 (2): 109-117
0114-5916/99/0002-0109/$04.50/0

The Medical Dictionary for Regulatory Activities (MedDRA)

Elliot G. Brown, Louise Wood and *Sue Wood*‡

Medicines Control Agency, London, England

Abstract

The International Conference on Harmonisation has agreed upon the structure and content of the Medical Dictionary for Regulatory Activities (MedDRA) version 2.0 which should become available in the early part of 1999.

This medical terminology is intended for use in the pre- and postmarketing phases of the medicines regulatory process, covering diagnoses, symptoms and signs, adverse drug reactions and therapeutic indications, the names and qualitative results of investigations, surgical and medical procedures, and medical/social history. It can be used for recording adverse events and medical history in clinical trials, in the analysis and tabulations of data from these trials and in the expedited submission of safety data to government regulatory authorities, as well as in constructing standard product information and documentation for applications for marketing authorisation. After licensing of a medicine, it may be used in pharmacovigilance and is expected to be the preferred terminology for international electronic regulatory communication.

MedDRA is a hierarchical terminology with 5 levels and is multiaxial: terms may exist in more than 1 vertical axis, providing specificity of terms for data entry and flexibility in data retrieval. Terms in MedDRA were derived from several sources including the WHO's adverse reaction terminology (WHO-ART), Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART), International Classification of Diseases (ICD) 9 and ICD9-CM. It will be maintained, further developed and distributed by a Maintenance Support Services Organisation (MSSO).

It is anticipated that using MedDRA will improve the quality of data captured on databases, support effective analysis by providing clinically relevant groupings of terms and facilitate electronic communication of data, although as a new tool, users will need to invest time in gaining expertise in its use.

In July 1997, at the 4th International Conference on Harmonisation, the M1 Expert Working Group agreed upon the structure and content of the implementable version [version 2.0 (v2.0)] of the Medical Dictionary for Regulatory Activities (MedDRA). Their objective was to produce a single, internationally acceptable, medical terminology for use in both the pre- and postmarketing phases of the regulatory process. This was intended to overcome the limitations of existing termino-

‡ Dr Susan Wood died suddenly in September 1998. She was director of the Post-Licensing Division of the UK Medicines Control Agency and chaired the International Conference on Harmonisation M1 Expert Working Group on medical terminology. MedDRA was conceived and came into fruition largely as a result of her vision and efforts.

Table I. Developmental history of the Medical Dictionary for Regulatory Activities (MedDRA)

Date	Event
1989	The UK Medicines Control Agency (MCA) identifies need for a single medical terminology for drug regulation to support its new computer databases
1991	New medical terminology introduced into MCA Adverse Drug Reactions On-line Information and Tracking (ADROIT) database
January 1993	Identification of need for a medical terminology to support the new European Community drug regulatory system
Second quarter 1993	Working party with representatives from the pharmaceutical industry and European Union regulators set up to assess wider applicability of MCA medical terminology
November 1993 to October 1994	Working Party reviews and amends MCA terminology, now called the Medical Dictionary for Drug Regulatory Affairs (MEDDRA)
December 1993	European Committee for Proprietary Medicinal Products approves MEDDRA project remit and objectives
September 1994	International consensus meeting recommends that MEDDRA [version 1 (v1.0)] should form the basis of the new standard medical terminology for drug regulation
October 1994	International Conference on Harmonisation (ICH) adopts MEDDRA v1.0 as the basis of the new standard medical terminology for drug regulation
November 1994	Release of MEDDRA v1.0 for evaluation and alpha testing
March 1995	First meeting of ICH M1 Expert Working Group. Remit to produce an implementable terminology and maintenance framework
March 1995 to July 1997	Meetings of M1 Expert Working Group: continuing review and development of the terminology
February 1996	International release of MEDDRA v1.5 for testing
July 1997	ICH agrees the 'implementable version' (v2.0) and adopts new name: the Medical Dictionary for Regulatory Activities (MedDRA)
December 1997	Call for tenders for Maintenance Support Services Organisation (MSSO) advertised
September 1998	Selection of MSSO by ICH Steering Committee
First quarter 1999	MSSO scheduled to commence services and distribute v2.0

logies including lack of specificity of data entry terms, limited data retrieval options and the need to use multiple terminologies, and to provide for long term maintenance by a Maintenance Support Services Organisation (MSSO) to ensure the evolution of the terminology in response to changing user needs.

1. Scope

MedDRA covers diagnoses, symptoms and signs, adverse drug reactions and therapeutic indications, the names and qualitative results of investigations, surgical and medical procedures, and medical/social history.[1] In general, only terms relevant to pharmaceutical regulatory affairs are included. MedDRA does not comprise a drug or device nomenclature and does not contain terms covering study design, patient demographics, numerical values or qualifiers such as those describing disease severity or frequency.

MedDRA is intended to cover medicinal and biologically derived products and the health effects of medical devices and can be used for recording adverse events and medical history in clinical trials, in the analysis and tabulations of data from these and in the expedited submission of safety data to government regulatory authorities. The terminology may be used in constructing standard product information, such as the summaries of product characteristics and in documentation in support of applications for marketing authorisation. After licensing of a medicine, it may be used in pharmacovigilance for data entry and for expedited and periodic reporting of adverse drug reactions. MedDRA is expected to be the preferred terminology for international electronic regulatory communication.

MedDRA does not include definitions of terms. However, there is an ongoing initiative on the part of the Council for International Organisation of

Medical Sciences (CIOMS) to provide standard definitions for terms which will be relevant to the use of MedDRA Preferred Terms, for example, in investigating signals of new adverse reactions.

2. Development of MedDRA

MedDRA is based upon the Medical Dictionary for Drug Regulatory Affairs (MEDDRA), which was created by the UK Medicines Control Agency (MCA) and was modified by a working party of representatives from pharmaceutical companies and European regulatory authorities. The developmental history of the terminology is summarised in table I.[2-4]

3. The Structure of MedDRA

The structure of MedDRA is shown in figure 1.[5] The basic units in MedDRA are the 'preferred terms' (PTs), each of which is a distinct descriptor for a condition covered by the scope of MedDRA: it is the term preferred for use in the regulatory environment, formatted according to MedDRA conventions. PTs are unambiguous, specific and self-descriptive: eponymous terms are only used if recognised internationally. Each PT is duplicated as a 'lowest level term' (LLT) and may be linked to 1 or more other LLTs, which are synonyms, lexical variants or alternative spellings. Each PT is represented only once under a particular 'system organ class' (SOC), to which it is connected vertically via a single 'high level term' (HLT), which in turn is fixed in location and represented only once in that SOC under 1 'high level group term' (HLGT). This arrangement represents the 'primary system organ class' location for the PT. However, the parallel vertical SOC axes are not mutually exclusive: a PT may also be linked to secondary locations in 1 or more other SOC, in which it is again placed under a specified HLT and HLGT, retaining its associated LLTs. The MedDRA SOCs are shown in table II.

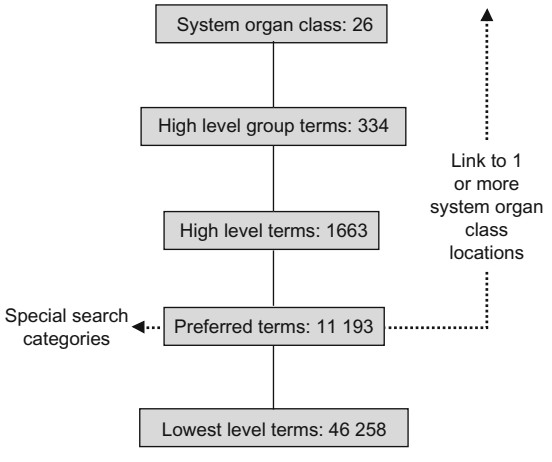

Fig. 1. The hierarchical structure of the Medical Dictionary for Regulatory Activities (MedDRA).

Table II. Medical Dictionary for Regulatory Activities (MedDRA) system organ classes: internationally agreed order

Infections and infestations
Neoplasms benign and malignant (including cysts and polyps)
Blood and lymphatic system disorders
Immune system disorders
Endocrine disorders
Metabolism and nutrition disorders
Psychiatric disorders
Nervous system disorders
Eye disorders
Ear and labyrinth disorders
Cardiac disorders
Vascular disorders
Respiratory, thoracic and mediastinal disorders
Gastrointestinal disorders
Hepato-biliary disorders
Skin and subcutaneous tissue disorders
Musculoskeletal, connective tissue and bone disorders
Renal and urinary disorders
Pregnancy, puerperium and perinatal disorders
Reproductive system and breast disorders
Congenital and familial/genetic disorders
General disorders and administration site conditions
Investigations
Injury and poisoning
Surgical and medical procedures
Social circumstances

Having multiple locations for a PT has the advantage that the way medical conditions are presented is not artificially constrained by their placement within the terminology. Thus, for example, cerebrovascular accident may be represented in

Table III. Example of a system organ class (SOC) hierarchy: hepato-biliary disorders SOC. Associated preferred terms and lowest level terms are not shown

HLGT: Bile duct disorders (excluding neoplasms)	
HLTs	Bile duct disorders infective and inflammatory
	Obstructive bile duct disorders (excluding neoplasms)
	Structural bile duct disorders including malformations
HLGT: Gall bladder disorders (excluding neoplasms)	
HLTs	Cholecystitis and cholelithiasis
	Gall bladder disorders NEC
HLGT: Hepatic disorders (excluding neoplasms)	
HLTs	Cholestasis and jaundice (all forms)
	Hepatic enzyme and function abnormalities
	Hepatic failure and associated disorders
	Hepatic fibrosis and cirrhosis
	Hepatic infections (excluding viral)
	Hepatic metabolic disorders
	Hepatic symptoms and signs
	Hepatic vascular disorders
	Hepatic viral infections
	Hepatocellular damage and hepatitis NEC
	Miscellaneous hepatic disorders
HLGT: Hepato-biliary neoplasms	
HLTs	Benign hepato-biliary neoplasms
	Hepato-biliary neoplasms NOS
	Malignant hepato-biliary neoplasms

HLGT = High Level Group Term; **HLT** = High Level Term; **NEC** = not elsewhere classified; **NOS** = not otherwise specified.

tabulations as a vascular or a neurological event, depending on context. HLGTs and HLTs facilitate data retrieval and presentation by providing clinically relevant groupings of terms for drug regulatory purposes (see table III).

Terms in MedDRA were included from several sources. Version 2.0 includes all PTs and 'included terms' from the latest version of the WHO Adverse Drug Reaction Terminology (WHO-ART) and its Japanese adaptation (J-ART, 1996), the 5th edition of the Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART) Preferred Terms and Glossary Terms, Hoechst Adverse Reaction Terminology (release 2.2) terms, International Classification of Diseases (ICD) 9 3- and 4-digit code terms and ICD9-CM (4th revision) 3-, 4- and 5-digit code terms, as well as terms from the Japanese adaptation of ICD9, MEDIS. These terms are included as LLTs in MedDRA: some are also PTs. Their source and original numerical code or symbol are stored in attribute fields linked to the MedDRA terms in order to facilitate the migration of legacy data at the time of transfer to using MedDRA.

Each MedDRA term has an associated unique numerical code but there is no hierarchical sequence, and location of terms within MedDRA does not reflect their position in source hierarchies. Vague, obsolete, misspelt or hybrid terms are flagged as non-current. These are retained in MedDRA as LLTs to preserve historical information, but will not be used for new data entry. ICD-10 terms have not been specifically incorporated into MedDRA v2.0, although this exercise may be undertaken in the future by the MSSO (see section 4).

At the time of writing, linguistic translations are complete down to, and including, PTs for French, Spanish and Japanese. Although the full terminology is written in British English, there are many American English alternatives among the LLTs. Translations are planned for German and Portuguese. The MSSO will provide additional translations if required.

The MedDRA user guide explains the development of the terminology and defines hierarchical levels and the rationale and conventions for their use. A noteworthy convention applies to investigations. These are represented only in the 'investigations' SOC; there are no secondary linkages. However, terms describing clinical conditions, e.g. hypoglycaemia and hyperkalaemia, are not found in the 'investigations' SOC: they are present only in other SOCs such as the 'disorders of metabolism and nutrition' SOC.

4. Maintenance Arrangements

MedDRA will be maintained, further developed and distributed by the MSSO: this organisation will also be responsible for user liaison and support, including facilitation of terminology implementation, although it will not have exclusive rights over the latter. At the time of writing, the MSSO is being

recruited by competitive tender and it is scheduled to release MedDRA v2.0 in the early part of 1999.

The maintenance framework, summarised in figure 2, has been developed to ensure:

- frequency of updates commensurate with user needs
- clinically validated translations of new terms
- evolution in response to advances in medical and scientific knowledge and the regulatory environment
- services to facilitate implementation
- mechanisms for user input into the maintenance process
- accountability to users with replacement of the MSSO if it is unsatisfactory
- availability of the terminology at a reasonable cost.

The International Federation of Pharmaceutical Manufacturers Associations will hold ownership of MedDRA in trust for the International Conference on Harmonisation Steering Committee and will award the MSSO a fixed term renewable licence. The MSSO will sublicence a Japanese Maintenance Organisation and issue licences to users elsewhere. Subscribers will be able to obtain the terminology in a variety of formats and to request changes. Terms proposed for addition by individual users or the MSSO, will only be added if they meet the predefined criteria for term additions and will be subject to medical review by staff employed by the MSSO. Major changes to the terminology, for example the restructuring of a SOC, will require consultation with users and the approval of the management board. The latter will approve service level fees and oversee the activities of the MSSO to ensure that it continues to meet user needs. It will report to the International Conference on Harmonisation Steering Committee, advising it on renewal of the MSSO contract, and will function at a political level to maintain the commitment of key stakeholders.

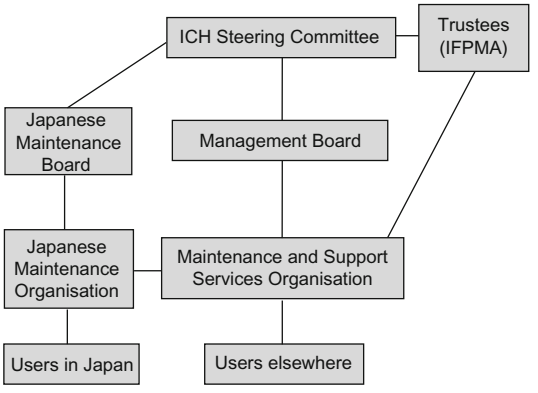

Fig. 2. The Medical Dictionary for Regulatory Activities (MedDRA) maintenance framework. **ICH** = International Conference on Harmonisation; **IFPMA** = International Federation of Pharmaceutical Manufacturers Associations.

5. Using MedDRA

Because of MedDRA's size and complexity, data entry will require the use of an autoencoder and/or a computerised search programme. It is intended that data entry should use LLTs. When a MedDRA LLT is selected for data entry, there is automatic assignment of PTs, HLT, HLGT and location in primary SOC together with secondary SOC linkages. Whilst MedDRA terms can be used in a database, the terminology does not include descriptors, such as disease severity, demographic terms, nor values for investigations. If a suitable LLT does not exist, the MSSO may allocate a new term. However, strict guidance has been provided to prevent uncontrolled proliferation.

There are a number of possible approaches to data retrieval. Cases comprising related medical concepts may be retrieved by identifying a relevant HLT, and selecting the appropriate PT. It is essential to also retrieve any appropriate PTs from the 'investigations' SOC. A decision must be made on whether to search only for terms located in a SOC as their primary location, or to include terms linked to it secondarily. Depending on the choice of output, tabular presentations including data from primary and secondary SOC locations may result in duplication of terms.

An example of a search using a primary plus secondary location strategy might be in retrieving reports relevant to, pulmonary oedema. Intuitively, a search might be based on the 'Respiratory dis-

Table IV. Extract from the 103 preferred terms in the haemorrhage special search category

Adrenal haemorrhage
Anastomotic ulcer haemorrhage
Antepartum haemorrhage
Auricular haematoma
Bleeding tendency
Bleeding varicose vein
Blood in stool
Broad ligament haematoma
Breast haemorrhage
Cardiac tamponade
Cephalhaematoma
Cerebral haemorrhage neonatal
Choroidal haemorrhage
Colitis haemorrhagic
Colonic haematoma
Colonic haemorrhage
Conjunctival haemorrhage
Coronary artery atheroma haemorrhage
Cystitis haemorrhagic
Diarrhoea haemorrhagic
Duodenal haemorrhage
Duodenal ulcer haemorrhage
Duodenitis haemorrhagic
Dysfunctional uterine bleeding
Ear haemorrhage
Ecchymosis
Epistaxis
Exsanguination
Extradural haematoma
Eye haemorrhage

orders' SOC, which includes the HLGT 'Lower respiratory tract disorders (excluding obstruction and infection)'. Under this HLGT are the HLTs: 'Lower respiratory tract inflammatory and immunologic conditions', 'Lower respiratory tract radiation disorders', 'Occupational parenchymal lung disorders' and 'Parenchymal lung disorders NEC' (not elsewhere classified), as well as, 'Pulmonary oedema (all forms)'.

The latter HLT includes the PTs: 'Adult respiratory distress syndrome', 'Capillary leak syndrome', 'Non-cardiogenic pulmonary oedema', 'Pulmonary congestion', 'Pulmonary oedema NOS' (not otherwise specified) and 'Pulmonary oedema post fume inhalation'. However, the PT 'Pulmonary oedema NOS' is only situated in this HLT as its secondary site. Its primary location is in the 'Cardiac' SOC. Searching the 'Respiratory' SOC alone using primary and secondary locations would find this term. However, a search for cases of pulmonary oedema based on primary SOC locations would have to encompass both the 'Respiratory' SOC and the 'Cardiac' SOC in order to retrieve all the relevant terms. The PTs 'Left ventricular failure' and 'Pulmonary oedema NOS' are present in their primary location under the HLT 'Left ventricular failure (all forms)', which is itself found under the HLGT 'Heart failure (all forms)' in the 'Cardiac' SOC.

Tabulation of data according to body site using primary as well as secondary SOC locations might duplicate cases associated with the PT 'Pulmonary oedema NOS', although this may be eliminated at the output stage. Either search strategy requires additional search of the 'Investigations' SOC, as investigation terms are not represented elsewhere in MedDRA.

In addition to these *ad hoc* searches, MedDRA includes some predefined searches comprising clusters of PTs which cut across SOCs and form 'Special Search Categories' (SSCs). These are PTs associated with broad clinical concepts which are not otherwise represented in 1 location in the terminology. Examples of SSCs are 'Haemorrhage' and 'Anaphylaxis'. An extract from the 103 PTs included in the 'Haemorrhage' SSC is shown in table IV.

Searching for terms included in SSC provides automatic identification of relevant cases. Fescharek et al.[6] described the use of MEDDRA v1.0, especially the SSC, in searches to characterise the safety profile of biological products, based on spontaneous adverse drug reaction reports. Users may create their own SSCs containing specified PTs to meet their particular search needs. However, these would not be part of the internationally agreed terminology.

6. Strengths and Weaknesses

It is expected that MedDRA will demonstrate several advantages over existing terminologies re-

garding medical validity and regulatory functional relevance although published comparisons between v2.0 of MedDRA and other terminologies are not available. MedDRA's richness should make it better able than other terminologies to represent precise medical concepts. Huntley et al.[7] reported that the testing of MEDDRA v1.0 found that it was more complete, accurate and flexible than other terminologies.

MedDRA has been designed to facilitate the flexible retrieval and presentation of data. This structure has proved successful within the Adverse Drug Reactions On-line Information and Tracking Database (ADROIT) used by the MCA for post-marketing drug safety monitoring as well as in their Product License User System (PLUS) marketing authorisation database. A second advantage for MedDRA is its unified nature, combining features of an adverse drug reaction and morbidity terminology, thus obviating the need to use separate dictionaries.

MedDRA is intended for use in summaries of product characteristics and should facilitate preparation of summaries of product characteristics databases. Brown and Clark[8] examined 1247 terms from UK summaries of product characteristics using MEDDRA v1.5. Overall, 78.9% of terms in the summaries of product characteristics and covered by the terminology's scope were represented adequately, ranging from 61.5% of terms in the dosage and administration sections to 89.7% of terms in the adverse effects sections.

Critically, MedDRA has been accepted internationally within the European Union (EU), the US and Japan as the standard for regulatory communication. As familiarity with the terminology increases for both industry and regulators, there could be savings in time and resource in its use. Certainly, the MSSO should save time currently spent in maintaining in house terminologies. However, of greater benefit would be regulatory acceptance of the reliability of company-encoded data without a need for recoding prior to entry on a regulatory database.[9]

MedDRA's size requires a computer for ease of handling, which could be a disadvantage for some potential users. Its size may be problematic for users in gaining familiarity with its content, and the lack of a logical code might pose a problem for some. Although the hierarchical structure has been extensively used in the pharmacovigilance environment at the MCA, its utility in the aggregation and presentation of clinical trial data remains to be confirmed. Brown et al.[10] compared MEDDRA v1.5 with COSTART in coding adverse event terms from a phase II dose-ranging clinical trial. No medically acceptable terms could be found for 10% of 378 different adverse event terms when COSTART glossary terms were used, compared with no acceptable terms being found in 2% of cases when using MEDDRA LLTs. Using the 2 terminologies to enter identical data in duplicate from a single data set resulted in apparent differences in the total numbers of different adverse events as well as in the frequency of individual events. It remains to be seen how MedDRA v2.0 will behave, but it would be expected that tables of adverse events showing frequencies of occurrence in clinical trials would differ according to which terminology was used.

In another study, White[11] examined 204 adverse event reports for 2 marketed medicines and compared the use of WHO-ART and MEDDRA v1.5 PTs in respect of the current labelling of the products. The 'expectedness' of the adverse events for purposes of expedited reporting to regulatory authorities was evaluated. In the case of 32 terms (15.7%), there were medically significant differences between the 2 terminologies, but these had no implications for labelling. Ten terms (4.9%) were considered to be medically significantly different and also affected expectedness in the labelling, as did 3 other terms for which the differences were not considered to be of medical significance. It was concluded that the specificity of MEDDRA could result in increasing the number of adverse events which are unlabelled and hence require expedited reporting.

In terms of the daily work of those who will use MedDRA, once existing systems have been

adapted and MedDRA installed, the impact is likely to be significant. Data entry should be simpler than with existing standard terminologies, provided an auto-encoder and search programme are available, because the large number of LLTs in MedDRA will facilitate exact matches with the original words that were used. There should be less need for judgement in data entry, and a saving on lengthy and resource-intensive dictionary updating exercises, in which new terms were added as a customisation of the standard terminologies. On the other hand, retrieval of data, analysis and presentation may be more complex with MedDRA, requiring a deeper understanding of medical terminology and of the medical concepts under investigation. There may need to be a more individual approach to analysing and presenting the data from each study or in relation to each drug safety issue being analysed. However, the results from these endeavours are likely to be considerably more meaningful and clinically relevant than those obtained with existing terminologies, although this remains to be demonstrated by study or by experience in use.

7. Implementation

The European Medicines Evaluation Agency is currently implementing v2.0 of MedDRA in its EudraWATCH European Union regulatory pharmacovigilance network. Tsutani[12] has described some of the implications associated with implementing MedDRA in Japan and the Far East. In July 1997, Brown and David[13] carried out a survey of how regulators in the EU, Japan and the USA intended to use the terminology. 15 regulatory authorities responded: most indicated that they were likely to use it for their own pharmacovigilance purposes within 9 months of availability and would require companies to use it for expedited adverse drug reaction reports or in periodic safety updates within 21 months of availability. Plans to use MedDRA for purposes such as standard product information or marketing authorisation applications were less well advanced. There was no consensus as to what levels (PTs, LLTs) should be used for the various regulatory purposes, or whether these could replace original (verbatim) reported terms. Since the publication of that paper, regulators in the EU have indicated that companies will be expected to use LLTs for electronic transmission of adverse reaction data, whilst the US Food and Drug Administration (FDA) appears likely to require PTs for this purpose.

It is unknown at the time of writing what the intentions of regulatory authorities elsewhere in the world are regarding implementation. Many use the WHO-ART and ICD9. For those authorities that handle small numbers of reports of adverse drug reactions and do not engage extensively in review of original data for licensing purposes, there might be little interest in using a new terminology, even if no immediate costs were involved. In other cases, a wait-and-see strategy might be adopted. However, it is to be hoped that all regulators would accept the use of MedDRA by pharmaceutical companies in the analysis and presentation of data for pharmacovigilance and other regulatory activities. A possible role of WHO in establishing global consensus in the use of the terminology has been described by ten Ham.[14]

8. Conclusions

The use of MedDRA should improve the quality of data captured on databases, support the effective analysis of data by providing clinically relevant groupings of terms and facilitate electronic communication of data by providing an internationally accepted standard. However, MedDRA is a new tool and users will need to invest time in gaining expertise in its use. Reaping the benefits of MedDRA will require widespread and well planned implementation of the terminology, regulatory authorities and industry cooperating to resolve issues as they arise and effective long term maintenance and evolution to meet a variety of user needs.[15]

References

1. Wood KL, Coulson RA, Wood SM. MEDDRA: the basis for the new international medical terminology for regulatory purposes. ESRA Rapporteur 1995; 2: 12-5
2. Mitchard M, Wood L. Regulatory communications. Eur Pharm Law Notebooks 1996; II: 139-55

3. Wood KL. The medical dictionary for drug regulatory affairs (MEDDRA) project. Pharmacoepidemiol Drug Saf 1994; 3: 7-13
4. Wood KL. Rapporteur's progress report. In: d'Arcy PFD, Harron DWG, editors. Proceedings of the Third International Conference on Harmonisation. Nov 1995, Yokahama. Belfast: Queens University Belfast Publications, 1996: 495-8
5. Wood KL, Wood SM. The international medical terminology for regulatory activities: a tool to improve the utilisation of regulatory data and to support its communication within and between organisations In: Mitchard M, editor. Electronic communication technologies – techniques and technologies for the 21st Century. Buffalo Grove (IL): Interpharm Press Inc., 1998: 299-332
6. Fescharek R, Dechert G, Reichert D, et al. Overall analysis of spontaneously reported adverse events: a worthwhile exercise or flogging a dead horse? Pharm Med 1996; 10: 71-86
7. Huntley K, Veverka MJ, Golden M. The FDAs medical dictionary for drug regulatory affairs alpha test. Drug Info J 1995; 29: 1133-43
8. Brown EG, Clark E. Evaluation of MEDDRA in representing medicinal product data sheet information. Pharm Med 1996; 10: 1-8
9. Brown EG. Medical terminology: a view from Europe. In: DArcy PFD, Harron DWG, editors. Proceedings of the Third International Conference on Harmonisation. Nov 1995, Yokahama. Belfast: Queens University Belfast Publications, 1996: 500-3
10. Brown DR, Brown EG, Moulvad TB. A comparison of two medical terminologies in coding and analysing clinical trial safety data. Int J Pharm Med 1997; 11: 85-9
11. White C. A preliminary assessment of the impact of MEDDRA on adverse event reports and product labeling. Drug Inform Assoc J 1998; 32: 347-62
12. Tsutani K. View from Japan. In: d'Arcy PFD, Harron DWG editors. Proceedings of the Third International Conference on Harmonisation. Nov 1995, Yokahama. Belfast: Queens University Belfast Publications, 1996: 503-12
13. Brown EG, David M. The medical dictionary for regulatory activities (MedDRA): a survey of regulatory authority approaches to implementation. Int J Pharm Med 1998; 12: 23-7
14. ten Ham M. WHO and international terminology. In: d'Arcy PFD, Harron DWG, editors. Proceedings of the Third International Conference on Harmonisation. Nov 1995, Yokahama. Belfast: Queens University Belfast Publications, 1996: 514-6
15. MEDDRA: setting a new standard in medical terminology. [editorial]. Int J Pharm Med 1997; 11: 248

Correspondence and reprints: Dr *Elliot G. Brown*, Medicines Control Agency, Market Towers, 1 Nine Elms Lane, London SW8 5NQ, England.
E-mail: browns@globalnet.co.uk