

**USA 2000--MedDRA™ MSSO International User Group Meeting
9 November 2000, San Diego, CA**

The agenda for the meeting was as follows:

1. MSSO Overview
2. JMO Overview
3. Status of Regulatory Implementation
4. Networking Break
5. Regulatory Pilot Projects
6. MedDRA Term Selection

MSSO Overview

Jim Mundell, Director, MSSO Maintenance

Mr. Mundell reviewed the past MSSO year and emphasized the recurring theme of communication. The User Groups primary mechanism is to promote communication between the MSSO and the user community. In an effort to expand the communication, the MSSO has provided additional avenues for subscribers to communicate with the MSSO, the comment page on the website, the helpdesk (AT&T worldwide tollfree), broadcast emails, and/or the User Group meetings that are sponsored by MSSO and JMO. The MSSO is continuing to improve communication from the MSSO to subscribers based on user feedback through the following areas: web site postings, the Newsletter "MedDRA Messenger," broadcast email messages, and User Group meetings, both MSSO/JMO sponsored and those sponsored by other groups.

Background statistics on the use of MedDRA were presented (see presentation for details). This past year, the web site use has increased markedly and has grown to be the primary source of information to support the use of MedDRA among the industry. Postings from this past year include policies and guidelines, MedDRA/ICH documents (comments on documents are requested), announcements, and downloadable consecutive data sets. Future postings will include Management Board abstracts, communication of translation information, proposed complex changes and communication with the MSSO through the web. During the past year, the MSSO has solicited feedback from the user community on the posting of the policies and guidelines that MSSO has provided. The results of the comment period were discussed (see presentation for details).

The status of MedDRA translations was presented. MedDRA is currently available in English and Japanese. All new and modified terms are translated into French, German, and Spanish by MSSO. The EU has provided a grant to respective countries to translate into French, German (2000), Spanish, and Portuguese (2000). The German and Portuguese translations were recently delivered to the MSSO and

the translations were completed to the preferred term (PT) level. The MSSO is in the process of establishing a process for validating, accepting, maintaining the translations on an ongoing basis, and distributing these translations to be presented to the Management Board.

Statistics on the change request processed the past two years were presented (see presentation for detail).

The objectives and goals for the Year 2000 are based on the feedback the MSSO has received. The primary objective for the MSSO is to undertake proactive maintenance activities with the assistance of the subscribers to review for quality, consistency and completeness of the MedDRA structure, and the placement of the LLT/PT terms. The MSSO has a number of goals for Y2000, first, the correction of all PT spelling issues and the completion and publication of the MedDRA rules by 1 September 2000, this has been completed. Second, the SOC by SOC review and the cross SOC review, this began on 1 November 2000. The results of these reviews will be posted on the web site for review and comments by industry. It is important that the MSSO gets feedback from the user community to ensure to completeness of the review. In Spring 2001, the MSSO expects to release an updated MedDRA Introductory Guide to reflect the SOC reviews. At the same time, complex changes from SOC reviews will be implemented after the comment period, as well as implement PT/LLT changes from SOC review and working group input.

During the past year, the MSSO has seen an increase in activities in all three regions and across all levels of industry. Training courses for Advanced MedDRA and a CRA course have been developed and are currently available. MSSO has been involved in providing implementation support to several companies, which the MSSO is looking to see how the information could be augmented to share with the MedDRA user community. In response to this, MSSO is in the process of developing computer-based-training courses for MedDRA. The same goes with data conversion activities.

In the coming year, several major changes are currently under negotiation with the Management Board, which may become effective very shortly. These include an addition of a core level to accommodate all the recent major mergers of companies, the reduction of MedDRA releases from quarterly to semi-annually beginning with MedDRA 4.0, elimination of diskettes as an available media format, the possibility of web distribution of MedDRA, and distribution of translations.

In conclusion, the MSSO has completed its first year of operation successfully, not only meeting but also exceeding Yr. 2 requirements of the contract. During this second year, MSSO has definite its goals as a direct response to the user requests and at the same time began the process of implementing contract changes to enable the MSSO to better serve the user community. The MSSO is continually working on improving our process to address users needs. Through it all, user

group meetings continue to be vital for information sharing between the MSSO and the user community.

The next User Group meeting will be held in conjunction with EURO/DIA on 6 March 2001, in Barcelona, Spain. Please visit the MSSO web site for details as they become available.

JMO Overview

Kazuo Hirayama, Managing Director, JMO

The JMO is the sister organization to the MSSO, established for the promotion and distribution of MedDRA in Japan. The organization is responsible for the maintenance of MedDRA/J and is an active participant in the International Medical Review process for MedDRA. The history of JMO and MedDRA/J follows in the same manner as that of the MSSO and MedDRA. Currently, MedDRA/J has a subscriber base of 231 subscribers, across all industries. Subscription to MedDRA/J is available as core services only, unlike with MedDRA and the MSSO. This past year, the number of change requests received by JMO is 113, of which 86 were accepted and sent to the MSSO. JMO has contracted with Quintiles Japan for maintenance services. The MedDRA/J change request process flow was presented (see presentation for detail).

The status of MedDRA/J implementation in Japan is as follows: 39% of subscribers have implemented MedDRA/J, 41% are currently examining MedDRA, with 20% taking no action yet. The objectives of implementation have been in areas such as spontaneous reports, post market reports, clinical study data, legacy database migration, and others (product information). The domestic use of MedDRA/J for regulatory reporting is as follows: 56% use J-ART, 19% use a combination of J-ART and MedDRA, 15% use MedDRA solely, and 10% have no reporting. The international exchange of information done in respect to MedDRA use is about 16% of by the Japanese industry compared to 22% for WHO-ART and those with no experience of international exchange of information, 9 % for COSTART, and the 31% for other terminology.

Expectations for the future from JMO are such that important training is essential to the promotion of MedDRA/J use in Japan, the continual process to improve the quality assurance process to ensure the quality of maintenance and distribution of MedDRA/J and to provide other services to subscribers.

Status of Regulatory Implementation

- Andrea Neal, Office of Post-Marketing Drug Risk Assessment, Center for Drug Evaluation & Research

Ms. Andrea presented the current status of MedDRA implementation for regulatory reporting from FDA.

The agency had issued the Advanced Notice of Proposed Rulemaking for electronic ADR Reporting earlier on November 5, 1998. This would implement MedDRA, M2 Standards for electronic submission and E2B data elements requirement, as a result of the federal mandate for FDA to be a paperless environment by 2002. In the advanced notice with regards to MedDRA, it was FDA's effort to solicit comments from the industry regarding exemptions, cost benefits versus cost burdens, and timeframes for implementing requirement. The feed back received is being taken into account for the proposed rule. Presently, the MedDRA requirements have moved from the proposed rule for electronic ADR Reporting to the proposed rule for Safety Reporting Requirements for Human Drug & Biological Products. This rule will implement the ICH standards for safety reporting. At the same time, by having MedDRA in the proposed rule, it means that MedDRA usage is required regardless of reporting means. The Safety Reporting Proposed Rule is currently in the Office of Management and Budget to undergo a review, which could last a maximum of ninety days. After the review, the rule will be published with a defined review and comment period, where industry can provide feedback, which will have to be taken into consideration at the writing of the final rule. All feedback received will be made public and available for review through the document on the FDA website. A defined implementation period will be set for the final rule. Therefore, the requirement of MedDRA is not too far off in the future; industry should start getting ready for MedDRA.

At CDER & CBER, with respect to MedDRA, FDA has simultaneously implemented both the MedDRA terminology and the new adverse event reporting system for both therapeutic biologics and human drug products. This was a significant change from the old practice. To date, FDA has three years experience since implementation. Currently, 750,000 reports have been entered into the database using MedDRA terms; FDA is coding and storing at the preferred term (PT) level. FDA has begun to see benefits from the switch to MedDRA, in that the safety evaluators are finding more granular and specific listing of terms and the hierarchical structure of MedDRA allows for advanced searching & retrieval functions, all of which are not available with COSTART. FDA is expecting to have payoff when electronic submission of report is realized full scale and MedDRA is widely used with uniformity. As a point of interest, MedDRA is suited not only for therapeutic biologics and human drugs, but it can also be used for vaccines. As a result, FDA is looking at possibly implementing MedDRA into the vaccine system as well.

Currently, FDA is receiving reports that are coded in MedDRA, in paper format, electronically via physical media and/or electronically through the gateway. For paper reports received not coded in MedDRA, FDA performs data entry, assigns appropriate MedDRA codes using event narratives for the basis of MedDRA term selection, and performs coding quality control. For those reports received that are

already coded in MedDRA, FDA is currently recoding the terms before performing quality control. As for the reports received electronically that are not coded in MedDRA, they receive the usual coding process based on the electronically received narrative before undergoing the quality control process. Those electronic reports already coded in MedDRA, FDA is in the process of developing a plan to “MedDRA enable” each of the manufacturers, who are participating in the pilot, and then followed by a quality control process. As a result, these reports are not currently going directly into the system; there are a few potential problems with quality control that FDA is facing with the reports that it is receiving. Foremost is the omission of a medical concept in the MedDRA coding box. Another problem is MedDRA not being used to its full potential due to the poor specificity of MedDRA terms being used when a more specific term exists. A few implementation issues, which companies will have to face as they begin to use MedDRA. Since MedDRA has a scientific content as well a number of technical issues. As a result, training is essential, which is readily available from the maintenance organization. Another issue is maintenance of the terminology, as versions become outdated and replaced; there is a lot of work involved. FDA has been sharing its experience with MedDRA over the past three years and has received good feedback from the industry. However, the FDA’s experience with MedDRA is not fully representative of the experience that industry is going to have as each company begins to implement MedDRA. Therefore, there is a particular need for a broad sharing of those experiences through user groups, such as the MedDRA User Group.

- Emer Cooke, Enterprise Directorate General European Commission

MedDRA implementation in the EU is occurring from two aspects, from the legal legislative perspectives and practical issues as identified in the examination of MedDRA. Unlike the FDA's practical experience in MedDRA during the recent years, the European Commission has been concentrating on getting the legislative framework ready to implement MedDRA, while trying to work in parallel with the practical aspects. In June of this year, the Directive 75/319/EEC was modified, in chapter 5A on Pharmacovigilance, to take account of the technical and scientific progress, as well as a number of the ICH activities. The Directive, effectively gives a mandate to Volume 9 of the Rules Governing Medicinal Products in the European Union, which is a basic compilation of all guidance of pharmacovigilance related issues. The Directive 2000/38, which is referred to previously was adopted on 5 June 2000. Included in it are the ICH definitions of adverse reaction, serious adverse reaction and unexpected adverse reaction, as well as slight changes to reporting requirements for ADRs. The Directive also referenced a data processing network to facilitate exchange of pharmacovigilance information between member states to ensure better pharmacovigilance among the member states. In addition, there is a more specific reference than in Volume 9 mentioned above, to the fact that the commission will publish a reference to an internationally agreed terminology, which will allow for the publishing of a reference to MedDRA. The Commission guidance will also include reference to internationally agreed formats

for reporting purposes. In terms of recommendation for MedDRA, thus far, the Notice to Marketing Authorization holders has been drafted and was published in January 1999. In the notice, there are three references to MedDRA. However, since the draft was written prior to the establishment of the maintenance organization, it referred to MedDRA when it is implemented; therefore update to the notice will be made to take into account the existence of the MSSO and the slight changes in the new directive adopted this year. A December version will be published to include a reference to MedDRA, which will elaborate more specifically on the three references to MedDRA previously mentioned, and will include a reference to dates of implementation.

From the practical aspects, the level of use of MedDRA has been worked on. There have been many debates on the level of use because in Europe, reporting is done at the lowest level term (LLT) in the hierarchical level, whereas in the US and Japan, the reporting is done at the preferred term (PT) level. A meeting was organized in Brussels, Belgium this past July, where regulators from EU, Japan and US worked together to come up with an agreement with respect to the use of the LLT and PT in the E2B message. The agreement was to use the PT in one of the fields and use LLT in the verbatim field of E2B message. However, slight modifications have been made to the agreement recently, in that another field is to be added to allow for the usage of both LLT and PT in the E2B message. This is believed to be an acceptable international solution. In terms of an implementation schedule, a brainstorming meeting between the member states was organized in November 1999. A result of the meeting is a set of provisional dates and it was agreed in principle that the use of MedDRA would become mandatory in Europe. This was further discussed this year at the 50th Pharmaceutical Committee. The agreed dates are January 2002 for single case reports received electronically and January 2003 for all ADR reporting. However, specific details have yet to be worked out, but this is a clear message that the use of MedDRA will be mandatory in the EU within a specified time frame. As for the translation status of MedDRA, there is a planned schedule for the translation of the 11 languages within the EU. Currently, German and Portuguese translations have been completed. Spanish and French have been translated to MedDRA 1.5; however, they are being updated to take into account MedDRA 3.0, so they are nearing completion. Recently the Greek translation has been contracted out. To finish out the translation for 2000, funding is available for the Dutch translation. There are a number of issues with respect to implementation of the translations that will have to be addressed. Foremost is the validation of the translations and acceptance criteria for translation. Equally important is the cross language consistency of the translation. The timing for addition of new terms is another issue to be solved. Fortunately, there is a strong commitment from the EU regulatory authorities for their involvement in this whole process. A meeting is planned for the end of 2000 or first quarter of 2001 with the MSSO and these translators to work out these issues. In the area of training, the needs have been identified. Due to the member states being at various stages of implementation, it creates a challenge when it comes to providing necessary training. However, the

Commission will organize the initial training to help the member states in the implementation. The "train the trainer" approach is expected to be used.

In conclusion, there is a real commitment to implement MedDRA in Europe. There are some issues remaining to be resolved. However, much progress has been made over the past eighteen months. At the same time, MedDRA is seen as a real potential for a multilingual terminology in Europe, which will provide great benefits not only for European patients but will allow for more efficient pharmacovigilance across the member states.

- Takashi Yasukawa, Ministry of Health and Welfare, Japan

A three-step process for the implementation plan is being undertaken in Japan. The steps consist of adoption of MedDRA/J as the adverse drug reaction terminology, pilot study based on E2B/M2 conducted by MHW and industry, and setting in place the electronic adverse drug reaction system barring no problems at the conclusion of the pilot study. As part of the adoption phase, an administrative notification of the use of MedDRA/J was officially issued on 28 Dec 99, in which MHW strongly recommended the use of MedDRA/J in adverse drug reporting beginning the end of March 2000. The scope of application affects ADR and infection case reports from industry in the history of ADRs and ADRs/infections, and the reporting level recommended is at the preferred term (PT) level. The notification is composed of the basic principle, date of effectuation, scope of application and notes. The basic principle is that MedDRA/J may be used in ADR and infection case reports from industry to MHW. However, J-ART remains applicable for the time being. However, if J-ART terms are used, they are being converted to MedDRA/J upon submission. In addition, MedDRA/J may also be used to describe ADRs in the following reports: Clinical trials, re-examination/re-evaluation of drug and/or package inserts (if possible).

At present, about 20% of all reports submitted from industry to MHW utilize MedDRA/J. MHW is expecting a gradual increase in this percentage. This increase in use will be a result of the resolution to the issue of the use PT-LLT as reporting term level, as agreed upon from the Brussels meeting earlier this year. Another contributing factor for this increase will be the implementation of the electronic reporting system for E2B/M2.

MHW has identified a few issues, which will affect MedDRA. Working in conjunction with the MSSO in the "MedDRA Term Selection: Points to Consider" MHW is expecting that this document will facilitate effective and efficient selection of MedDRA terms. MHW believes that numeric code in reports will be necessary for rapid exchange of information among the multiple language regions. Version control is another issue since MedDRA/J is revised regularly. Since multiple versions of MedDRA/J may be used in a submitted report, it is necessary to indicate the version number of MedDRA/J in the report so that MHW can manage

the data in an appropriate manner. Fortunately, this issue has been agreed at the recent ICH meeting. Finally, MHW is looking at the possible expansion of the application scope of MedDRA to "indication for use" in E2B data element and also PSUR. In this respect, every user of MedDRA should actively submit change requests if there are terms not currently in MedDRA, thereby not only improving the content of MedDRA but also possibly expanding the application scope of MedDRA.

Regulatory Pilot Projects

- Dr. Bill Gregory, Pfizer Inc., AERS

The US experience with MedDRA and the electronic safety data-reporting pilot is presented. The US pilots represent cooperative ventures between industry and regulators. The progress made thus far is step-wise progress, in the learning is done in increments and the learning is from shared experiences of other companies as well as regulators. Achievements to date have been significant; however, they are just the beginning.

A quick overview of the tools for electronic reporting includes the relevant ICH standards and FDA Rule on Electronic Records (21 CFR Part 11). In the case of individual case safety reporting, ICH Topic E2B outlines the data elements, of which, there are approximately 309 possible data fields, many are repeatable; ICH Topic M1 reference the use of MedDRA as the terminology and ICH Topic M2 detailing the format, security and transport of the report. In addition, to be in compliance with the US FDA Electronic Records Rule (21 CFR Part 11), audit trails of the reporting is necessary. As a result, there is an interdependence of E2B, M2 and MedDRA throughout the process. The ICH-compliant electronic reporting process is explained (see presentation for details).

The current status of the two US pilots for individual case safety reports are presented. The initial pilot plan was developed in April 1996, referred to as the "proof of concept," was kept as simple as possible, recognizing the tools available at the time. The focus was on non-expedited "periodic" reports that are required to be submitted to the FDA and limited to marketed products only. In addition, a decision not to encrypt the data was made as well as the use of physical media for producing the records. Results came in July 1998, when the first records were successfully delivered to FDA's ICH-compliant AERS database. By November of that year, two companies began regular submission of periodic reports on physical media. However, presently, this pilot is dormant due to the upgrade from version 1.0 of the M2 SGML DTD to version 2.0 SGML DTD. The current pilot, referred to as the "ePrompt," was developed in early 1999, focusing on the expedited reports to the FDA. At the same time, over the wire transmission using encrypted data was decided upon. In addition, it included for regulatory compliant purposes, a test to see if an electronic acknowledgement of receipt is possible. The goal of this pilot was elimination of paper reports since in both pilots, paper reports were required to

be submitted simultaneously with the electronic report. The statistics of the ePrompt first six months of operation is presented (see presentation for details). As of October 2000, three companies have begun submitting expedited reports to FDA in production-ready electronic format on a regular basis. With these pilots in respect to MedDRA, its use remains voluntary for participation in the pilots, with FDA selecting and encoding adverse events terms from free text in the narrative to MedDRA version 1.9 at the preferred term (PT) level for storage. The goal is to have the agreed E2B data fields to be coded in MedDRA by the sender for reporting purposes such that re-coding by the receiver is not needed.

The issues with MedDRA are identified. Foremost is the issue of the use of LLT versus PT, which relates to reaction/event term. A mechanism is needed to resolve the debate concerning the inclusion of both PT and LLT in the E2B message. This concern, however, may be resolved in the very near future, as eluded in the previous presentation by the European Commission. From the industry's perspective as far as search is concerned, it is essential to have a separate field for Reporter verbatim. The concern of whether MedDRA data should be exchanged as text or code, it is desirable to use the 8-digit code, which would eliminate the problem of which language to use if text is selected. As for the issue of version control, it is a consensus that E2B must provide a means to transport the MedDRA version number with each term used. The use of MedDRA terms should be encouraged. The real advantage of MedDRA is in communication for reporting.

Expectations for the future from industry are such that important modifications to E2B/M2 will be issued, that MedDRA will continue to mature, and that electronic exchange of ICSRs between the three Regions will enhance uniform interpretation and implementation of ICH standards.

- Steen Ottosen, Lunbeck, Eudrawatch

The EU Pilot Project on E2B Submission is presented. The current status of the pilot has been 444 submissions including 1090 cases that have been submitted by June 2000 from companies to EMEA, they do not include the submissions between participating companies. Active participation in the pilot is relatively small compared to the number of participants in the pilot project group. The next step in the project will be establishing global communication, with the intent to participate in the three regions pilot using the current tools available (email, s-mime security, Templar and/or XMLbus). It is the pilot's intent to have parallel FDA case exchange so this is currently being explored. Future MHW participation is desired, however, this has not been explored at this time. A major issue in the pilot is the need for a unique case identification due to the complexity of European reporting requirements. In respect to MedDRA, it is the multilingual characters that is a big issue faced in the pilot. It has been suggested by the pilot to use XML instead if the SGM currently being used to identify those multilingual characters are being used. This is an important issue in the EU due to the many languages and character sets

available. The issues of translation have come often in the pilot. Foremost is the LLT level translation, which is problematic in the EU due to multiple concepts available for selection. Therefore, the suggestion of the use of numeric codes is essential to user's ability to match the medical terms. Synchronization of the translations is a big issue. Currently, there is the translation embedded within MedDRA from the MSSO and then there is the Japanese translation of MedDRA. However, in the future as the terminology gets translated into the 11 languages of the member states, synchronization of these translations will be a big issue so that it is fully understandable. Another issue to come up has been the issue of MedDRA at the LLT versus PT level. However, this issue may have been resolved or will be resolved very shortly based on the previous presentations just given. In terms of MedDRA and the pilot, no major problems have been identified apart from the translation issue. Expectations for the future from the pilot group's perspective such that MedDRA and electronic submission will be globally mandatory by 1 January 2003. The use of XML to support the local languages in Europe due to the multilingual character sets, inclusion of FDA and MHW participation in the global compliance testing, particularly in global communication, with the use of S-MIME email as a global communication vehicle.

- Tadao Akiyama, Pharmacia & Upjohn, MHW

The experience of using MedDRA in Japanese industry is presented since the regulatory pilot project in Japan primarily focuses on the data transmission via the internet as opposed to MedDRA. The focus of this presentation will be from the point of view data management and information management as opposed to the medical point of view.

MedDRA's background in Japan begins with the regulation, which made the use of MedDRA/J acceptable from industry to MHW as of 31 March 2000; with J-ART being continued to be accepted for the mean time. Reporting that are affected by the regulation are adverse reaction in expedited report, periodic safety report, re-examination document and adverse reaction section in package insert. The regulation also recommended the use of preferred term (PT) in expedited reports. MedDRA/J is the terminology being used in Japan, provided by JMO. It consists of the same terms and codes as MedDRA, the Japanese terms and characters, as well as some additional files that are not a part of the English MedDRA. It is important to point out that the English term and the Japanese term in the terminology are not a one-to-one relation. The structure of MedDRA/J is presented (presentation for details). MedDRA can be implemented in the following areas such as safety information management, including clinical trial and marketed products, regulatory reporting, including single case report and summary report, and product information.

There are great benefits to MedDRA. Foremost is that it is available worldwide, global maintenance for its development. The terminology allows for precise

communication global and local companies because the MedDRA codes remain the same no matter what language is being used. Another benefit is that MedDRA is provided as electronic files.

There are three types of coding with MedDRA. First, is the coding of new reported information, this is the coding of reported term to MedDRA term. Second, is legacy data transfer, this is the coding of existing coded term to MedDRA term. In terms of legacy data transfer, consideration must be made as to whether to code from J-ART or from the reported term and how the process should be verified and validated. Third, is re-coding, this is the coding from old version to current version of MedDRA. In terms of re-coding, it may be necessary for summary reports, if so how should this be done. Standard procedures need to be established; guidance from the MSSO is essential. How the process should be verified and validated is another issue. For all three types of coding, version control is very important and must be resolved, in terms of both tools and business process. Finally, training strongly recommended for both Case Manager and IT personnel in the handling of MedDRA.

Expectations for the future of MedDRA from the Japanese industry are such that MedDRA applicable fields in E2B to be determined and a standard is applied to the coding of terms to MedDRA, to eliminate the variety of coded term to MedDRA, not only within an industry, but worldwide, that currently exists due to the many choices available in MedDRA. In addition, the frequency of MedDRA release, an increase to 2 byte Kana in MedDRA/J, the addition of version information in the ASCII files, should help in the management of MedDRA.

MedDRA Term Selection

Dr. Maggie Westland, Amgen, Rapporteur, MedDRA Term Selection Working Group

The Term Selection: Points to Consider Working Group is pleased to announce the completion of Release 2.0 of the document entitled "Application to Adverse Drug Reactions and Adverse Events." The framework of the document is different from the previous release. It is a companion document to "MedDRA Introductory Guide" version 3.2. It is important to note that this document is being evolved along with the MedDRA dictionary itself and is in the process of being endorsed by the ICH Steering Committee. During the drafting of the document, all comments received from the industry by the MSSO//JMO on the previous release of the document were considered. Comments were modified to best meet global user needs. More and better examples have been added, which will provide more guidance to the industry. At the same time, more thoughts about how input affects output are available in this document release.

Future expectation for this document is such that it continues to be a "living document," in that as MedDRA is developed so does the document, the joint

release of the document by both MSSO and JMO upon the completion of translation, to be release by mid-December 2000, continued feedback from user community is essential, a deadline for the comment period is yet to be determined, so do provide comments to help facilitate the development of the document. Other important activities include, addressing changes needed due to MedDRA 4.0, writing guidance for Medical history, Laboratory, Indications, Output strategies, and the use of Social Circumstances and Procedures SOCs, and finally, updating "points to consider" following future "complex changes" to MedDRA. There are several issues that have been identified as being "out of scope" for the Working Group, which will be referred back to the Management Board and MSSO for handling. These issues include version control and some "complex change" issues. Finally, there are two recommendations to ICH, which the Working Group believe will be helpful for future sessions. These include the need for ICH to establish a process to monitor and/or cross-link all working groups on MedDRA related issues and most importantly, they need to understand who they are and what they are charged with, and whether it impacts on our activities.