MedDRA概述、编码规则及使用时的考虑

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ICH药物警戒相关指南研讨会
Beijing, China. 17 March 2018

Agenda

• Basic of MedDRA use (MedDRA使用的基本信息)
  – When, where, and how MedDRA is used
• Getting started with MedDRA (准备引入/使用MedDRA)
  – Stakeholders in MedDRA community (MedDRA社会成员)
  – MSSO’s roles (MSSO的职责)
  – Implementing MedDRA (引入MedDRA)
  – MedDRA data sharing (MedDRA数据共享)
Agenda (cont)

- MedDRA terminology and MedDRA user Guides (MedDRA术语和用户指南)
  - Fundamentals of MedDRA terminology (MedDRA术语基本点)
  - MedDRA maintenance (MedDRA维护)
  - Download MedDRA (如何下载MedDRA)
  - ICH Points to Consider (PTC) documents (ICH考虑要点文档)
  - Condensed PTC documents in Chinese (ICH考虑要点文档精要版-中文版)

- MSSO Services (MSSO服务范围)
  - Help Desk (服务台)
  - Training (培训)
  - Tools (软件工具)
  - MedDRA.org website (MedDRA官方网站)

Basics of MedDRA Use (MedDRA使用的基本信息)
  - When, Where, and How MedDRA Is Used
What is MedDRA?

Med = Medical
D = Dictionary for
R = Regulatory
A = Activities

《监管活动医学词典》

MedDRA’s Purpose

• Facilitate the exchange of clinical information through standardization (通过标准化促进临床信息交流)
• Important tool for product evaluation (评估), monitoring (监测), communication (交流), electronic records exchange (交流), and oversight (监督管理)
• Supports coding (编码) (data entry) and retrieval (检索) and analysis (分析) of clinical information about human medical products including pharmaceuticals (化学药), biologics (生物制品), vaccines (疫苗), and drug-device combination products (药物—器械综合产品)
When to use MedDRA

MedDRA Definition

- MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry (药监部门和制药业). The terminology is used through the entire regulatory process (整个监管过程中), from pre-marketing to post-marketing, and for data entry (数据输入), retrieval (检索), evaluation (评估), and presentation (展示).

Where MedDRA is Used

- Individual Case Safety Reports (ICSR) (个例安全报告)
- Safety Summaries
- Clinical Study Reports (临床研究报告)
- Investigators’ Brochures (临床研究者手册)
- Core Company Safety Information
- Marketing Applications (上市申请)
- Publications
- Prescribing Information (处方信息)
- Advertising
- Regulatory Authority and Industry Databases
MedDRA’s Scope

- Information included in MedDRA
  - Medical conditions
  - Indications (适应症)
  - Investigations (tests 检查, results 检查结果)
  - Medical and surgical procedures (手术及医疗操作)
  - Medical, social, family history (病史, 家史, 社会史)
  - Medication errors (用药错误)
  - Product quality issues (产品质量问题)
  - Drug-device combination product issues
  - Pharmacogenetic (药物基因学) terms
  - Toxicologic (毒理) issues
  - Standardised MedDRA Queries (标准 MedDRA 分析查询)

How MedDRA Is Used

- ICH E2B (R3) – Individual Case Safety Report (个例安全报告)

<table>
<thead>
<tr>
<th>Element ID</th>
<th>E2B(R3) Element Name</th>
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</thead>
<tbody>
<tr>
<td>B.1.7.1.c.a.2</td>
<td>Structured Medical History Information (disease / surgical procedure / etc.)</td>
</tr>
<tr>
<td>B.1.8.c.f.2</td>
<td>Indication</td>
</tr>
<tr>
<td>B.1.8.g.2</td>
<td>Reaction</td>
</tr>
<tr>
<td>B.1.8.h.b1</td>
<td>Reported cause(s) of death</td>
</tr>
<tr>
<td>B.1.9.4.c.b1</td>
<td>Autopsy-determined cause(s) of death</td>
</tr>
<tr>
<td>B.1.10.2.1.c.a.2</td>
<td>Structured information (disease / surgical procedure / etc.) – parent/child report (parent)</td>
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<tr>
<td>B.1.10.8.c.f.2</td>
<td>Indication - parent/child report (parent)</td>
</tr>
<tr>
<td>B.2.1.1.b</td>
<td>Reaction/event in MedDRA terminology</td>
</tr>
<tr>
<td>B.3.2.c2</td>
<td>Test Name [MedDRA code]</td>
</tr>
<tr>
<td>B.4.3.7.c.a2</td>
<td>Indication in MedDRA terminology</td>
</tr>
<tr>
<td>B.5.3.c.2</td>
<td>Sender’s diagnosis/syndrome and/or reclassification of reaction/event</td>
</tr>
</tbody>
</table>
Getting Started with MedDRA (准备引入/使用MedDRA)

Stakeholders in MedDRA Community (MedDRA社区成员)

• MedDRA community
ICH MedDRA Management Committee Members (MedDRA管理委员 会成员)

MSSO’s Roles (MSSO 的职责)

- **Distribute** (颁发) MedDRA: deliver MedDRA to subscribers worldwide
- **Maintain** (维护) MedDRA: process users’ change requests
- **Develop** (开发) MedDRA: further develop MedDRA to keep up with the changes in medicine and meet the regulatory needs
- **Provide** (提供) user support
  - Free Help Desk service
  - Free training: face-to-face, webinar, videocast
  - Free user group meetings held in US, Europe, and China, and more...
ISO Certification (ISO证书)

- MSSO certified as ISO 9001:2015 compliant
  - ISO 9001:2015 standard is an internationally recognized quality management system standard
  - Developed by the International Standards Organization (ISO)
- MSSO has held ISO certifications continuously since 2003
- Involves:
  - Inspection of SoPs
  - Inspection of records to support the use of SoPs
  - Interviews with MSSO staff to ensure understanding of processes

Implementing MedDRA (引入MedDRA)

- Establish an implantation team
  - Set goals and objectives
- Have an implementation plan to consider
  - Define roles and responsibilities
    - Who is responsible for getting a MedDRA subscription?
    - Who is responsible for IT?
    - Who is in charge of communication?
    - Who is responsible for data conversion (if applicable)?
  - Identify impacts to your organization’s standard operating procedures
  - Plan for staff training: who, when, and what
- Include IT considerations: database, system, and tools
  - Set implementation timeline
Obtaining MedDRA Subscription (订阅MedDRA)

• A valid MedDRA subscription is required for any person/organization to use MedDRA
• Step by step instruction on how to apply for MedDRA subscription and pay for MedDRA invoice (commercial organizations) are available in Chinese at: https://www.meddra.org/chinese-subscription-rates
  – 如何订阅 MedDRA
  – 如何递交公司年销售额: only for commercial organizations
  – 如何支付 MedDRA 的 invoice: only for commercial organizations

MedDRA Subscription Rates (MedDRA订阅费)

• Enterprise wide subscription (以公司为单位)
• Free subscription (免费订户)
  – Nonprofit organizations (非盈利机构)
  – Regulatory authorities (监管机构)
• Paid subscription (付费订户)
  – Software developers (软件开发公司)
  – Commercial organizations (盈利机构), such as pharma companies, CROs
  • Sliding scale subscription fee based on annual revenue
  • Example, A company with annual revenue (年销售额) less than $1 million (630万人民币) pays $162 (1020人民币) per year.
2018 MedDRA订阅费

- Commercial 0-2 subscription rates reduced in 2018
- Reduction (减价) is a reflection of the continued success of MedDRA as a global standard in public health
- Costs of maintaining and developing MedDRA are distributed over a wider base
  - While still providing the same high standard of tools and services to MedDRA users
  - In fact, expanding services to include more translation and more software tools

2018 MedDRA订阅费表

<table>
<thead>
<tr>
<th>MedDRA Subscription Types</th>
<th>2018 Annual Subscription Rates</th>
<th>Additional Rates for Japanese Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory Authority</td>
<td>$0 USD</td>
<td>$0 USD</td>
</tr>
<tr>
<td>Non-Commercial / Non-Profit</td>
<td>$0 USD</td>
<td>$688 USD</td>
</tr>
<tr>
<td>Commercial (Parent Company Annual Revenue or Turnover)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
  Level 0 (Annual Revenue < $1 Million) | $102 USD | $650 USD |
  Level 1 (Annual Revenue $1-$10 Million) | $650 USD | $650 USD |
  Level 2 (Annual Revenue $10-$20 Million) | $2,527 USD | $668 USD |
  Level 3 (Annual Revenue $20-$500 Million) | $4,591 USD | $668 USD |
  Level 4 (Annual Revenue $500 Million-$1 Billion) | $10,646 USD | $668 USD |
  Level 5 (Annual Revenue $1-$5 Billion) | $43,795 USD | $668 USD |
  Level 6 (Annual Revenue $5-$20 Billion) | $57,694 USD | $668 USD |
  Level 7 (Annual Revenue > $20 Billion) | $74,100 USD | $668 USD |
| System Developer            | $2,091 USD                      | $668 USD                                |

76% of all MedDRA users pay no fee or $688 (or less)
Many software tools available to support the use of MedDRA
- Several provided free with the MedDRA subscription
  - Two browsers (Desktop 桌面浏览器 and Web-Based 网页浏览器)
  - MedDRA Version Analysis Tool (MVAT) 版本分析工具
- Need for software tools should be driven by the volume of data to be supported (软件类别取决于数据量)
  - With small amounts of data users can use simple software tools (e.g., free MSSO browsers, spreadsheets)
  - Larger implementations should consider commercial data management software products
  - List of third-party software tools on MedDRA website

At MedDRA.org

Commercial tools
- checklist
- drug risk assessment software
- drug database software
- database software
- database software
- database software
- database software
- database software
- database software
- database software
- database software
- database software
IT Considerations (cont)

- Build robust MedDRA safety database based on the knowledge of
  - Structure and relations of MedDRA tables
  - Versioning impact
  - Data retrieval needs
  - Describe the relationships among MedDRA tables.

MedDRA Data Sharing (MedDRA 数据共享)

- MSSO Statement on MedDRA Data Sharing is posted at (MSSO关于MedDRA数据共享的声明)
  [https://www.meddra.org/subscription/process](https://www.meddra.org/subscription/process)
- According to MedDRA Subscription Agreement (MedDRA订阅规定)
MedDRA Users Profile (用户概况)

- As of Dec 2017
  - 5,000 Subscribing organizations (MSSO+JMO)
  - 115 Countries
- Graph shows types of subscribing organizations

MedDRA Users by Region and Top 20 Countries

<table>
<thead>
<tr>
<th>Country</th>
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<td>United States</td>
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<td>United Kingdom</td>
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<td>Japan</td>
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<td>Austria</td>
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<td>Portugal</td>
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</tbody>
</table>
MedDRA Terminology and MedDRA User Guides (MedDRA 术语和用户指南)

**Fundamentals of MedDRA terminology (MedDRA 术语基本点)**

MedDRA Hierarchy (纵向结构)

- System Organ Class (SOC) 系统器官分类 (27)
- High Level Group Term (HLGT) 高位组语 (337)
  - High Level Term (HLT) 高位语 (1,738)
  - Preferred Term (PT) 首选语 (22,499)
- Lowest Level Term (LLT) 低位语 (77,248)
MedDRA System Organ Classes (系统器官分类)

- 血液及淋巴系统疾病
- 心脏器官疾病
- 各种先天性家族性遗传性疾病
- 耳及迷路类疾病
- 内分泌系统疾病
- 眼器官疾病
- 胃肠系统疾病
- 全身性疾病及给药部位各种反应
- 肝胆系统疾病
- 免疫系统疾病
- 感染及侵染类疾病
- 各类损伤、中毒及手术并发症
- 各类检查
- 代谢及营养类疾病
- 各种肌肉骨骼及结缔组织疾病
- 良性、恶性及性质不明的肿瘤（包括囊状和息肉状）
- 各类神经系统疾病
- 妊娠期、产褥期及围产期状况
- 产品问题
- 精神病类
- 各类手术及医疗操作
- 血管与淋巴管类疾病

MedDRA and Coded Cases

Use MedDRA hierarchy to retrieve cases
• MedDRA Term Selection: Points to Consider (MedDRA术语选择: 考虑要点)

• MedDRA Data Retrieval and Presentation: Points to Consider (MedDRA数据检索和展示: 考虑要点)

• Developed by an ICH working group
  – Regulators and industry representatives from ICH regions
  – WHO
  – MSSO and JMO
• Updated twice yearly with each MedDRA release
• Available on MedDRA and JMO websites
  – English and Japanese (只有英文版和日文版)
  – Word (“clean” and “redlined”), PDF, HTML formats
  – “Redlined” document identifies changes made from previous to current release of document
ICH M1 Points to Consider Working Group (PtC WG)

- Regulators and industry from EU, US, and Japan
- MFDS, Republic of Korea
- Health Canada, Canada
- MSSO
- JMO

Meeting 13-15 November 2017, Geneva, Switzerland

Condensed PTC Documents in Chinese

- Condensed (精要版) PTC documents are translated into all other MedDRA languages
  - Contain all PTC principles with fewer examples
- Will be available to users in late half of 2018
• **New addition to PTC Document, focus on**
  – Data quality
  – Medication errors
• **Will be available to users in late half of 2018**

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**Fundamentals of MedDRA terminology (cont)**

• **MedDRA languages** (MedDRA语言版本)
MedDRA Maintenance

- MedDRA is a term set updated based on user feedback information.
  - User feedback information
  - MSSO actively maintains and responds.
- Users can submit modification requests, which are reviewed by MSSO.
  - MedDRA changes
  - MedDRA Chinese translation modifications
  - MSSOrequest@meddra.org
  - Each organization: up to 100 CRs per month
  - For simple changes (simple change requirements) (PT and LLT levels), notification of final disposition within 7-10 working days
  - Complex changes (complex change requirements) above PT level received all year round. Posted for users’ comments mid-year.

MedDRA Maintenance (Cont.)

- They update twice a year.
  - September 1: X.1 English version (only simple changes)
  - September 15: MedDRA’s translation version
  - March 1: X.0 English version (complex and simple changes)
  - March 15: MedDRA’s translation version
MedDRA Release Zipped Package (版本文件压缩包)

- Release documents include:
  - MedDRA Introductory Guide* (MedDRA入门指南)
  - SMQ Introductory Guide* (标准MedDRA分析查询入门指南)
  - What’s New document*
  - Distribution File Format Document* (MedDRA发布文件格式文档)
  - Detail Change Request Report
  - SMQ Spreadsheet
  - Version Report
    * Translated in all MedDRA languages

What to do with the Contents of the Zip File (压缩包)?

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<thead>
<tr>
<th>Item</th>
<th>Who should receive it?</th>
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<tbody>
<tr>
<td>MedAscl Directory</td>
<td>IT staff to load MedDRA</td>
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<tr>
<td>SEQAscl Directory</td>
<td>IT staff to review changes</td>
</tr>
<tr>
<td>Readme</td>
<td>All users</td>
</tr>
<tr>
<td>SMQ Spreadsheet</td>
<td>Those using SMQs</td>
</tr>
<tr>
<td>SMQ Introductory Guide</td>
<td>Those using SMQs</td>
</tr>
<tr>
<td>Version Report</td>
<td>Those interested in version changes</td>
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<tr>
<td>What’s New</td>
<td>All users</td>
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<td>Detail Report</td>
<td>Those interested in version changes</td>
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<td>Distribution File Format</td>
<td>IT staff to load MedDRA</td>
</tr>
<tr>
<td>MedDRA Introductory Guide</td>
<td>All users</td>
</tr>
</tbody>
</table>
Download MedDRA (如何下载 MedDRA)

Click on Downloads

Enter Subscriber ID and password
Download MedDRA (cont)

- Select the version and language(s)
  - Password protected zip file
- Save the zip file to your computer

Extract the MedDRA Files

- Zip file structure and contents
  - Select a file to extract
  - Enter Unzip password from Welcome letter
MedDRA Transition Date (版本转换日期) (ICSR个例安全报告)

- A new release version of MedDRA should become the ICSR reporting version on the first Monday of the second month after it is released.
- To synchronize this event over the ICH regions, the MSSO recommends midnight GMT, Sunday to Monday, for the switchover.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>1 March</td>
<td>MedDRA X.0 released</td>
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<tr>
<td>1st Monday of May</td>
<td>MedDRA X.0 becomes the reporting version</td>
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<tr>
<td>1 September</td>
<td>MedDRA X.1 released</td>
</tr>
<tr>
<td>1st Monday of November</td>
<td>MedDRA X.1 becomes the reporting version</td>
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</tbody>
</table>

MSSO Services (MSSO 服务范围)
Free Help Desk Service (免费服务台)

- MSSO Help Desk: mssohelp@meddra.org
- Hours of operation: 5:00 – 17:00 US Eastern Time.
- Users may ask a variety of questions
  - Subscription
  - Tools
  - Change request
  - Training
  - Meeting

Free Training (免费培训)

- Formats
  - Face-to-face sessions (课堂培训), webinars (网上培训), videocasts (视频培训)
- Languages
  - English, French, German, Spanish, Mandarin Chinese
- Locations
  - Worldwide and “virtual”
Free Training (cont)

Face-to-face sessions - Full Day (课堂培训)
• Coding with MedDRA (MedDRA 编码)
• MedDRA: Safety Data Analysis and SMQs (MedDRA: 安全性数据分析和SMQs)
• Getting Started with MedDRA (per request)
• 自2010年，每年在中国办一次
  – 今年九月在上海办培训，具体时间未定

Free Training (cont)

Webinars – 1 hour (网上培训)
• Introduction module
  – MedDRA Overview
  – Getting Started with MedDRA
• Coding module
  – MedDRA Coding Basics
  – Advanced MedDRA Coding
• Data analysis module
  – Data Analysis and Query Building with MedDRA
  – Standardised MedDRA Queries (SMQs)
• What’s New webinar

YouTube Channel with recorded videocasts and webinars
Free Training (cont)

• Free videocasts on MedDRA website (视频培训)
  – Short videocasts on a variety of MedDRA-related topics
  – Available in several different languages
  – Can be downloaded or viewed directly on website
  – Available to all

Videocasts (视频培训)

<table>
<thead>
<tr>
<th>Videocast Language</th>
<th>Chinese</th>
<th>English</th>
<th>French</th>
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<tbody>
<tr>
<td>Getting Started with MedDRA</td>
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<td>Introduction to the Points to Consider (PTC) Documents</td>
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<td>MedDRA Structure and Scope</td>
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<td>Primary SOC Allocation in MedDRA</td>
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<td>MedDRA Desktop Browser 4.0 Enhancements</td>
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<td>MedDRA Web-Based Browser (WBB)</td>
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<td>The Top 12 Things to Know about the MedDRA Website</td>
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</table>
Summary of 2017 Training

- 63 face-to-face sessions (45 subscriber, 18 regulator):
  - 1,736 attendees
  - Central/South and North America, Europe, Asia/Eurasia, Scandinavia

- 27 webinars:
  - 2,705 connections
  - Central/South and North America, Europe, Asia/Eurasia, Africa, Australia, Scandinavia

Free Tools (免费工具)

- Desktop Browser (MDB) 桌面浏览器
- Web-based Browser (WBB) 网页浏览器
- MedDRA Version Analysis Tool (MVAT) 版本分析工具
- Web-based Change Request Tool (WebCR)
- Self Service Application (SSA) 自助服务工具
MedDRA.org Website

- Online interface with MedDRA users
- Source of information for
  - Subscribing to MedDRA: 订阅MedDRA
  - Renewing subscription: 续约MedDRA执照
  - Downloading MedDRA: 下载 MedDRA
  - News and Events: 新闻和活动通知
    - MedDRA activities, such as training, meetings
  - Access MSSO tools: MedDRA 工具
  - Points to Consider documents: 考虑要点文档
  - MSSO Best Practice documents: 最佳规范文档
  - MSSO training materials: 培训文档
  - Recorded webinars and videocasts: 录的网上培训课程和视频
  - Frequent asked questions (FAQs): 经常问的问题

Translations of MedDRA

- Your MedDRA subscription includes the following languages
  - English, Chinese, Czech, Dutch, French, German, Hungarian, Italian, Portuguese, Spanish
- MedDRA Japanese translation requires an additional fee.
Chinese MedDRA WeChat Group (MedDRA群)

- Set up and run by users in China
- Have a few hundred members
- Provide platform to ask questions about MedDRA subscription, coding, data sharing, etc.
- Free to participate
- MSSO is a member of the group
- Contact me if you are interested in joining the group: 若想加入，请与我联系

Paying Subscription by Credit Card 信用卡付订阅费

- New feature coming later in 2018
- For Level 0-2 commercial subscribers
- Goal is to make paying MedDRA subscription easier for lower revenue users 方便用户
MSSO Contacts

- Website
  - www.meddra.org
- Email
  - mssohelp@meddra.org
- Frequently Asked Questions
  - www.meddra.org/faq

Questions?