

MSSO/JMO MedDRA User Group Meeting

MedDRA and the Electronic Safety Data Reporting Pilots: US Experience

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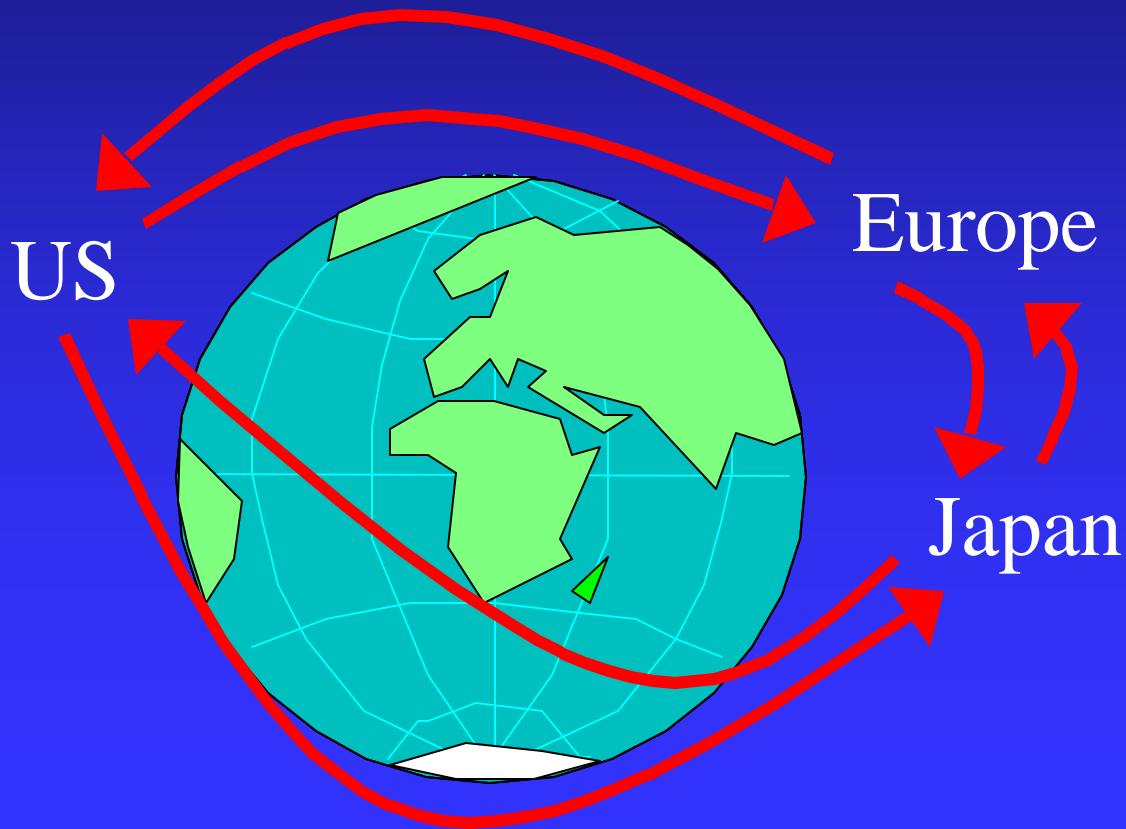
Agenda

1. Overview
2. Important Tools for Electronic Reporting
 - ◆ ICH Topics E2B, M1, and M2
 - ◆ FDA Rule on Electronic Records (21 CFR Part 11)
3. Status of the Two US Pilots
4. MedDRA Issues
5. Expectations for the Future

1. Overview

The Vision

Two-way (send/receive) global capability: *But will the ultimate Receiver have a high fidelity copy of the original Sender's content?*



Perspective

- ◆ Uniform interpretation and implementation of ICH standards and specifications, including MedDRA, will be key factors in the eventual success of (paperless) electronic safety reporting
- ◆ US Pilots
 - Represent cooperative ventures between Industry and Regulators
 - Progress is step-wise; learn from shared experience
 - Achievements to date are significant, but represent only the beginning

2. Important Tools for Electronic Reporting

The Relevant ICH Standards

Content of Individual Case Safety Report

Data elements, ICH Topic E2B

Terminology, ICH Topic M1 (MedDRA)

Format

Data (field) attributes, ICH Topic M2

Electronic Data Interchange, ICH Topic M2

Security (encryption, non-repudiation), ICH Topic M2

Transport (physical media & Internet), ICH Topic M2

*In addition, compliance with the US FDA
Electronic Records Rule (21 CFR Part 11),
which requires audit trails, is necessary.*

ICH E2B Data Elements

17 JULY 1997 STEP 4 DOCUMENT

~309 possible data fields; many repeatable

Minimal elements

- ⇒ A.2 Identifiable reporter
- ⇒ B.1 Identifiable subject
- ⇒ B.2 Event
- ⇒ B.4 Suspect drug

Other elements

- A.1.10 ID number
- A.1.7 Date of most recent information
- A.3.1.2 Sender
- A.3.2 Receiver

MedDRA



MedDRA Coding in E2B Message: Examples

- ⇒ B.1.7 Relevant medical history/conditions
 - ⇒ B.1.8 Relevant history (indication/reaction)
 - ⇒ B.1.10.7 Relevant medical history (parent)
 - ⇒ B.2.i.2 Reaction(s)/event(s)
 - ⇒ B.4.k.11 Indication for use in case
 - ⇒ B.4.k.17.2 Which reaction/event recurred?
 - ⇒ B.4.k.18.1 Reaction assessed
 - ⇒ B.5.3 Sender's diagnosis/re-classification
- more*

Interdependence of E2B, M2, and MedDRA

Example: Use of M2 transport specifications with one E2B data element, B.2.i.2 (Reaction/event term), and MedDRA text:

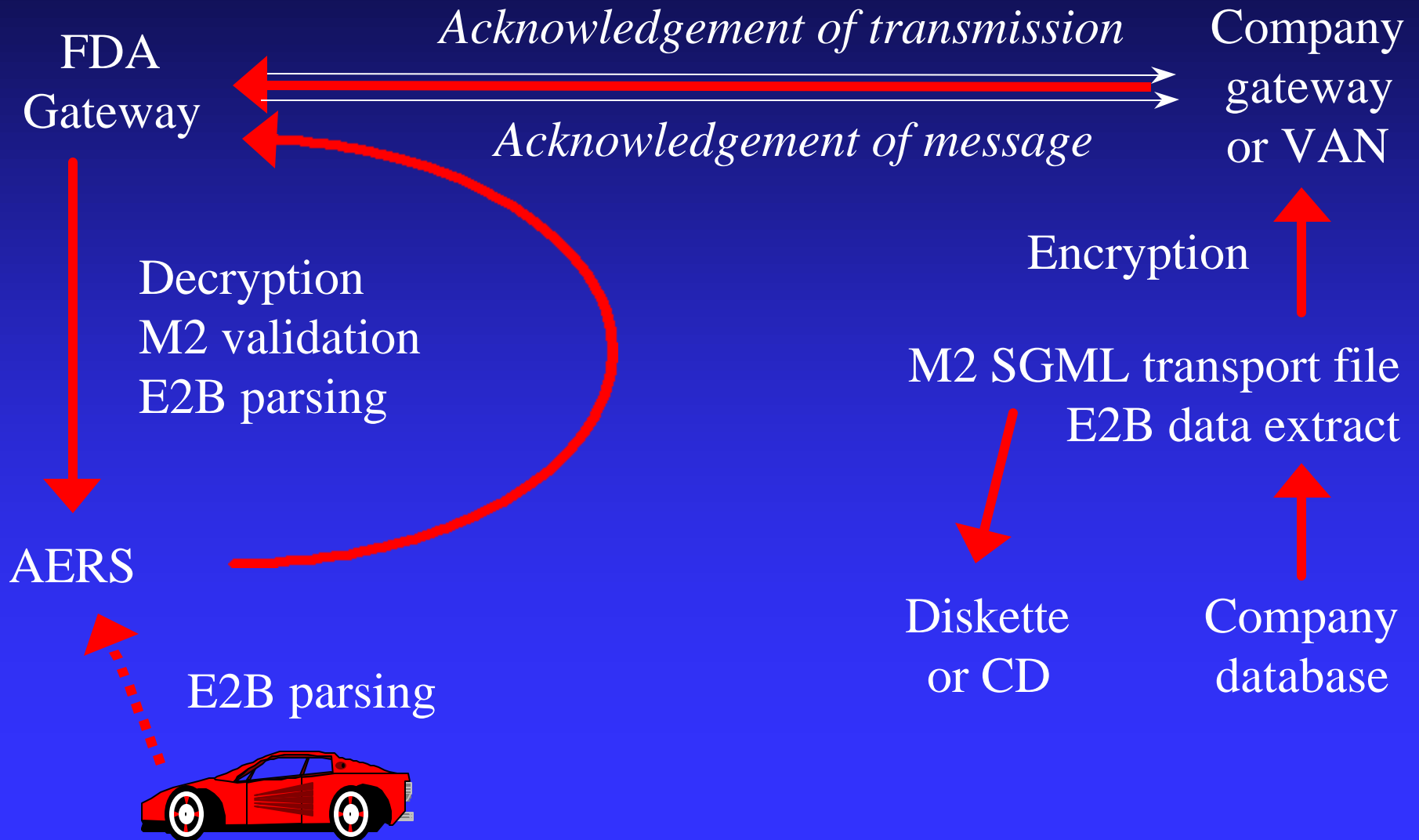
```
<reaction term>
```

```
Abdominal Pain Nos
```

```
</reactionterm>
```

Version 1.0 of the M2 DTD specification was used in the initial pilot. Version 2.0 of the M2 DTD specification, which can accommodate electronic acknowledgement of receipt, is now being used.

ICH-Compliant Electronic Reporting



3. Status of the Two US Pilots

PhRMA/FDA Electronic Pilots

Individual Case Safety Reports

First Pilot (proof of concept)

- ◆ April 1996 - Initial pilot plan developed
 - Non-expedited “periodic” reports, marketed products
 - Non-encrypted data on physical media (diskette/CD)
- ◆ July 1998 - *Results!*
 - First records successfully delivered to FDA’s ICH-compliant AERS database
- ◆ November 1998 - Two companies began regular submission of periodic reports on physical media
- ◆ This pilot is now dormant

PhRMA/FDA Electronic Pilots

Individual Case Safety Reports (Continued)

Current Pilot (“ePrompt”)

- ◆ April 1999 - Initial pilot plan developed
 - Expedited (15-day) reports
 - Encrypted data over the Internet
 - Trading Partner Agreement Required
 - Electronic acknowledgement of receipt
 - Goal: *Eliminate paper reports*
- ◆ November 1999
 - FDA ready to accept test files with new M2 DTD

PhRMA/FDA Electronic Pilots

Individual Case Safety Reports (Continued)

ePrompt Snapshot: November 1999 - April 2000

| <u>Manufacturer</u> | <u>Total files submitted</u> | <u>Number passed</u> | <u>Number failed</u> | <u>Total ICSRs</u> |
|---------------------|------------------------------|----------------------|----------------------|--------------------|
| A | 20 | 19 | 1 | 19 |
| B | 3 | 0 | 3 | 0 |
| C | 112 | 100 | 12 | 223 |
| D | 4 | 2 | 2 | 16 |
| E | 3 | 1 | 2 | 3 |
| F | 15 | 10 | 5 | 10 |
| G | 3 | 1 | 2 | 20 |
| H | 1 | 0 | 1 | 0 |

PhRMA/FDA Electronic Pilots

Individual Case Safety Reports (Continued)

Current Pilot (“ePrompt”)

- ◆ October 2000 - Three companies began submitting expedited reports to FDA in production-ready electronic format on a regular basis.

NB: Regulatory changes that will permit electronic filing without paper copies are required prior to Full Production.

PhRMA/FDA Electronic Pilots

Individual Case Safety Reports (Continued)

- ◆ Current use of MedDRA
 - MedDRA use remains voluntary
 - FDA currently selects and encodes adverse event terms from free text in report narrative (B.5.1)
 - MedDRA version 1.9
 - MedDRA Preferred Term (English) is stored
- ◆ Goal: Agreed E2B data fields are to be coded by the Sender for reporting purposes such that re-coding by the Receiver is not needed.

4. MedDRA Issues

MedDRA: LLT vs PT

Reaction/event term

- ◆ Current: Since 1997
 - B.2.i.1 Reporter verbatim
 - B.2.i.2 MedDRA text (English)
- ◆ Mechanism is needed to resolve the debate concerning inclusion of both PT and LLT in the E2B message
 - A separate field for Reporter verbatim is *essential*
 - Should MedDRA data be exchanged as text (which language?) or 8-digit unique code?

MedDRA: Version

- ◆ Consensus that E2B must provide a means to transport the MedDRA version number *with each term* used (case level association would be inadequate)
 - Would require a new optional E2B field linked to each field in which a MedDRA term (number or text) *could* be used; would trigger M2 changes
 - Version number is needed for “internal” communication
 - Version number would not be needed for reporting purposes

MedDRA: Principles

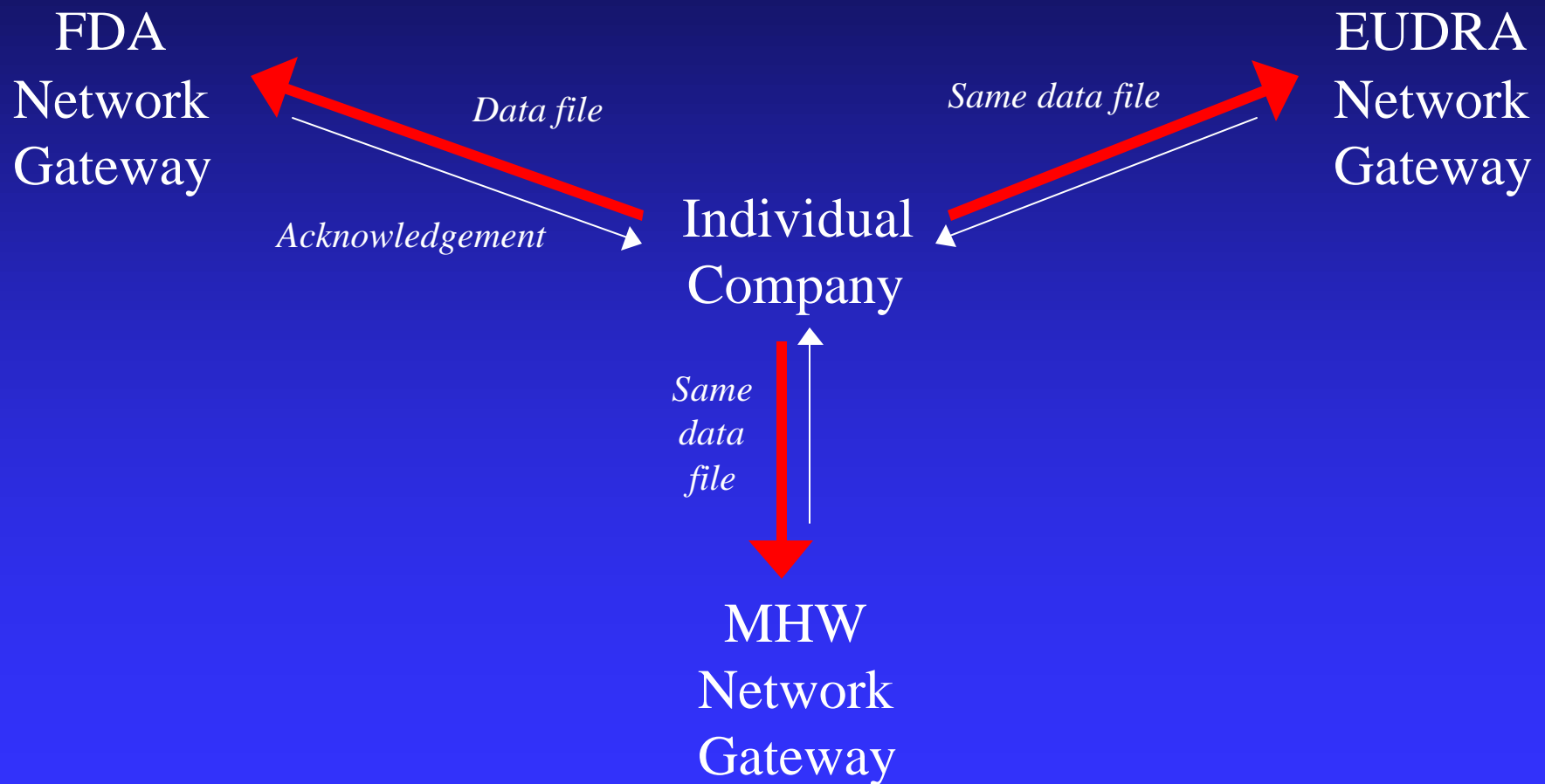
- ◆ Use of MedDRA terms should be encouraged
 - Promote medical accuracy & consistent usage
 - Enhance data retrieval for medical analysis
- ◆ MedDRA's advantage is in communication (e.g., reporting)
 - Data entry using MedDRA should be optional
 - If MedDRA terms are resident in a database, re-coding upon release of a new MedDRA version should be optional
 - Semi-annual (annual) versioning is desirable

5. Expectations for the Future

Expectations

- ◆ Important modifications to E2B/M2 will issue
- ◆ MedDRA will continue to mature
 - PTs will be comprised of unique medical concepts
 - Data entry and database re-coding will be optional
 - New versions will be released semi-annually (annually), with algorithm(s) for Provisional Terms
 - Numeric codes will be used for communication
- ◆ Electronic exchange of ICSRs between the three Regions will enhance uniform interpretation and implementation of ICH standards

Anticipated Three-Region Pilot



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