FDA AND ADVERSE EVENT REPORTING
FDA Mission

FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

FDA is responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health.

FDA has responsibility for regulating the manufacturing, marketing and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.
What is an Adverse Event?

An adverse event is any undesirable experience associated with the use of a medical product in a patient.
What is a Serious Adverse Event?

The event is serious and should be reported to FDA when the patient outcome is:

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability or Permanent Damage
- Congenital Anomaly/Birth Defect
- Required Intervention to Prevent Permanent Impairment or Damage (Devices)
- Other Serious (Important Medical Events)
FDA AE Reporting Regulations: Drugs

21CFRPart11, Section: 314.80

Adverse drug experience. Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: An adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action.
FDA AE Reporting Regulations:

Devices

21CFR803.3

**Medical Device Reporting (or reportable event)**

1. An event that user facilities become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury; or

2. An event that manufacturers or importers become aware of that reasonably suggests that one of their marketed devices:
   
   i. May have caused or contributed to a death or serious injury, or
   
   ii. Has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.
Types of FDA AE Reporting

- Mandatory Adverse Event Reporting
  - Leveraging Standard Form 3500a

- Voluntary Adverse Event Reporting
  - Leveraging Standard Form 3500
Mandatory AE reporting: MedWatch Standard Form 3500A

For use by users/facilities, importers, distributors and manufacturers for MANDATORY reporting

A. PATIENT INFORMATION

1. Patient Identifier

2. Age at Time of Event:
   - [ ] Under 18
   - [ ] 18 years or over
   - [ ] Date of Birth:
     - [ ] Male
     - [ ] Female

3. Sex

4. Weight

5. Date of Event (mm/dd/yyyy)

B. ADVERSE EVENT OR PRODUCT PROBLEM

2. Outcomes Attributed to Adverse Event (Check all that apply)
   - [ ] Death
   - [ ] Disability or Permanent Damage
   - [ ] Life-threatening
   - [ ] Congenital Anomaly/Birth Defect
   - [ ] Hospitalization - Initial or prolonged
   - [ ] Other Serious (Important Medical Events)
   - [ ] Required Intervention to Prevent Permanent Impairment/Damage (Device)

3. Date of Event (mm/dd/yyyy)

4. Date of This Report (mm/dd/yyyy)

5. Describe Event or Problem

C. SUSPECT PRODUCT(S)

1. Name (Give labeled strength & mf/lbl)

2. Dose, Frequency Route Used

3. Therapy Dates (If unknown, give duration/ from/to or best estimate)

4. Diagnosis for Use (Indication)

5. Event Altered After Use Stopped or Dose Reduced?

6. Event Reappeared After Reintroduction?

7. Exp. Date

8. Lot #

9. NDC# or Unique ID

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
Voluntary AE reporting:
MedWatch Standard Form 3500

For VOLUNTARY reporting of adverse events, product problems and product use errors

<table>
<thead>
<tr>
<th>A. PATIENT INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patient Identifier</td>
</tr>
<tr>
<td>2. Age at Time of Event or Date of Birth:</td>
</tr>
<tr>
<td>3. Sex</td>
</tr>
<tr>
<td>□ Female</td>
</tr>
<tr>
<td>□ Male</td>
</tr>
<tr>
<td>4. Weight</td>
</tr>
<tr>
<td>lb or kg</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check all that apply:</td>
</tr>
<tr>
<td>□ Adverse Event</td>
</tr>
<tr>
<td>□ Product Problem (e.g., defects/malfunctions)</td>
</tr>
<tr>
<td>□ Product Use Error</td>
</tr>
<tr>
<td>□ Problem with Different Manufacturer of Same Medicine</td>
</tr>
<tr>
<td>2. Outcomes Attributed to Adverse Event</td>
</tr>
<tr>
<td>(Check all that apply)</td>
</tr>
<tr>
<td>□ Death: (mm/dd/yyyy)</td>
</tr>
<tr>
<td>□ Disability or Permanent Damage</td>
</tr>
<tr>
<td>□ Life-threatening</td>
</tr>
<tr>
<td>□ Congenital Anomaly/Birth Defect</td>
</tr>
<tr>
<td>□ Heart failure, sudden or unexpected</td>
</tr>
<tr>
<td>□ Other Serious (Impaired Medical Condition)</td>
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<table>
<thead>
<tr>
<th>2. Dose or Amount</th>
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<tbody>
<tr>
<td>#1</td>
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<td>#2</td>
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<thead>
<tr>
<th>3. Dates of Use (If unknown, give duration) from/to (or best estimate)</th>
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<tbody>
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<td>#1</td>
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<td>#2</td>
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<tr>
<th>4. Diagnosis or Reason for Use (Indication)</th>
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<tbody>
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<td>#1</td>
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<td>#2</td>
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<thead>
<tr>
<th>5. Event Abated After Use Stopped or Dose Reduced?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes</td>
</tr>
<tr>
<td>□ No</td>
</tr>
<tr>
<td>□ Doesn’t Apply</td>
</tr>
<tr>
<td>#1</td>
</tr>
<tr>
<td>#2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. Event Reappeared After Reintroduction?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes</td>
</tr>
<tr>
<td>□ No</td>
</tr>
<tr>
<td>□ Doesn’t Apply</td>
</tr>
<tr>
<td>#1</td>
</tr>
<tr>
<td>#2</td>
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</tbody>
</table>

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<tr>
<th>7. Expiration Date</th>
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<tr>
<td>#1</td>
</tr>
<tr>
<td>#2</td>
</tr>
</tbody>
</table>
FDA MedWatch Program
(What not to report via MedWatch)

- Vaccines: Report vaccine events to the Vaccine Adverse Event Reporting System (VAERS) online at https://vaers.hhs.gov/esub/step1
- Investigational (study) drugs: Report investigational (study) drug adverse events as required in the study protocol and send to the address and contact person listed in the study protocol.
- Mandatory reporting by regulated industry:
  - Drugs and Biologics
  - Devices
  - Dietary supplements
- Reporting on Veterinary Medicine Products
Background on ICH

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry of Europe, Japan and the US to discuss scientific and technical aspects of drug registration.
ICH Work Products

ICH Guidelines
MedDRA

Electronic Standards
E2B R3
electronic Common Technical Document (CTD)
All adverse event reporting should comply with International Conference on Harmonisation (ICH) adverse event reporting requirements:

E2B(R2): Current standard in use for Adverse Event Reporting

E2B(R3): Constrained version of HL7 ICSR Release 3 standard currently being tested and piloted by various regional members of ICH (US, Japan and EU)
The *ASTER Project

ADE Spontaneous Triggered Electronic Reports

David Westfall Bates, MD, M.Sc.
Chief of the Division of General Internal Medicine at the Brigham and Women's Hospital; Professor of Medicine at Harvard Medical School and Professor of Health Policy and Management at the Harvard School of Public Health (Co-Director of the Program in Clinical Effectiveness)

Jeffrey A. Linder, MD, MPH, FACP - PI of *ASTER
Assistant Professor of Medicine, Harvard Medical School
Division of General Medicine and Primary Care, Brigham and Women's Hospital, Boston MA
Adverse Event Reporting Information Flow

1. Physician discontinues drug due to Adverse Event (AE)
2. EHR System creates XML data file
3. EHR System sends XML data file via RFD
4. Physician completes and submits AE form
5. XML data file is received and pre-populates AE form
6. AE form is displayed to physician
7. AE Form data is stored in AE repository as an AE report
8. AE report data coded (MedDRA)
9. Transmit message to FDA
10. Create an ICSR message
11. Set serious flag (Y/N)
12. Receive message
13. Adverse event message is displayed (MedWatch form)
Adverse Event Report

The information on this form will be submitted to FDA as an adverse event report. You need to complete the Event Detail section.

Patient Initials: [Name]
Patient Record Number: [ID]

Suspect Drug: [Drug]
Date Drug First Prescribed: [Date]

Event Details:
- [ ] Resulted in death
- [ ] Was life-threatening
- [ ] Resulted in inpatient hospitalization or in prolonging inpatient hospitalization
- [ ] Resulted in a disability or incapacity which is persistent or medically significant
- [ ] Resulted in a congenital anomaly or birth defect (of the patient's child)
- [ ] Medically important for other reasons (e.g., allergic bronchospasm, blood dyscrasias, convulsions, etc.)
- [ ] None

Primary Adverse Event:
Allergic reaction to asthma medicine

Please confirm the earliest date of occurrence:
Monday, October 20, 1997

Description of event:
[Drug] discontinued due to adverse event: Allergic reaction to asthma medicine

Do you want your identity withheld from the drug manufacturer?
- [ ] Yes
- [ ] No
Patient Information

Patient Initials: tms
Patient Birth Date: 19970303

Patient GP Medical Record Number: pmrn10230405060708
Patient Onset Age: 00023

Patient Specialist Record Number: pshn12345678975654
Patient Weight: 210 kg

Patient Hospital Record Number: phrn112334566776
Patient Gender: Female

Text for relevant medical history and concurrent conditions:
Patient has a history of diabetes, heart disease, and asthma. Patient was hospitalized for insulin shock in 1994 for 2 weeks. Despite doctor’s warnings, patient continues to smoke and does not exercise regularly. A proper diet would help tremendously. Patient has a history of mental illness in the family; patient was institutionalized for mild depression in 1990 for eight months. Depression is being treated with prescription drugs; patient has never been hospitalized for severe asthma.

• Patient Medical History Episodes
• Relevant Past Drug History
• Lab Results
• Patient Death
• Adverse Reactions
• Medications
SDC AE/PSE WG

• **Goal:**
  – Validate, test and pilot the S&I SDC interoperability standards that specify how electronic health records (EHRs) can capture and transmit structured data for Patient Safety Event (PSE) and Adverse Event (AE) reporting

• **Objectives:**
  – Identify **Common Data Elements** (CDEs) and associated value sets, leveraging AHRQ Common Formats, that can be used for PSE and AE reporting from EHRs
  – Identify **structured forms/templates** these CDEs will populate, leveraging AHRQ Common Formats and FDA Form 3500/3500a
  – Develop PSE and AE Reporting **end-to-end workflow** (from EHR system to AHRQ Repository and from EHR system to FDA repository)
  – Identify 2 or more organizations to test and **pilot** the SDC Implementation Guide in a production or near production environment
Data Element Example: Can be a Question/Response Set on a Form

Data Element **Attributes**
(identified in database where data element is maintained)

<table>
<thead>
<tr>
<th>Attribute NAME</th>
<th>Attribute VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>id:</strong></td>
<td>123XYZ</td>
</tr>
<tr>
<td><strong>version:</strong></td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Name:</strong></td>
<td>Sex</td>
</tr>
<tr>
<td><strong>Preferred question text:</strong></td>
<td>Sex</td>
</tr>
<tr>
<td><strong>Creation Date:</strong></td>
<td>Jan 20, 2014</td>
</tr>
</tbody>
</table>

Value Domain/Value Set **Attributes**
(identified in database where value domain is maintained)

<table>
<thead>
<tr>
<th>Attribute NAME</th>
<th>Attribute VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name:</strong></td>
<td>Administrative_Gender</td>
</tr>
<tr>
<td><strong>Version:</strong></td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Max character quantity:</strong></td>
<td>6</td>
</tr>
<tr>
<td><strong>Permissible value:</strong></td>
<td>Female</td>
</tr>
</tbody>
</table>
FDA Drug & Common Formats Data Element Overlap

FDA Drug Data Elements
- Patient Identifiers
- Provider /reporter Identifiers
- Preexisting Medical History
- Frequency
- Indication
- NDC code
- Relevant Tests/Laboratory Data Including Dates

AHRQ Common Formats Data Elements
- Route of Administration/
- Expiration Date
- Product Use error

- Stage of Process, when event occurred?
- Compounded preparation
- …
FDA Device & Common Formats
Data Element Overlap

FDA Device Data Elements:
- Concomitant Medical
- Products and Therapy Dates
- User Facility or Importer Name/Address
- Relevant Tests Lab Data, Including Dates
- Other Relevant History, Including Preexisting Medical Conditions
- …

AHRQ Common Formats Data Elements:
- Was a device intended for a single use reused in the event or unsafe condition?
- Report Date
- Gender
- UDI
- Model No.
- Serial No.
- Reporter's Job
- Briefly describe the location where the event occurred or where the unsafe condition exists
- Patient's Medical Record No.
- Was any intervention attempted in order to "rescue" the patient (i.e., to prevent, to minimize, or to reverse harm)?
- …
Questions