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FDA AND ADVERSE EVENT REPORTING

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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.

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What is an Adverse Event?

An adverse event is any undesirable experience associated with the use of a medical product in a patient.

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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)

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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.

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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.

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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

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Form Approved: OMB No. 0910-0291, Expires: 6/30/2015
See OMB statement on reverse.

U.S. Department of Health and Human Services
Food and Drug Administration

MEDWATCH

FORM FDA 3500A (2/13)

For use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting

Page 1 of ____

Mfr Report #

UF/Importer Report #

FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier — In confidence
2. Age at Time of Event: or Date of Birth:
3. Sex — Female / Male
4. Weight — lbs or kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. Adverse Event and/or Product Problem *(e.g., defects/malfunctions)*
2. Outcomes Attributed to Adverse Event *(Check all that apply)*
   - Death: *(mm/dd/yyyy)*
   - Life-threatening
   - Hospitalization - initial or prolonged
   - Required Intervention to Prevent Permanent Impairment/Damage (Devices)
   - Disability or Permanent Damage
   - Congenital Anomaly/Birth Defect
   - Other Serious (Important Medical Events)
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 & mfr/labeler)* — #1, #2
2. Dose, Frequency & Route Used — #1, #2
3. Therapy Dates *(If unknown, give duration)* from/to *(or best estimate)* — #1, #2
4. Diagnosis for Use *(Indication)* — #1, #2
5. Event Abated After Use Stopped or Dose Reduced? — #1 Yes No Doesn't Apply; #2 Yes No Doesn't Apply
6. Lot # — #1, #2
7. Exp. Date — #1, #2
8. Event Reappeared After Reintroduction? — #1 Yes No Doesn't Apply; #2 Yes No Doesn't Apply
9. NDC# or Unique ID
10. Concomitant Medical Products and Therapy Dates *(Exclude treatment of event)*

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Voluntary AE reporting: MedWatch Standard Form 3500

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MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

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

Page 1 of 3

Form Approved: OMB No. 0910-0291, Expires: 6/30/2015
See PRA statement on reverse.

FDA USE ONLY
Triage unit sequence #

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event or Date of Birth:	3. Sex	4. Weight
In confidence		☐ Female ☐ Male	lb or kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☐ **Adverse Event** ☐ **Product Problem** *(e.g., defects/malfunctions)*
   ☐ **Product Use Error** ☐ **Problem with Different Manufacturer of Same Medicine**

2. **Outcomes Attributed to Adverse Event** *(Check all that apply)*
   ☐ Death: _____ *(mm/dd/yyyy)*
   ☐ Life-threatening
   ☐ Hospitalization - initial or prolonged
   ☐ Disability or Permanent Damage
   ☐ Congenital Anomaly/Birth Defect
   ☐ Other Serious (Important Medical Events)

2. Dose or Amount	Frequency	Route
#1			
#2			

3. **Dates of Use** *(If unknown, give duration) from/to (or best estimate)*
   #1
   #2

4. **Diagnosis or Reason for Use** *(Indication)*
   #1
   #2

5. **Event Abated After Use Stopped or Dose Reduced?**
   #1 ☐ Yes ☐ No ☐ Doesn't Apply
   #2 ☐ Yes ☐ No ☐ Doesn't Apply

8. **Event Reappeared After Reintroduction?**
   #1 ☐ Yes ☐ No ☐ Doesn't Apply
   #2 ☐ Yes ☐ No ☐ Doesn't

6. **Lot #**

7. **Expiration Date**

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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

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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)

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E2B

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)

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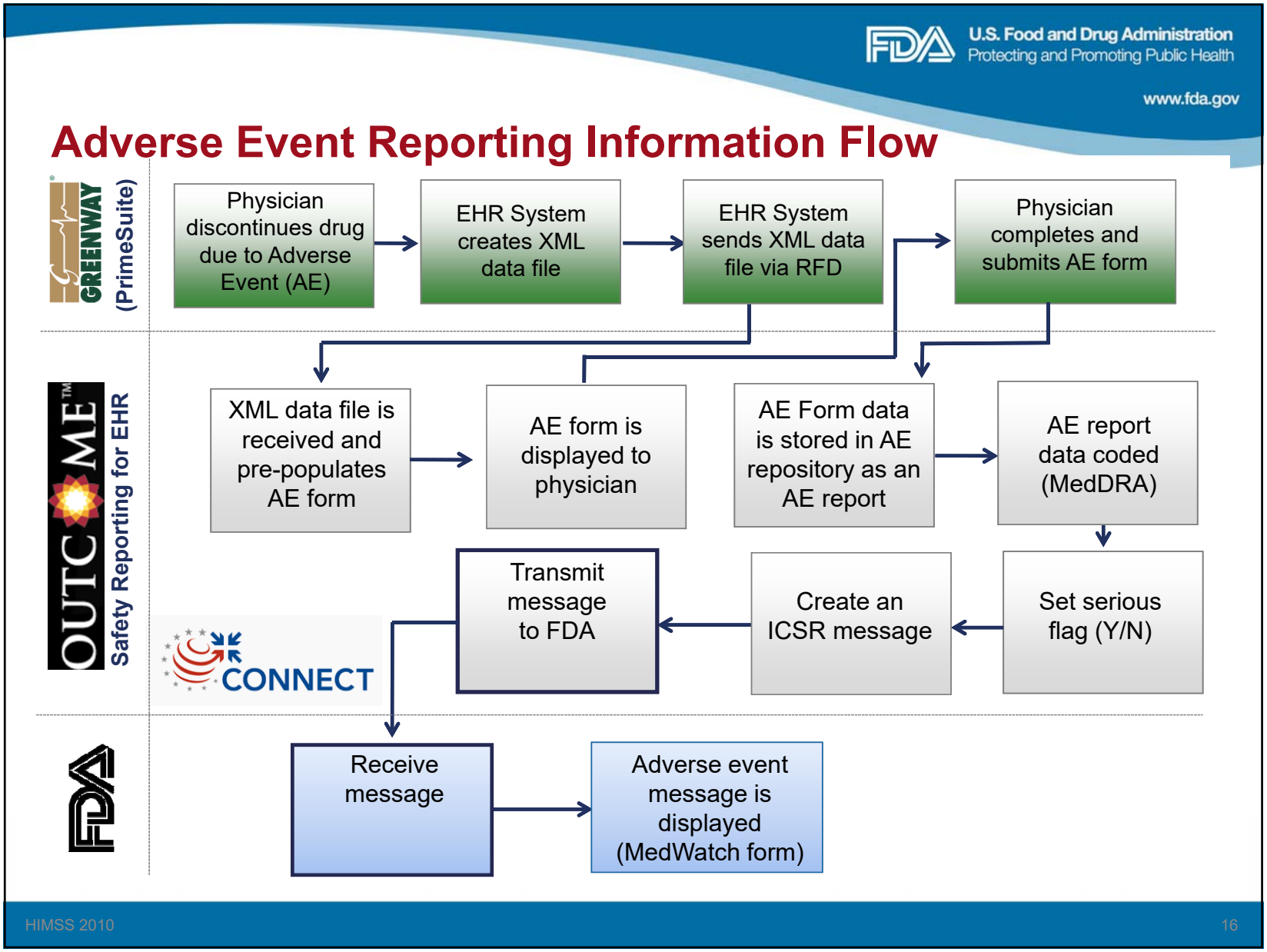
ADVERSE EVENT REPORTING FROM EHRS


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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Adverse Event Reporting Information Flow
GREENWAY (PrimeSuite)
Physician discontinues drug due to Adverse Event (AE)
EHR System creates XML data file
EHR System sends XML data file via RFD
Physician completes and submits AE form
OUTCOMES™ Safety Reporting for EHR
XML data file is received and pre-populates AE form
AE form is displayed to physician
AE Form data is stored in AE repository as an AE report
AE report data coded (MedDRA)
Set serious flag (Y/N)
Create an ICSR message
Transmit message to FDA
CONNECT
FDA
Receive message
Adverse event message is displayed (MedWatch form)
HIMSS 2010
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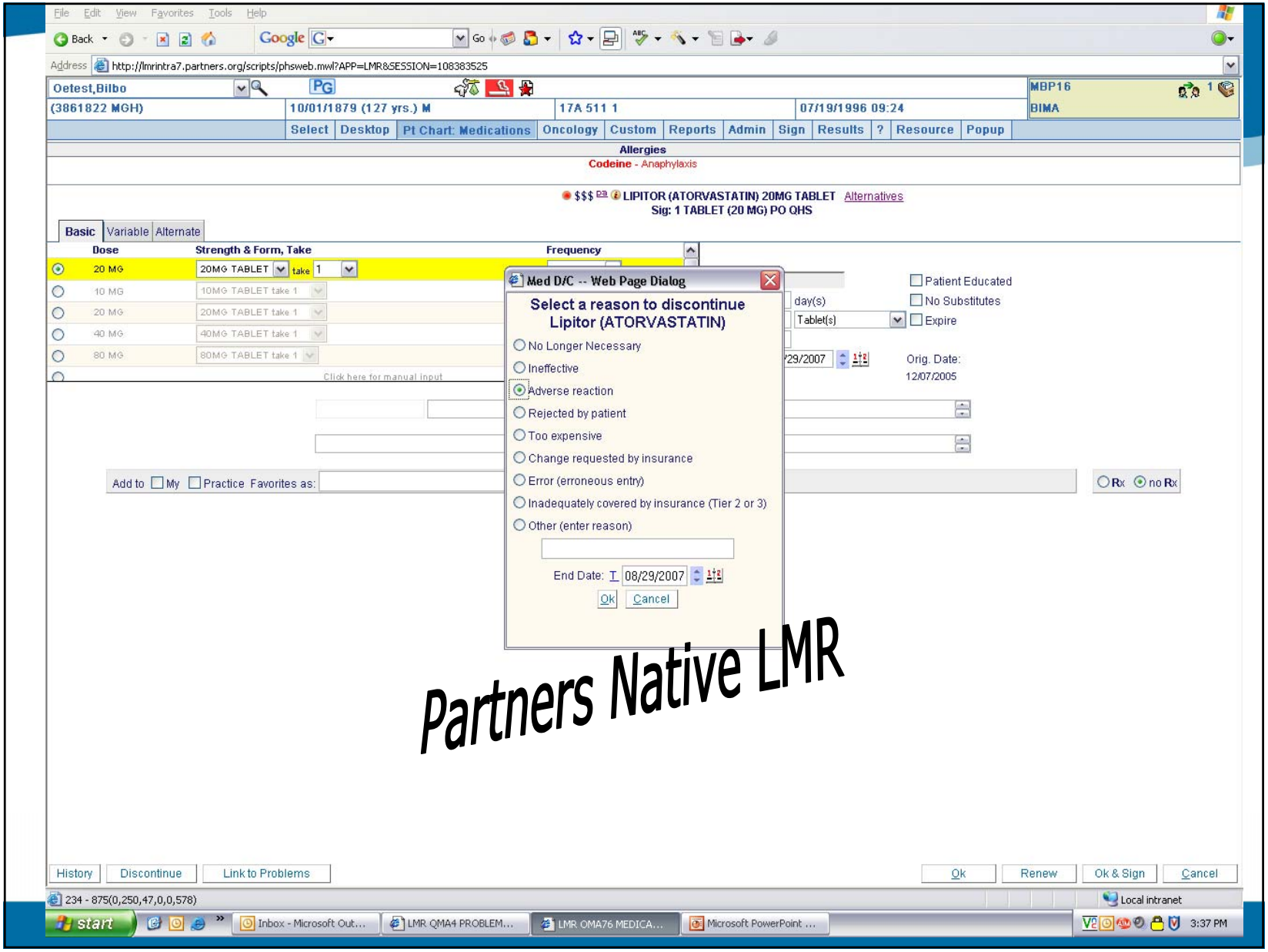
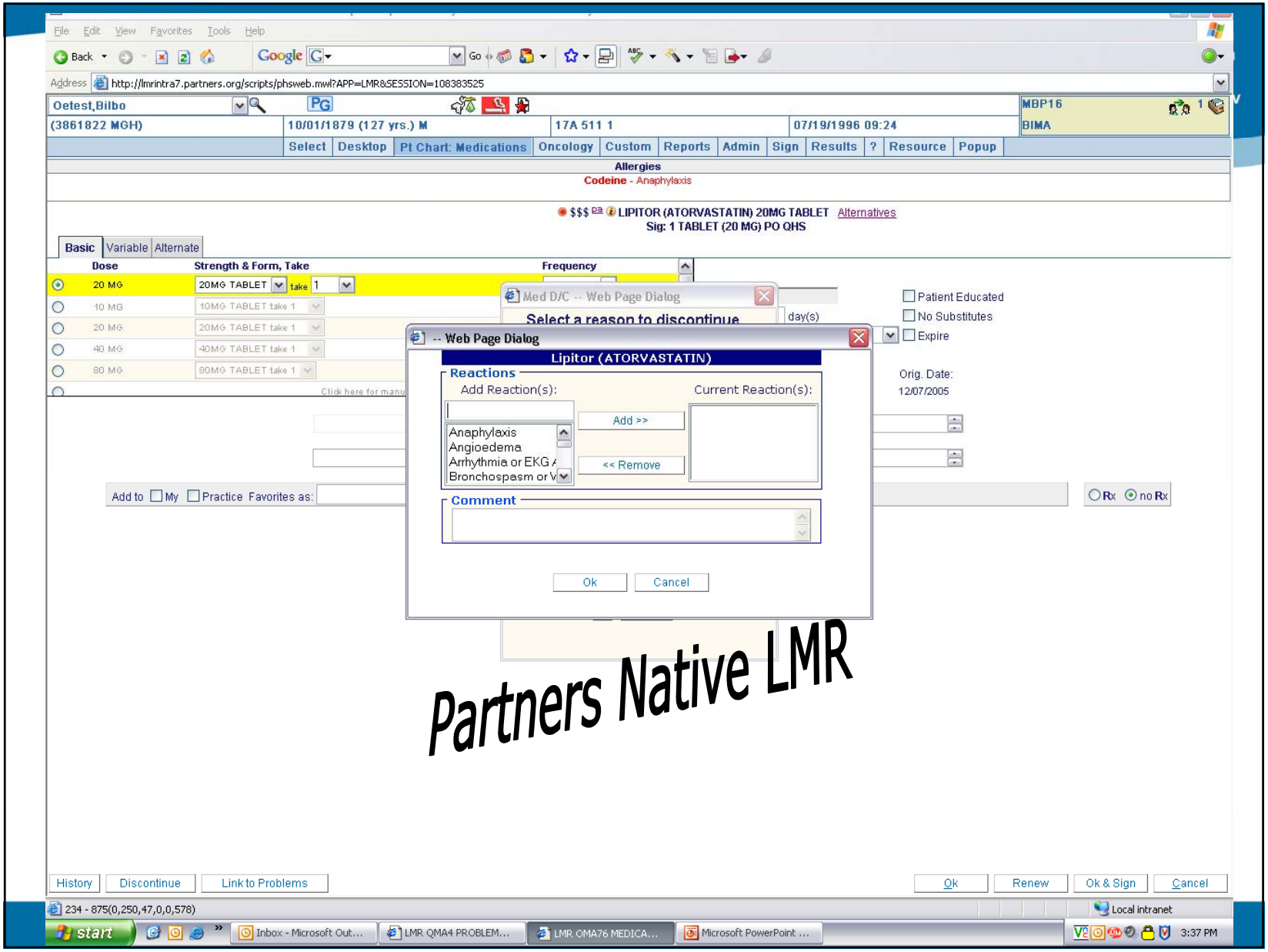
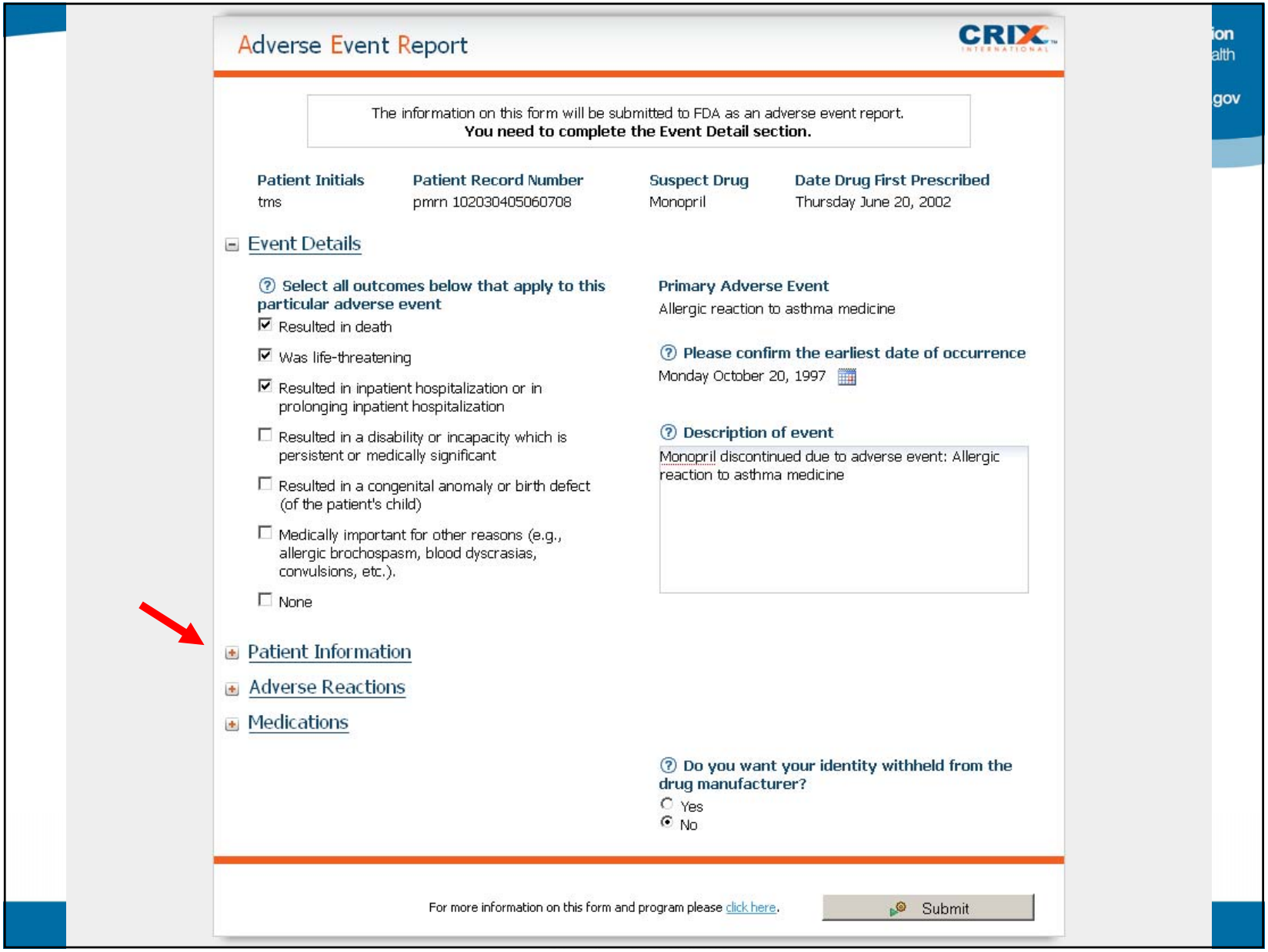
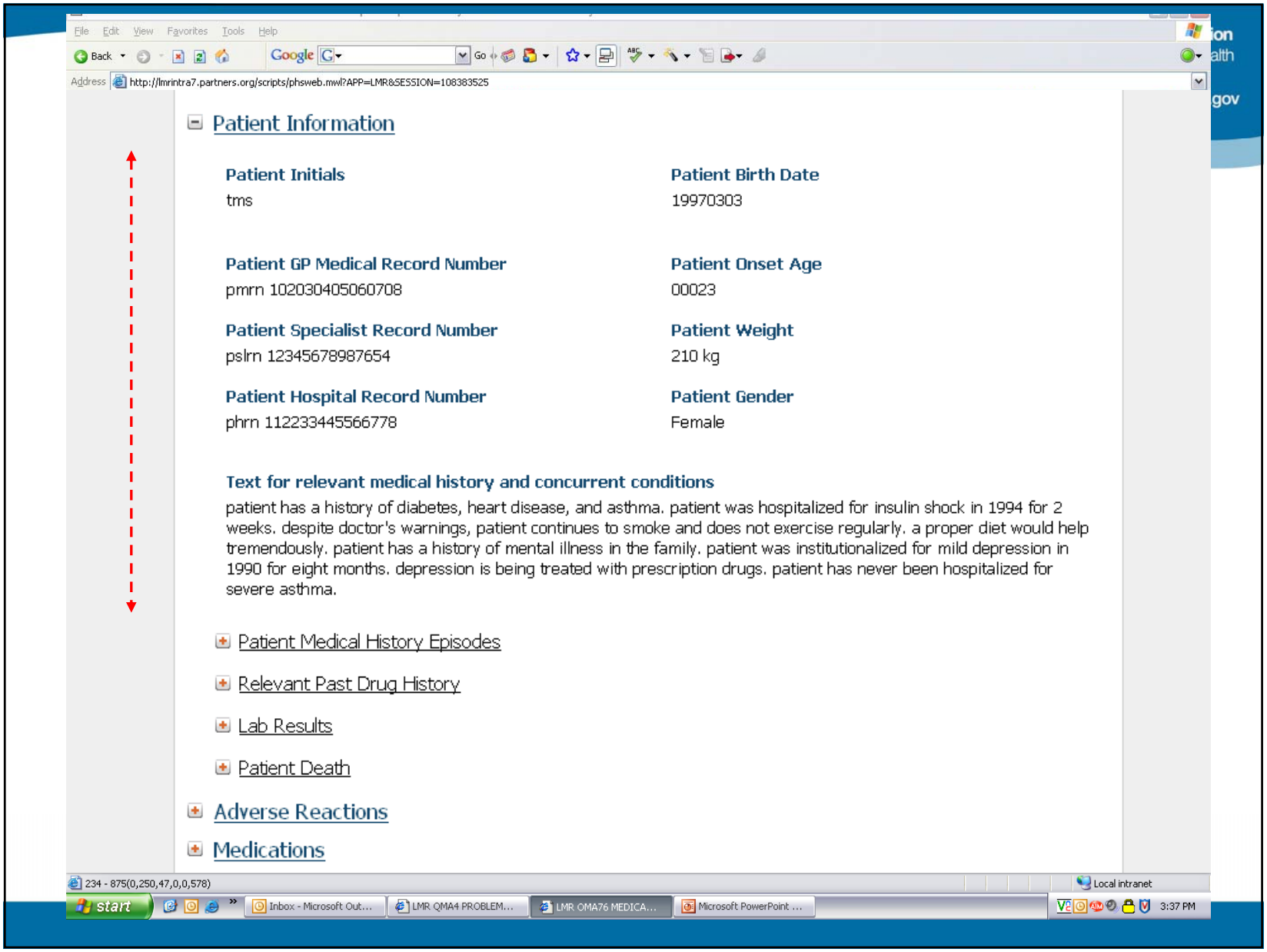
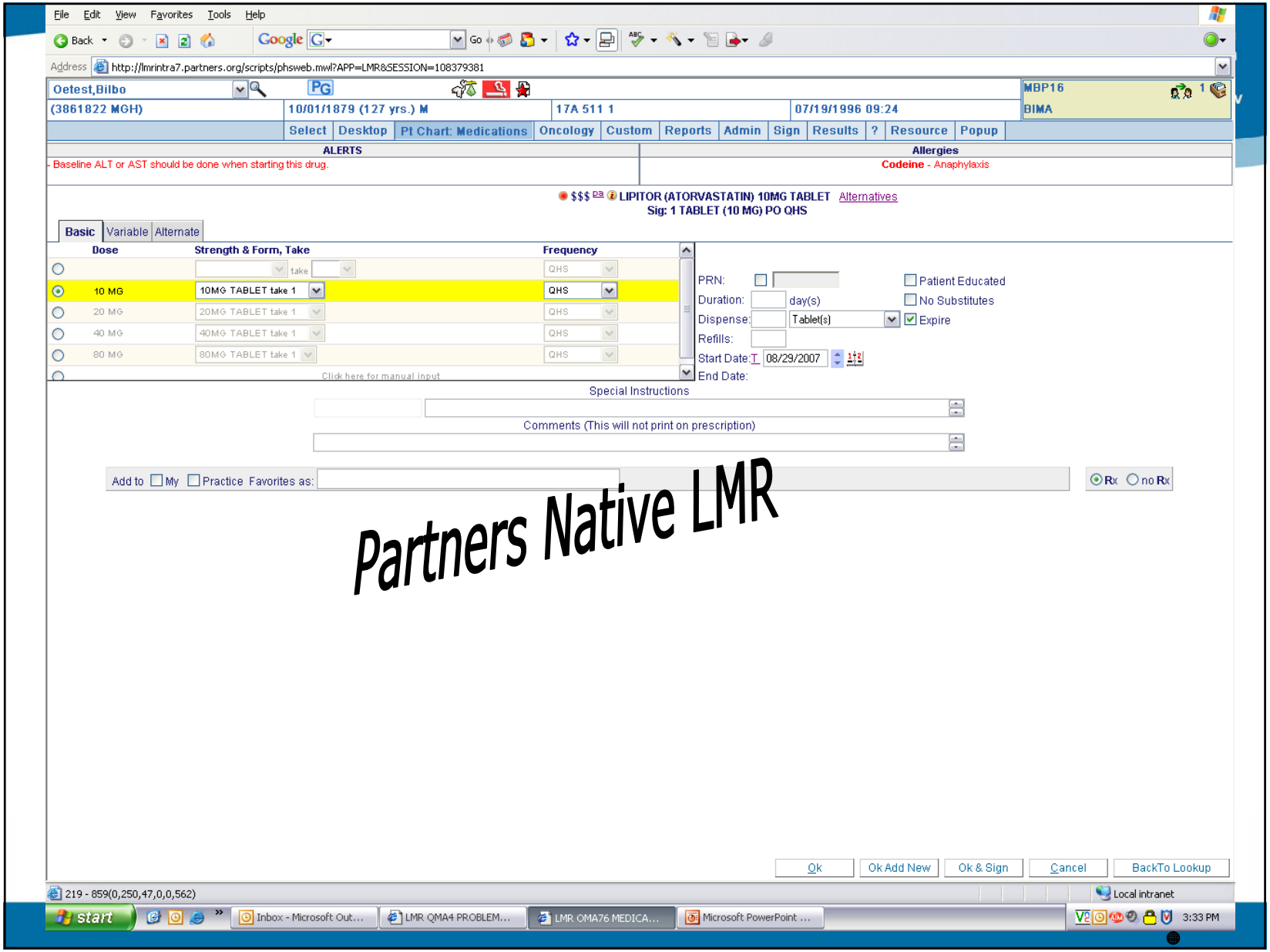

Oetest,Bilbo
(3861822 MGH)
10/01/1879 (127 yrs.) M
17A 511 1
07/19/1996 09:24
MBP16
BIMA
Select Desktop Pt Chart: Medications Oncology Custom Reports Admin Sign Results ? Resource Popup
Allergies
Codeine - Anaphylaxis
LIPITOR (ATORVASTATIN) 20MG TABLET Alternatives
Sig: 1 TABLET (20 MG) PO QHS
Basic Variable Alternate
Dose
Strength & Form, Take
Frequency
20 MG
10 MG
20 MG
40 MG
80 MG
Click here for manual input
Med D/C -- Web Page Dialog
Select a reason to discontinue Lipitor (ATORVASTATIN)
No Longer Necessary
Ineffective
Adverse reaction
Rejected by patient
Too expensive
Change requested by insurance
Error (erroneous entry)
Inadequately covered by insurance (Tier 2 or 3)
Other (enter reason)
End Date: T 08/29/2007
Ok Cancel
Patient Educated
No Substitutes
Expire
Orig. Date: 12/07/2005
Add to My Practice Favorites as:
Rx no Rx
History Discontinue Link to Problems
Ok Renew Ok & Sign Cancel
Partners Native LMR


Partners Native LMR
Oetest,Bilbo
(3861822 MGH)
10/01/1879 (127 yrs.) M
17A 511 1
07/19/1996 09:24
MBP16
BIMA
Select Desktop Pt Chart: Medications Oncology Custom Reports Admin Sign Results ? Resource Popup
Allergies
Codeine - Anaphylaxis
LIPITOR (ATORVASTATIN) 20MG TABLET Alternatives
Sig: 1 TABLET (20 MG) PO QHS
Basic Variable Alternate
Dose
Strength & Form, Take
Frequency
20 MG
20MG TABLET take 1
10 MG
40 MG
80 MG
Med D/C -- Web Page Dialog
Select a reason to discontinue
-- Web Page Dialog
Lipitor (ATORVASTATIN)
Reactions
Add Reaction(s):
Current Reaction(s):
Anaphylaxis
Angioedema
Add >>
<< Remove
Comment
Ok
Cancel
Patient Educated
No Substitutes
Expire
Orig. Date:
12/07/2005
Add to My Practice Favorites as:
Rx no Rx
History Discontinue Link to Problems
Ok Renew Ok & Sign Cancel


Adverse Event Report
CRIX INTERNATIONAL
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
tms
Patient Record Number
pmrn 102030405060708
Suspect Drug
Monopril
Date Drug First Prescribed
Thursday June 20, 2002
Event Details
Select all outcomes below that apply to this particular adverse event
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 brochospasm, 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
Monopril discontinued due to adverse event: Allergic reaction to asthma medicine
Patient Information
Adverse Reactions
Medications
Do you want your identity withheld from the drug manufacturer?
Yes
No
For more information on this form and program please click here.
Submit


File Edit View Favorites Tools Help
Back
Google
Address http://lmrintra7.partners.org/scripts/phsweb.mwl?APP=LMR&SESSION=108383525
Patient Information
Patient Initials
tms
Patient Birth Date
19970303
Patient GP Medical Record Number
pmrn 102030405060708
Patient Onset Age
00023
Patient Specialist Record Number
pslrn 12345678987654
Patient Weight
210 kg
Patient Hospital Record Number
phrn 112233445566778
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
234 - 875(0,250,47,0,0,578)
Local intranet
start
Inbox - Microsoft Out...
LMR QMA4 PROBLEM...
LMR QMA76 MEDICA...
Microsoft PowerPoint ...
3:37 PM


File Edit View Favorites Tools Help
Back
Address http://lmrintra7.partners.org/scripts/phsweb.mwl?APP=LMR&SESSION=108379381
Oetest,Bilbo
(3861822 MGH)
10/01/1879 (127 yrs.) M
17A 511 1
07/19/1996 09:24
MBP16
BIMA
Select Desktop Pt Chart: Medications Oncology Custom Reports Admin Sign Results ? Resource Popup
ALERTS
- Baseline ALT or AST should be done when starting this drug.
Allergies
Codeine - Anaphylaxis
$$$ LIPITOR (ATORVASTATIN) 10MG TABLET Alternatives
Sig: 1 TABLET (10 MG) PO QHS
Basic Variable Alternate
Dose
Strength & Form, Take
Frequency
10 MG
10MG TABLET take 1
QHS
20 MG
20MG TABLET take 1
40 MG
40MG TABLET take 1
80 MG
80MG TABLET take 1
Click here for manual input
PRN:
Duration:
day(s)
Dispense:
Tablet(s)
Refills:
Start Date: 08/29/2007
End Date:
Patient Educated
No Substitutes
Expire
Special Instructions
Comments (This will not print on prescription)
Add to My Practice Favorites as:
Rx no Rx
Partners Native LMR
Ok Ok Add New Ok & Sign Cancel BackTo Lookup
219 - 859(0,250,47,0,0,562)
Local intranet
start
Inbox - Microsoft Out...
LMR QMA4 PROBLEM...
LMR OMA76 MEDICA...
Microsoft PowerPoint ...
3:33 PM

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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

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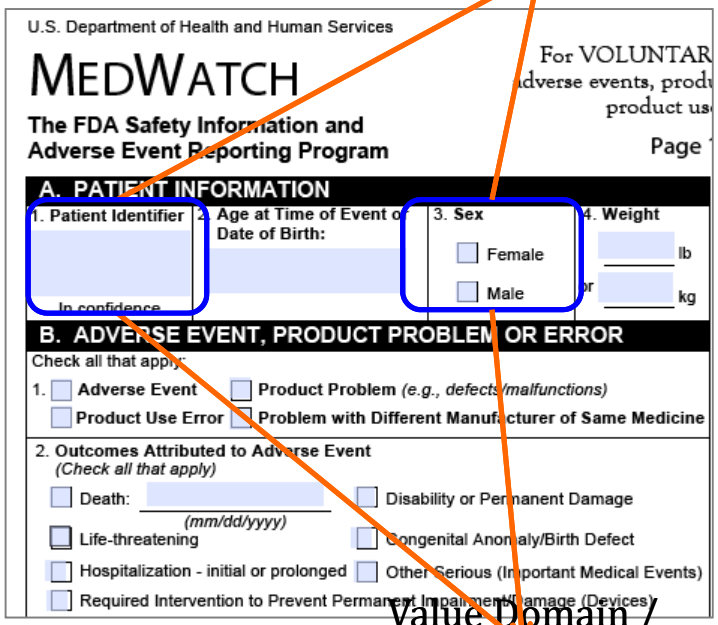
Data Element(s)


U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTAR
dverse events, prod
product us

Page

A. PATIENT INFORMATION

1. Patient Identifier | 2. Age at Time of Event o Date of Birth: | 3. Sex Female Male | 4. Weight lb kg

In confidence

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. Adverse Event | Product Problem *(e.g., defects/malfunctions)*
Product Use Error | Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event *(Check all that apply)*

Death: *(mm/dd/yyyy)* | 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 (Devices)

Value Domain / Value Set (free text or answer list / coded list)

Data Element *Attributes*

(identified in database where data element is maintained)

Attribute NAME	Attribute VALUE
•*id*:	123XYZ
•*version*:	1.0
•*Name*:	Sex
•*Preferred question text*: Sex	
•*Creation Date:*	Jan 20, 2014
•…	

Value Domain/Value Set *Attributes*

(identified in database where value domain is maintained)

Attribute NAME	Attribute VALUE
Value Domain	
• *Name*:	Administrative_Gender
• *Version*:	1.2
• *Max character quantity:*	6
• *Permissible value:*	Female

FDA Drug & Common Formats:
Data Element Overlap

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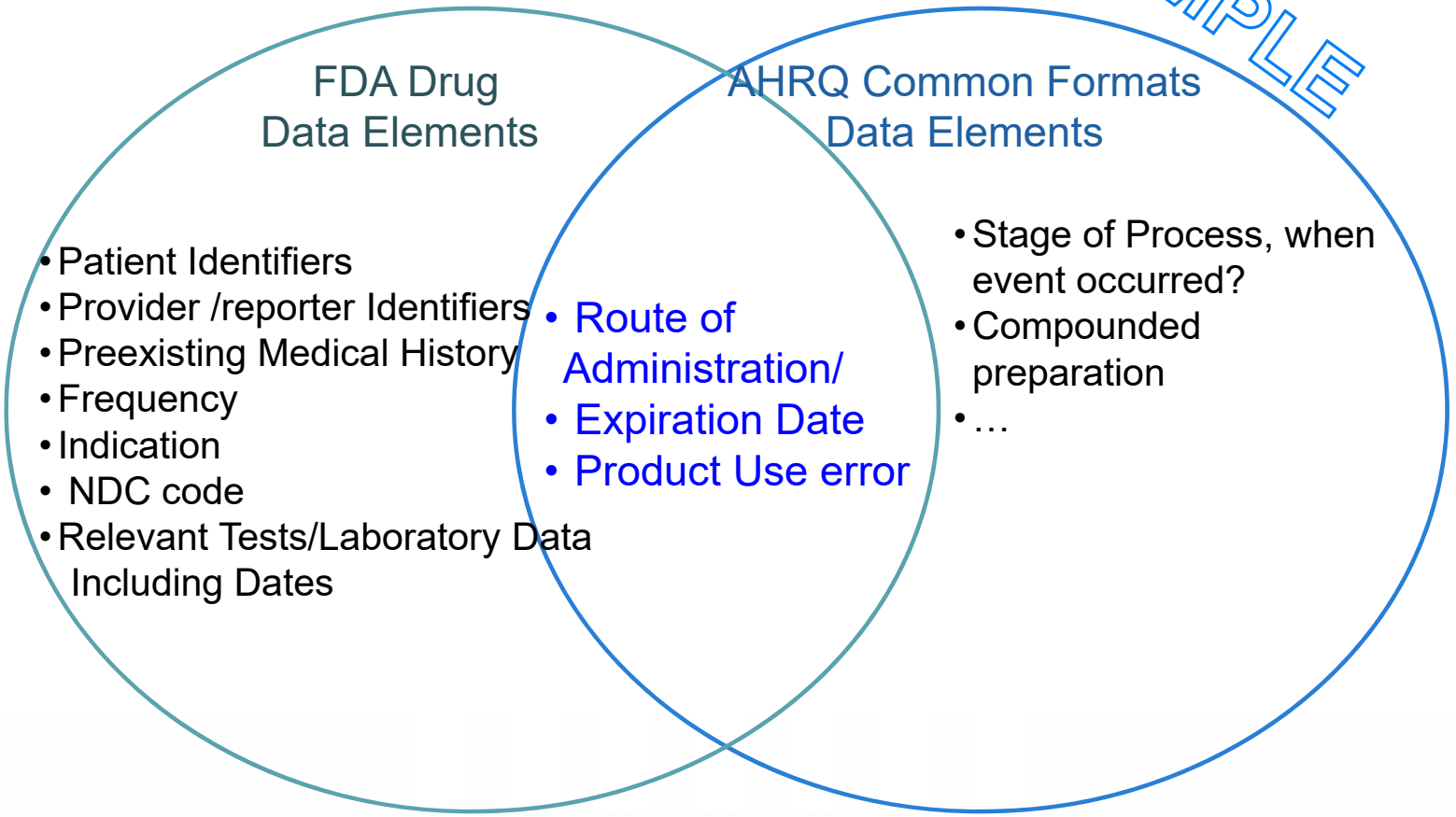
SAMPLE



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FDA Device & Common Formats:
Data Element Overlap

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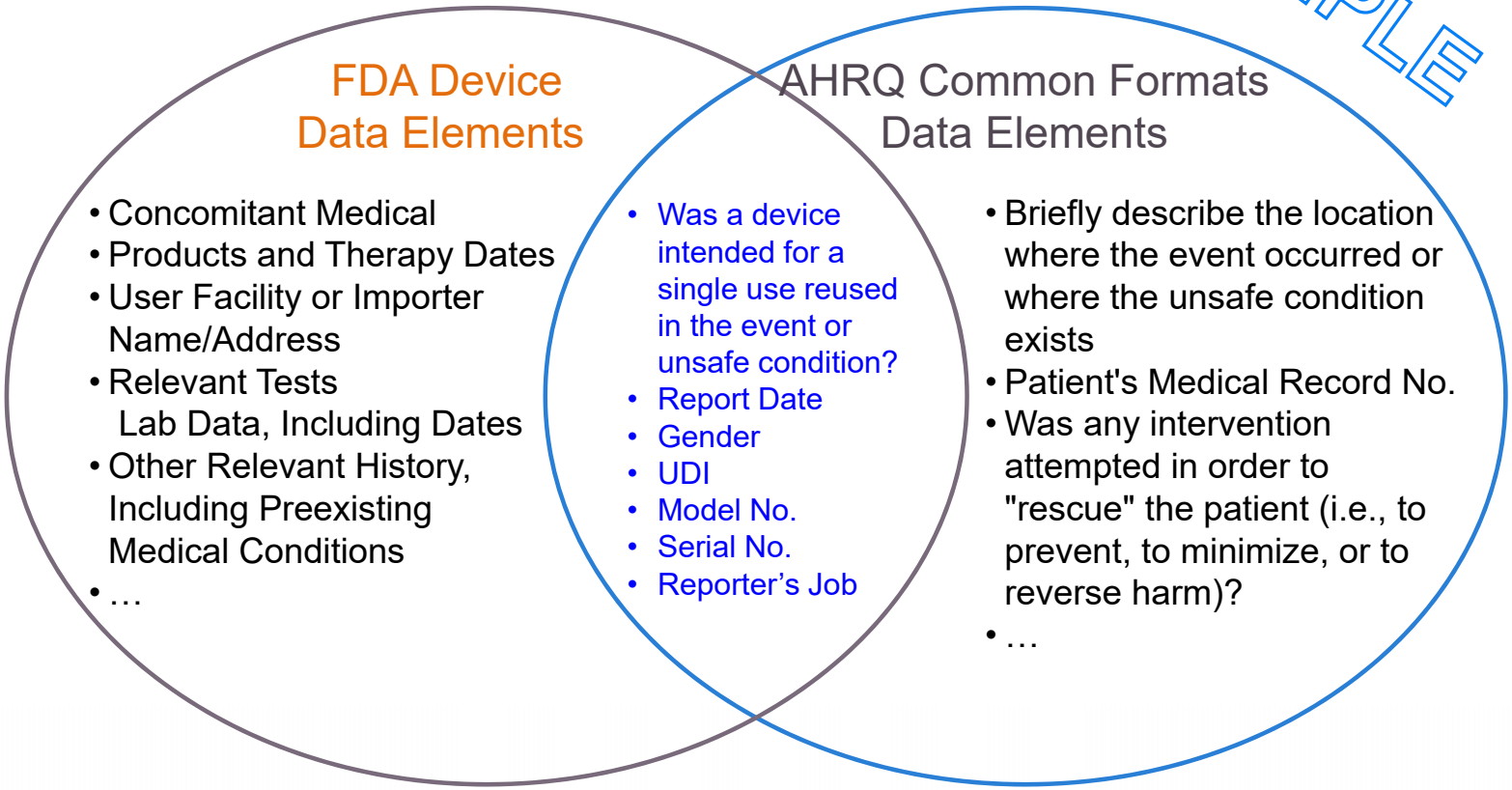
SAMPLE



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Questions