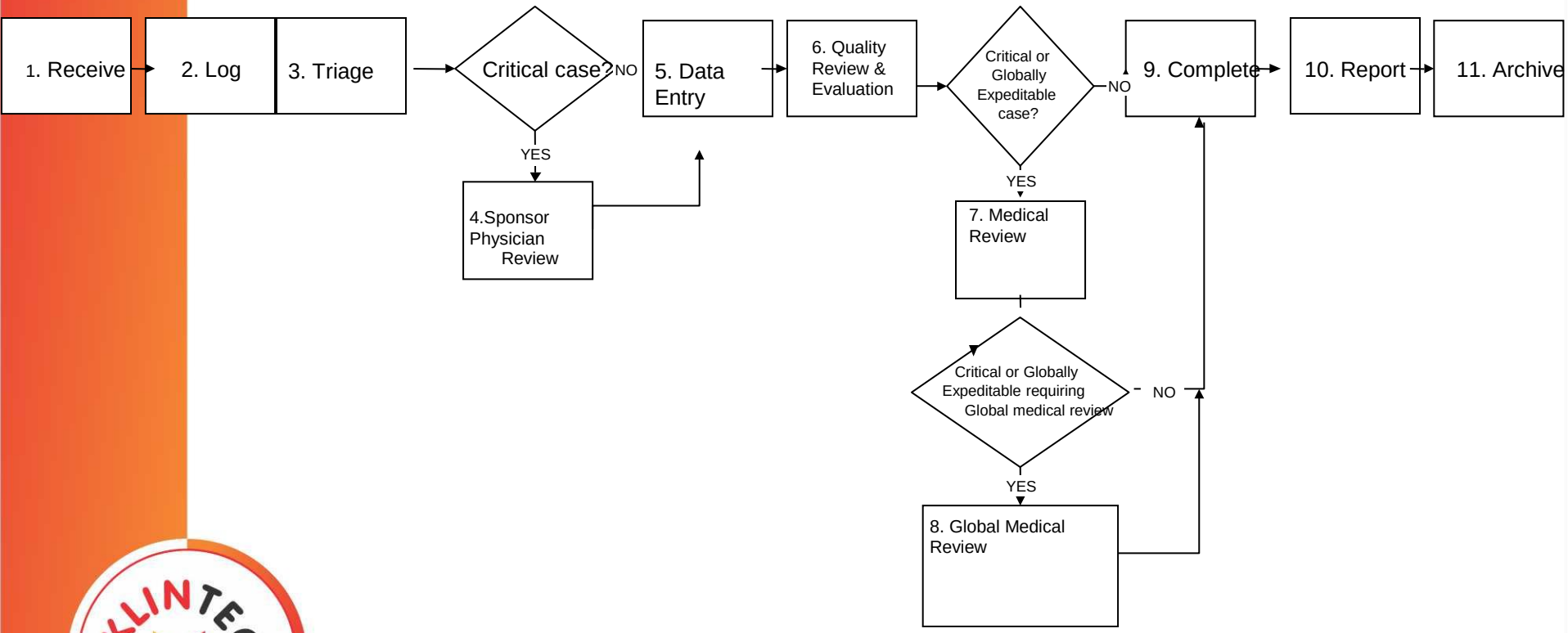
Processing of individual cases (ICSRs)

Global Case Handling Process Overview

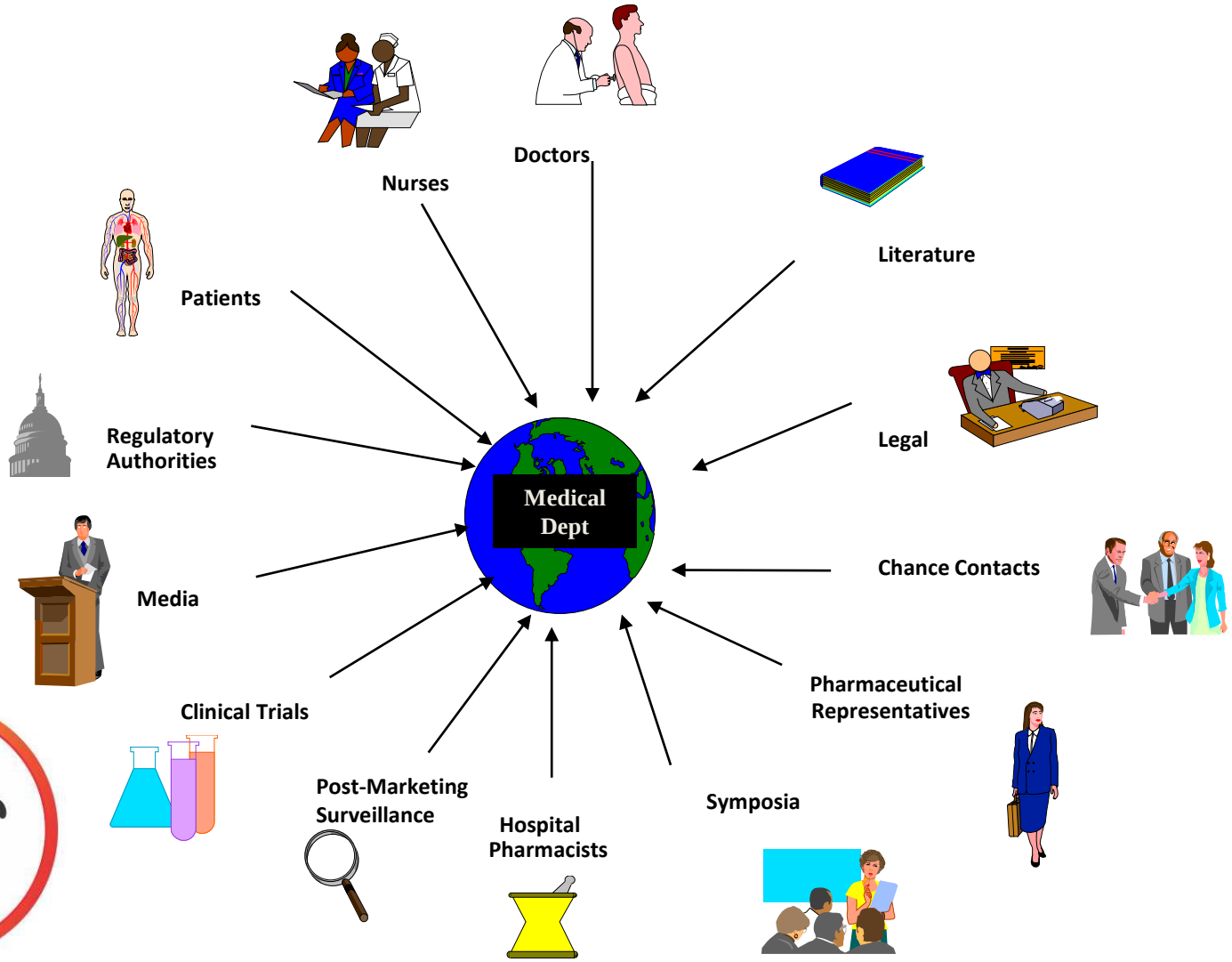


Steps in case handling

- AE Occurs : Receive – Triage-Process- Review - Complete
- Based on pharmacovigilance policies, regulations and guidance documents, the process can be summarized as follows:
    1. Creation of individual case from multiple source of safety information such as clinical trials, safety call centers, spontaneous reports, literature searches, internet monitoring
    2. Processing of each case and assessment of its relationship to the investigational product
    3. Reporting to the regulatory authorities and other stakeholders, either as an expedited report or as a part of an aggregate report

Chaplain V @ PhUSE 2014

Sources of AEs



Acknowledgement – Why?

- Encourages further reporting
- Ensures cooperation if more info is wanted
- Builds company image
- Protects the company
- Assists marketing, improves liaison, ensures future prescriptions
- No acknowledgement = more duplicates

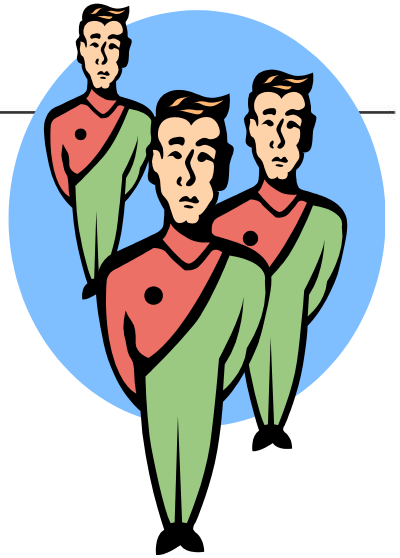
Triage origins!!!

- A process for sorting injured people into groups based on their need for or likely benefit from immediate medical treatment. Triage is used in hospital emergency rooms, on battlefields, and at disaster sites when limited medical resources must be allocated
- **1.** (Medicine) the principle or practice of sorting casualties in battle or disaster or other patients into categories of priority for treatment
- **2.** (Government, Politics & Diplomacy) the principle or practice of allocating limited resources, as of food or foreign aid, on a basis of expediency rather than according to moral principles or the needs of the recipients

Triage

- Assess case for validity as per regulations
- Duplicate search
- Determine regulatory clock start date
- Is the case initial or follow up
- Assess AE terms
- Is the case serious? Expected? Related?
- Is it active or blinded?
- Determine reporting priority
- Send for processing

Duplicate Search



- Common phenomenon
  - Multiple agencies
  - Greater awareness
  - Strict regulations
- Significance to further processing: If follow up, could alter case seriousness & reporting timelines
- Damage potential :
  - Can mislead signal detection systems, improper generation of signals
  - Regulatory action if delayed

Duplicate Search

- Patient, reporter, product , event & permutations
- Patient – identification, location, study
- Reporter – address ,city, street, hospital, HCP/ consumer,
- Change of reporter from consumer to HCP makes case medically confirmed
- Change of info could diminish seriousness of case
- Event – new additions to past report could change seriousness
- Causality – HCP could change his mind about the causality

Case processing

- Assign identification # and assign for data entry
- Perform data entry
- Coding (AE terms, drugs)
- Identify missing case elements
- Followup for completion
- Prepare narrative
- Review

Case narrative- importance

- Provides summary of events to readers who do not have access to original data sets
- Seen/used by various groups
  - case reviewers to decide seriousness, upgrade etc
  - affiliates to triage for their countries,
  - regulatory authorities,
  - during preparation of PSURs and other summary reports
- Essential to follow company & CIOMS guidelines, ensure completeness, chronology and sufficient detail to come to a conclusion

It should be ready to be pasted into any report

Review

- Quality
  - Check for accuracy
  - Check for consistency
  - Check for completeness
- Medical and scientific
  - Confirm triage
  - Check case for medical sense
  - Request non routine follow up if appropriate
  - Make company causality assessment for upgrades or in absence of investigator causality

Medical review contd

- Appropriateness of the AE terms selected.
- Confirmation of the seriousness classification of the AE terms.
- Agreement with the listedness/expectedness classification of AE terms, outcome classification. coding of AEs, concomitant conditions, and medical history.
- Review of the narrative -it makes clinical sense and includes all important elements
- Authoring the company clinical comment, including determination of the company causality assessment, when appropriate.
- Identification of any specific additional information needed for medical assessment purposes other than routine follow-up requests required for case completion.
- Upgrade or downgrade to the case's regulatory reportability
- Identification of potential safety signals.
- A rapid and clearly understood error resolution process must support case review

Drug Safety Physician

Drug-safety physicians are often confronted, especially in relation to spontaneous reporting, with incomplete information on observed adverse events. To make the best use of the information received, they need medical commonsense, experience and — when collecting additional information — communication skills.

Having collected all the needed information available, the drug-safety physician is supposed to write a medical evaluation — including a diagnosis, a comment on the causal role of the drug in question, and alternative explanations—and a discussion of any action that needs to be taken.

Reporting ADRs, Clinical Terms & Definitions for their use. CIOMS handbook,1999

Case completion

- Case reviewed
- Incorporate requested changes
- Request expedited report (if required) with attachments & supporting correspondence
- Distribute globally
- Produce and forward expedited report (if reqd)
  - Send to reg authorities as appropriate
  - Circulate to internal company personnel
  - Send to external partners (licensees, distributors)
- Generate requested follow up (if required)
- Archive case

Forms

- Various forms are used to report AEs
- 3500A (Medwatch Form)
- Council for International Organization of Medical Science (CIOMS I Foreign) or other form if approved in advance

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day	Month	Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP	

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

CDSCO
Central Drugs Standard Control Organization
Directorate General of Health Services,
Ministry of Health & Family Welfare, Government of India,
Nirman Bhawan, New Delhi - 110011
www.cdsco.nic.in

For VOLUNTARY reporting of Adverse Drug Reactions by health care professionals

Report #

To be filled in by Pharmacovigilance centres receiving the form.

A. Patient information

1. Patient Identifier Initials _____ In confidence
2. Age at time of event: or _____ Date of Birth:
3. Sex: ☐ M ☐ F
4. Weight_____ Kgs

B. Suspected Adverse Reaction

5. Date of reaction started (dd/mm/yy):
6. Date of recovery (dd/mm/yy):
7. Describe reaction or problem

12. Relevant tests/ laboratory data, including dates

13. Other relevant history, including pre-existing medical conditions (e.g., allergies, race, pregnancy, smoking alcohol use, hepatic/ renal dysfunction, etc.)

14. Seriousness of the reaction
- ☐ Death (dd/mm/yy)_____
- ☐ Life threatening
- ☐ Hospitalization-initial or prolonged
- ☐ Disability
- ☐ Congenital anomaly
- ☐ Required intervention to prevent permanent impairment/ damage
- ☐ Other (specify)_____

15. Outcomes
- ☐ Fatal
- ☐ Continuing
- ☐ Recovering
- ☐ Recovered
- ☐ Unknown
- ☐ Other (specify)_____

C. Suspected medication(s)

Sl. No.	8. Name (brand and / or generic name)	Manufac-turer (if known)	Batch No. / Lot No. (if known)	Exp. Date (if known)	Dose used	Route used	Frequency	Therapy dates (if unknown, give duration)		Reason for Use or prescribed for
								Date started	Date stopped	
I										
II										
III										
IV										

Sl. No. As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced, dose
I										
II										
III										
IV										

11. Concomitant medical products and therapy dates including self medication and herbal remedies (exclude those used to treat reaction)

D. Reporter (see confidentiality section in first page)

16. Name and Professional Address: _____
_____
_____
Pin code: _____ E-mail: _____
Cell No. / Tel. No. with STD Code: _____
Speciality: _____ Signature:

17. Occupation

18. Date of this report (dd/mm/yy)

VACCINE ADVERSE EVENT REPORTING SYSTEM

VAERS

24 Hour Toll Free Information 1-800-822-7967
P.O. Box 1100, Rockville, MD 20849-1100
PATIENT IDENTITY KEPT CONFIDENTIAL

For CDC/FDA Use Only

VAERS Number _____

Date Received _____

Patient Name:

Last First M.I.

Address

City State Zip

Telephone no. (____) _____

Vaccine administered by (Name):

Responsible Physician _____

Facility Name/Address

City State Zip

Telephone no. (____) _____

Form completed by (Name):

Relation to Patient ☐ Vaccine Provider ☐ Patient/Parent ☐ Manufacturer ☐ Other

Address *(if different from patient or provider)*

City State Zip

Telephone no. (____) _____

1. State | 2. County where administered | 3. Date of birth mm / dd / yy | 4. Patient age | 5. Sex ☐ M ☐ F | 6. Date form completed mm / dd / yy

7. Describe adverse events(s) (symptoms, signs, time course) and treatment, if any

8. Check all appropriate:
- ☐ Patient died (date mm / dd / yy)
- ☐ Life threatening illness
- ☐ Required emergency room/doctor visit
- ☐ Required hospitalization (_____days)
- ☐ Resulted in prolongation of hospitalization
- ☐ Resulted in permanent disability
- ☐ None of the above

9. Patient recovered ☐ YES ☐ NO ☐ UNKNOWN

10. Date of vaccination mm / dd / yy Time _____ AM PM

11. Adverse event onset mm / dd / yy Time _____ AM PM

12. Relevant diagnostic tests/laboratory data

13. Enter all vaccines given on date listed in no. 10

	Vaccine (type)	Manufacturer	Lot number	Route/Site	No. Previous Doses
a.					
b.					
c.					
d.					

14. Any other vaccinations within 4 weeks prior to the date listed in no. 10

	Vaccine (type)	Manufacturer	Lot number	Route/Site	No. Previous doses	Date given
a.						
b.						

15. Vaccinated at:
- ☐ Private doctor's office/hospital
- ☐ Public health clinic/hospital
- ☐ Military clinic/hospital
- ☐ Other/unknown

16. Vaccine purchased with:
- ☐ Private funds
- ☐ Public funds
- ☐ Military funds
- ☐ Other/unknown

17. Other medications

18. Illness at time of vaccination (specify)

19. Pre-existing physician-diagnosed allergies, birth defects, medial conditions(specify)

20. Have you reported this adverse event previously?
- ☐ No
- ☐ To health department
- ☐ To doctor
- ☐ To manufacturer

Only for children 5 and under

22. *Birth weight* _____ lb. _____ oz.

23. *No. of brother and sisters*

Only for reports submitted by manufacturer/immunization project

21. Adverse event following prior vaccination (check all applicable, specify)

	Adverse Event	Onset Age	Type Vaccine	Dose no. in series
☐ In patient				
☐ In brother or sister				

24. *Mfr./imm. proj. report no.*

25. *Date received by mfr./imm.proj.*

26. *15 day report?* ☐ Yes ☐ No

27. *Report type* ☐ Initial ☐ Follow-Up

Health care providers and manufacturers are required by law (42 USC 300aa-25) to report reactions to vaccines listed in the Table of Reportable Events Following Immunization. Reports for reactions to other vaccines are voluntary except when required as a condition of immunization grant awards.

Form VAERS-1(FDA)

Print | Next Page | Reset Form | Delete Page | Delete Multiple Pages

Form Approved: OMB No. 09 10-029 1, Expires 12/31/11
See OMB statement on reverse.

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

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

Mfr Report # Mfr_Report

UF/Importer Report # UF_Importer_Report

FDA Use Only

MEDWATCH

FORM FDA 3500A (6/10)

General Instructions

Page of ____

A. PATIENT INFORMATION

Section A - Help

1. Patient Identifier: 10416 — In confidence

2. Age at Time of Event: 13 Years
or
Date of Birth: 06/23/1997

3. Sex: ☐ Female ☑ Male

4. Weight: ____ lbs or 44 kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

Section B - Help

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)*: 06/11/2011

5. Describe Event or Problem
DESCRIBE

C. SUSPECT PRODUCT(S)

Section C - Help

1. Name *(Give labeled strength & mfr/labeler)*
#1 NAME_1
#2 NAME_2

2. Dose, Frequency & Route Used
#1 DOSE_1
#2 DOSE_2

3. Therapy Dates *(If unknown, give duration from/to (or best estimate))*
#1 THERAPY_1
#2 THERAPY_2

4. Diagnosis for Use *(Indication)*
#1 DIAGNOSIS_1
#2 DIAGNOSIS_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 LOT_1
#2 LOT_2

7. Exp. Date
#1 EXPDATE_1
#2 EXPDATE_2

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

9. NDC# or Unique ID
NDC_1

10. Concomitant Medical Products and Therapy Dates *(Exclude treatment of event)*
CONCOMITANT