Emnet Coordinating Center

ABS-AS-40091

PhV and Complaint Management

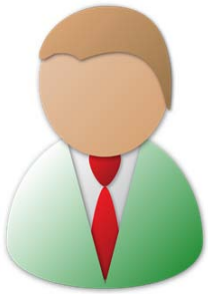
Global Patient Safety & PhV

9/21/15

Agenda:

- Serious adverse event or related SABA event journey
- ABS-AS-40091 AE report form (including tips and study specifications)
- Regulatory obligations - SUSARs
- Follow up and queries
- Pregnancy reports
- Additional Reports
- SAE management plan
- Product Complaint Management

SAE/related SABA AE Journey



Investigator

Teva LSO

Teva Safety Database

Filing System

Emnet Coordinating Center

LSO

AE Report Form

CIOMS XML

Study Specifications

- Although study personnel will inquire concerning specific asthma exacerbation symptoms at the ED interview and follow-up interview, eg, throat tightness, limitation of activities, patients will not be asked whether they are currently experiencing any unusual symptoms or medical problems
- Nevertheless, serious and non-serious adverse events (other than asthma symptoms) and pregnancies reported by the patients during these interviews will be recorded and reported to the investigator (and attending physician at the ED interview). Patients at the follow-up interview who report adverse events will be encouraged to contact their primary care provider for further assistance; patients without a primary care provider or who report serious adverse events will be encouraged to go to their local ED for evaluation.

Study Specifications

- Complete the Teva ABS-AS-40091 AE Report Form only for
  - non-serious adverse events considered to be related to a Teva SABA inhaler (ie, ProAir HFA or ProAir RespiClick) by the study investigator
  - all serious non-asthma adverse events regardless of relationship
- Worsening of, or hospitalization for, asthma exacerbation symptoms at the ED visit in which the patient was enrolled, or during the 2-week follow-up period, will not be considered an adverse event.
- Period for recording and reporting adverse events
  - starts after the clinical study patient has signed the informed consent form and ends after completion of the 2-week follow-up period (ie, completion of the follow-up telephone call and medical record review).

AE reporting form

ABS-AS-40091 Adverse Event Report Form

http://
:vanet.teva.corp/si

Instructions for Completing Protocol ABS-AS-40091 Adverse Event Form

http://
:vanet.teva.corp/si

AE Follow Up Reports

- Follow-up reports should be completed and sent when:
  - new clinically significant data are obtained;
  - there is a significant change in the subject's condition;
  - upon event resolution;
  - requested by Teva Pharmacovigilance.
- When new information becomes available: complete the AE reporting form

ABS-AS-40091 AE Reporting Practical Tips

- When possible, a diagnosis, not a list of signs/symptoms, should be reported as the SAE.
- Surgeries are not SAEs (report the reason for the surgery i.e. Appendectomy - Appendicitis).
- Use medical terminology.
- Always specify the exact start and stop dates.
- Causality should be given by the investigator for each reported event for every suspected medication.
- Source documents should be summarized in the case narrative.

When does the reporting clock start ticking?

When a Teva representative receives from an Investigator a ADR report (with at least, patient, ADR and investigational drug information), the regulatory

reporting clock starts.

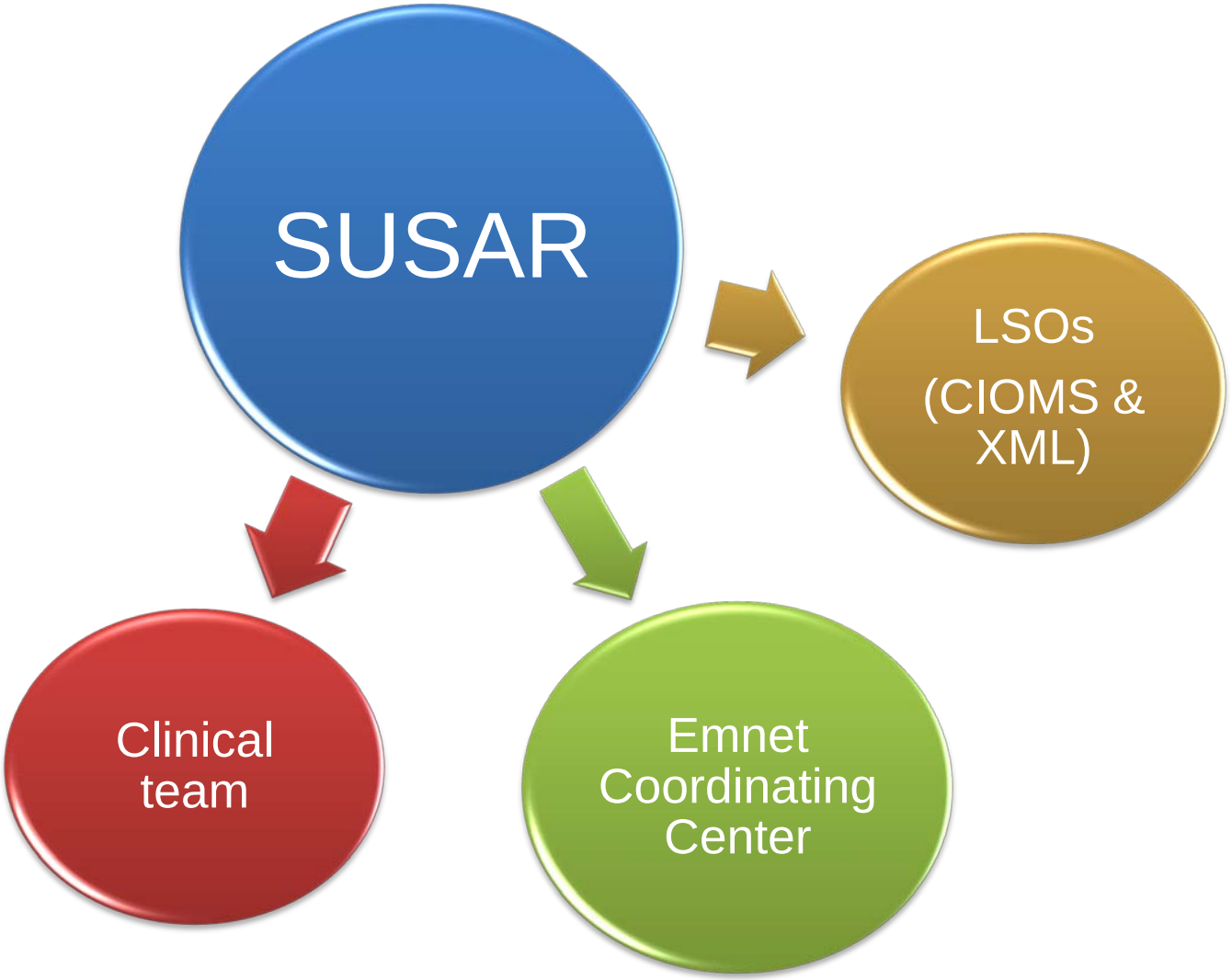
Investigators are required to report a ProAir HFA or ProAir RespiClick related AE or any SAE within **24 hours** of becoming aware of the event. Additional information (follow-up) should be sent to Teva Pharmacovigilance by the site within **24 hours** of the site becoming aware of the event.

Expedited Reports Timeline

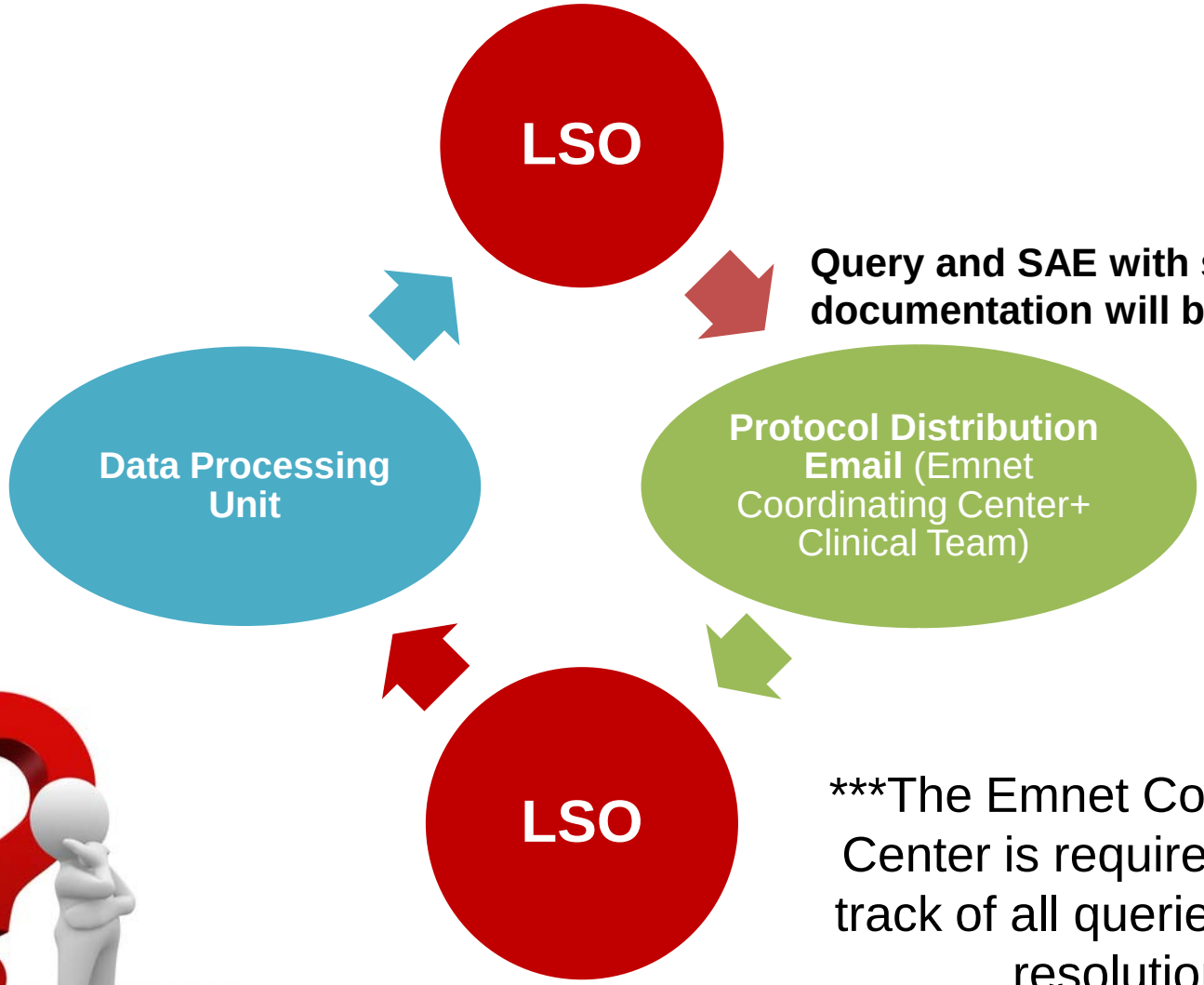
SUSAR need to be submitted as soon as possible:

Type of Suspected Adverse Reaction	Submission Timeline (Authorities/ Ethic committees/ Investigators)
Fatal, life-threatening + unexpected	7 days
Other seriousness criteria + unexpected	15 days

Distribution of CIOMS/XML



FU/queries regarding SAEs



***The Emnet Coordinating Center is required to keep track of all queries through resolution

Pregnancy Reports

- All pregnancies reported by patients should be reported to a Teva representative, even if they do not include an *Adverse Event.*
- The pregnancy reporting procedure is the same as the AE reporting procedure.
  - When a subject's pregnancy is confirmed: complete Clinical Trial Pregnancy Form.
  - When new information becomes available or the pregnancy comes to an end: complete Clinical Trial Pregnancy Form.
  - If the pregnant subject experiences an SAE complete AE report form.

Tracking Submissions

- PhV's goal is 100% Compliance

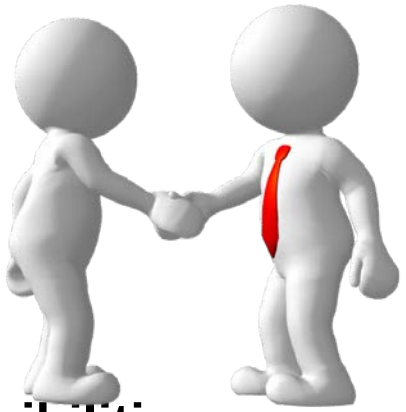
- LSO – submissions tracked electronically
- Emnet Coordinating Center– document all notifications of submissions

Reconciliation reports

- The protocol distribution group will receive the following quarterly reports:
  - **Cumulative line listing**: include all SAEs (related and not related) and adverse events considered to be related to a Teva SABA inhaler (ie, ProAir HFA or ProAir RespiClick) from the beginning of the study.
  - **Listing of new or changed information**: only new SAE/Teva related SABAs and new follow-ups received during the previous month will come up in this report.

SAE Management Plan (SMP)

- The draft SAE management plan is available.
- It includes:
  - **Objective**
  - **Standard Operating Procedures**
  - **Teva Responsibilities**
  - **Emnet Coordinating Center Responsibilities**
  - **AE Form and Instructions**
  - **Pregnancy Form and Instructions**



Emnet Coordinating Center

ABS-AS-40091

Clinical Product Complaints

DATE

Clinical Product Complaints

- Defined as a problem or potential problem with the physical quality or characteristics of a clinical device used in a clinical research study sponsored by Teva.
- Examples
  - unexpected or unanticipated taste or odor or both
  - broken or cracked inhaler
  - inhaler not working correctly or appears defective in some manner
  - incorrect packaging or incorrect or missing labeling

Clinical Product Complaints

- Patients may spontaneously complain about their SABA rescue inhaler during the ED interview and follow-up interview (ie, without prompting by the interviewer), but will not be asked about any clinical product complaints

Clinical Product Complaint Reporting Requirements

- Record all generic or brand name SABA inhalers made by any manufacturer on the Visit Form or Follow-up Form. In the source document also document any actions taken to resolve the complaint and to preserve the safety of the patient.
- Additional Reporting Requirements:
  - Complaints concerning other SABA inhalers should also be reported and the inhaler sent back to the appropriate manufacturer.
  - Complaints concerning SABA rescue inhalers marketed by Teva in the US (ie, ProAir HFA and ProAir RespiClick)
    - must be emailed to Teva's Quality Department at QAS@tevausa.com **within 48 hours** of becoming aware of the event.
    - It is required that the Teva SABA inhaler be sent back to the sponsor for investigative testing whenever possible.

Clinical Product Complaint Reporting Requirements

- Required Email Information:
  - indicate how was the complaint initiated, ie, during the course of a non-interventional, observational study of acute asthma patients at an emergency department interview / follow-up interview (chose 1)
  - clinical protocol number
  - investigational center number and study investigator name
  - name of person receiving the complaint
  - patient identifier (patient study ID)
  - Teva SABA inhaler name: ProAir HFA or ProAir RespiClick
  - NDC#
  - Lot#
  - Expiration date
  - product available for return? Yes/No
  - product was taken or used according to instructions? Yes/No
  - description or nature of complaint
  - associated adverse event? Yes/No
- NOTE: Reporting a complaint must not be delayed because not all the required information can be immediately obtained. Known information must be immediately reported. The sponsor will collaborate with the investigator to obtain any outstanding information

Adverse Events or Serious Adverse Events Associated with a Product Complaint

- If there is an adverse event or serious adverse event associated with a Teva SABA rescue inhaler, the protocol defined AE Reporting process should be followed.

Questions?