SOPP 8508.2: Procedures for the Vaccine Safety Team

Version #1

Effective Date: May 9, 2008

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1. Purpose

This SOPP describes the procedures that the Center for Biologics Evaluation and Research (CBER) staff should routinely follow to coordinate rapid responses to complex vaccine safety issues, as well as to provide advice to the CBER Office of the Director on additional vaccine safety data and policy needs. This SOPP describes the process for communication within CBER among points of contact in the Office of Biostatistics and Epidemiology (OBE), Office of Vaccine Research and Review (OVRR), Office of Compliance and Biologics Quality (OCBQ), Office of the Director (OD), and the Office of Communication, Training and Manufacturers Assistance (OCTMA). This SOPP also describes the communication process with other units within the Food and Drug Administration (FDA) as well as stakeholders external to the Department of Health and Human Services (HHS).

2. Definitions

VAERS

The Vaccine Adverse Event Reporting System (VAERS) is a national vaccine safety surveillance program co-managed by the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC).
Please refer to this web link for more information on VAERS:
http://www.vaers.hhs.gov/[1]

Risk Management

FDA views risk management of medical products as an iterative process encompassing the assessment of risks and benefits, the minimization of risks, and the maximization of benefits. For the majority of products, routine risk minimization measures, such as labeling, are sufficient to minimize risks and preserve benefits.
Only a few products are likely to merit consideration for additional risk minimization efforts identified as Risk Evaluation and Mitigation Strategy (REMS) in The Food and Drug Administration Amendments Act (FDAAA) of 2007, Title IX. The Vaccine Safety Team (VST) is not the decision making body for REMS, although the VST may provide advice on such a risk management tool.

Recall

21 CFR 7.3(g) defines a recall as a firm's removal or correction of a marketed product that the FDA considers to be in violation of the laws we administer and against which we would initiate a legal action.

Market Withdrawal

21 CFR 7.3(j) defines a market withdrawal as a firm's removal or correction of a distributed product that involves a minor violation that would not be subject to legal action by the FDA or involves no violation.

Vaccine Safety Team

The Vaccine Safety Team (VST) consists of CBER representatives from OBE, OCTMA, OCBQ, OD, and OVRR. The key purpose of the VST is to coordinate CBER rapid responses to vaccine safety issues that involve complex intra-Center interactions and to serve as a resource to CBER to identify data and policy needs pertaining to vaccine safety. The VST is chaired or co-chaired by a member from OVRR and/or OBE/Division of Epidemiology (DE). A regulatory project officer (RPO) assists in the planning and management of the VST.

3. Background

Safe and effective vaccines are important to U.S. public health. Concerns about vaccine safety may weaken public confidence in vaccination programs. The main processes to ensure vaccine safety are 1) assessments of the Investigational New Drug Application (IND) and the pre-market Biologics License Application (BLA) by vaccine review committees and 2) the continued post-market assessments of data, including reports from the Vaccine Adverse Event Reporting System (VAERS), lot release, and inspections of manufacturing facilities. Finally, risk communication and information about vaccine effectiveness need to be available to the public so it and the health care community are able to make the best possible health decisions.

The CBER managed review process is established to handle these functions and address the majority of safety issues that arise during a vaccine's lifecycle from preclinical to postmarketing development. Overall, the safety of vaccines in this country is high and the public can have confidence that these products are safe and effective. CBER has formed the Vaccine Safety Team (VST) to provide CBER rapid coordination, communication, and follow-up on safety issues involving complex intra-Center interactions. The VST will also serve as a resource to the Center for identifying data and policy needs.

4. Policy

Vaccine safety assessments continue as part of the life cycle of a vaccine from pre-marketing to post-marketing. Pre-market Biologics License Application (BLA) and Biologic License Application Supplements (BLS) review committees and pharmacovigilance staff in OBE/DE are responsible for ensuring that safety issues are identified, addressed, and adequately

monitored. At times, complex vaccine safety issues arise that need greater coordination, management, and rapid cross-CBER response. The VST will receive these issues from review staff, CBER's Office of the Director, or other offices. The VST will coordinate a response to these issues and ensure they are addressed.

At other times, the VST may serve CBER as a resource for identifying data and policy needs regarding vaccine safety issues. These data and policy recommendations will be communicated to the Office of the Director, CBER.

CBER staff who become aware of a potential or existing vaccine safety issue that needs assistance from the VST will communicate, as appropriate, to the VST co-chairs, or RPO, or their Office VST team member (Appendix 1). Coordination with other CBER or FDA units will be conducted as appropriate by the VST.

Examples of some emergency, complex vaccine safety issues, or data or policy needs that may benefit from VST serving as a resource include:

- Reports to VAERS or inspectional results or manufacturing issues that raise concerns about vaccine safety;
- Policy development for vaccine safety guidances and REMS; or
- Advising on a vaccine safety research agenda for the Center.

5. Responsibilities and Procedures

A. VAERS Reports and Inspectional/Manufacturing Issues

OBE Responsibilities

The Office of Biostatistics and Epidemiology (OBE) is the official contact for VAERS and is responsible for processing and review of the reports. OBE is also responsible for forwarding those reports to the appropriate contacts within CBER for further action and follow-up.

If OBE staff identifies VAERS adverse event reports that need a rapid response and complex coordination, the staff will immediately:

- Inform OBE management, who, if they concur with the determination, will
- Inform the VST co-chairs, or RPO, and the OBE VST points of contact (Appendix 1).
- The initial determination from OBE should include the need to notify other Center components (including CBER senior management: Directors of the CBER IOD, OVRR, OBE, OCTMA, OCBQ).

VAERS adverse events are also discussed at the VAERS Rounds, a periodic meeting (e.g. bi-monthly) run by OBE. VST members are invited to keep abreast

of developing safety concerns. Ad hoc meetings resulting from evaluation of incoming VAERS reports can also be scheduled.

OCBQ Responsibilities

If a complex vaccine safety issue involves or potentially involves manufacturing or could result in a possible vaccine shortage, the Office of Compliance and Biologics Quality (OCBQ) will follow up with the manufacturer in conjunction with vaccine product reviewer, if needed.

Information received from the manufacturer will be summarized by OCBQ and forwarded to the VST co-chairs directly or via the OCBQ VST team member (App. 1) if greater CBER coordination for responses is needed.

Should the VST recommend further investigation, OCBQ, Division of Inspections and Surveillance (DIS) will issue an assignment to the Office of Regulatory Affairs (ORA) to perform a field investigation and serve as the primary contact with ORA. Results from investigations will be shared with the VST.

OVRR Responsibilities

The reviewers in the Office of Vaccines Research and Review (OVRR) may contact the co-chairs, or RPO, or OVRR member of the VST to obtain assistance with the coordination of complex, emergency safety issues through discussion and determination of the next steps.

OVRR team members update the VST, on an ad hoc basis, on new and emerging vaccine safety concerns that give rise to policy and data safety needs based on the review and regulation of vaccines.

OVRR Regulatory Project Managers (RPMs) will archive records pertaining to significant decisions and actions for the administrative record (21 CFR 10.70) regarding a product, including the discussion and outcome of VST interactions.

OCTMA Responsibilities

The Office of Communication, Training and Manufacturers Assistance (OCTMA) will encourage consumers, health care providers and manufacturers to report suspected adverse events to VAERS for follow up by OBE. The OCTMA VST member may bring novel vaccine safety questions to the VST for assistance in drafting responses and, if necessary, creating policy to address emerging issues.

OD Responsibilities

The Emergency Operations Manager (EOM) in CBER's Office of the Center Director (OD) is the official contact in CBER for the Office of Crisis

Management in the Office of the Commissioner, FDA. If the Emergency Operations Manager (EOM) receives information about a potential vaccine safety issue from the Office of Crisis Management/Office of Emergency Operations, the EOM will disseminate this information to the VST co-chairs and other appropriate points of contact.

The EOM will also communicate information about the VST activities to CBER OD Management as needed.

VST Joint Responsibilities

If at any time, the Vaccine Safety Team (VST) determines an issue to be a significant public health concern:

- CBER senior management (Directors of the CBER IOD, OVRR, OBE, OCTMA, OCBQ) will be alerted and decisions regarding the need to follow-up with the appropriate contacts with others will be made.
- Any additional information will be communicated to all who have been previously contacted, so that everyone involved is up-to-date.
- The co-chairs of the VST will then determine if the matter is complete or not and seek concurrence with others on the VST.
- The VST co-chair and/or RPO will send an e-mail to those involved, to this effect.
- The VST will track and monitor these issues as received and initiate and coordinate responses.
- The VST will maintain all appropriate documentation for discussions and decisions. Documentation will also be included in the appropriate product administrative record.

All VST members are responsible for having access to their Offices' emergency contact lists for Office-specific expertise and resources.

B. Recalls and Market Withdrawal

The EOM will notify OCBQ's Division of Case Management (DCM) of information regarding recalls or market withdrawals. If the EOM is informed of a recall or market withdrawal involving a vaccine based on significant safety concern, the EOM will immediately inform the VST co-chairs, RPO, and a OCBQ VST member, and appropriate points of contact. If appropriate, other members of the VST will be contacted to determine next steps, consistent with established CBER and FDA recall policies/procedures (Part 7 of FDA's Regulatory Procedures Manual) For example, the VST may recommend notification of other CBER or FDA, HHS units, or the public.

C. Other Reports or Contacts

The CBER Office that is contacted from an outside agency (e.g. CDC or HRSA), the public, or other FDA offices about an adverse event involving a vaccine should contact the vaccine product division in OVRR. If the OVRR product division director or designee deems the matter is complex and needs a rapid response by CBER management and the VST, the product division director or designee may contact the VST co-chairs, or RPO, or Office VST team members. After a determination of next steps, the VST members will be contacted. If appropriate, CBER Office Directors will be contacted.

When necessary, OCBQ will issue an assignment to ORA to perform a field investigation or inspection. Any additional information will be communicated to all who have been previously contacted, so that everyone involved is up-to-date. The VST co-chairs will determine if the actions by the VST are complete or not and seek concurrence with others on the VST. The VST co-chairs will send an e-mail to those involved that includes the decision and any additional information deemed appropriate by the VST chair/co-chairs.

Other times, CBER may be contacted on safety policy issues from other governmental or non-governmental entities, and CBER OD may determine that these issues are appropriate for VST discussion and action. The VST co-chairs and RPO may also determine that an issue facing CBER is appropriate for VST input and initiate VST discussion on these items.

VST information, including meeting minutes, can be found on the CBER intranet VST page.

Discussion with CBER Senior Management

There will be an ad-hoc meeting of the VST with CBER senior management (Directors of the CBER IOD, OVRR, OBE, OCTMA, OCBQ) when a major event is identified. On a semi-annual basis, the VST will brief CBER OD and provide a written summary of all follow-ups of VST actions.

6. References

Web links to the references below can be found in the list following the History Section

VAERS Information
FDA's Regulatory Procedures Manual

7. Effective Date

May 20, 2008

8. History

Written/Revised	Approved	Approval Date	Version Number	Comment
VST/Houn	R. Yetter	May 9, 2008	1	First Issuance of this SOPP

References

- VAERS Information