Step 9: BOB Monitors Manufacturer's Compliance With Established Regulations; BOB Reviews the Safety and Efficacy of Licensed Vaccines

Source(s) of Authority: For products licensed before July 1, 1972, BOB uses 21 CFR 601.25 to establish review procedures to determine that licensed products are safe, effective, and not misbranded under prescribed, recommended or suggested conditions of use. For all licensed products, FDA can use 21 CFR 601.5 to revoke a license and 21 CFR 601.6 to suspend a 1icense. Implicit] y, these two sections give FDA authorit, to establish product review procedures.

Procedures and Processes: Under 21 CFR 601.5, the FDA Commissioner can determine the appropri - ateness of any licensed biological product based on the following criteria:

- Uninspectable conditions of manufacturing facilities
- No product available for inspection
- Failure of manufacturer to report major changes as described in 21 CFR 601.12
- Failure of manufacturer to comply with standards for product characteristics such as safety, purity, and potency
- Evidence that the product is either misbranded, unsafe, or ineffective for all intended uses.

Federal regulations do not precisely specify the procedures the FDA Commissioner uses to collect data to evaluate which, if any, of these criteria are met. Some evaluation appears to be clone by BOB staff; some may be done with the assistance of advisory panels. The FDA Commissioner also may hold public hearings (2 I CFR 601 .7).

Under 21 CFR 601.25, the FDA Commissioner uses the following procedures to review at his or- her discretion at least those biological products licensed prior to 1972:

1. Appoints advisory review panel(s) to do the following:
   —Evaluate the safety and efficacy of licensed products
   —Review the labeling of licensed products
   —Advise the Commissioner as to which products are safe, effective, and not misbranded.
2. Solicits data and views from the public regarding licensed biological products through the *Federal Register*.
3. Considers the conclusions of the advisory review panel.
4. Publishes in the Federal ***Register*** a proposed order that designates which products should remain licensed without further testing, which need further testing, and which should be withdrawn from interstate commerce.
5. Receives and reviews comments, and 60 days after publication of the proposed order, publishes in the Federal *Register* a final order.

Step 10: Based on Its Findings in Step 9, BOB Acts in One of Three Ways:

- **Leaves License Intact Without Requiring Further Testing**
- **Requires Manufacturer To Conduct Further Testing**
- **Removes Product From Commerce**

Source(s) of Authority: BOB derives its authority to revoke a product license from 21 CFR 601.5 and its authority to suspend a license from 21 CFR 601.6. Other authorities to remove a product from commerce are 21 USC 334 (seizure) and 21 USC 331 (injunction). Also, 21 CFR 601.25 permits the FDA Commissioner to revoke a license based upon data from a formal review.

Procedures and Processes: No comment.

Appendix 3.4
TYPES OF DATA BOB USES TO EVALUATE THE SAFETY AND EFFICACY OF BIOLOGICAL PRODUCTS

1. Product label(s) and all other labeling (including labeling for export)
2. Representative advertising used during the past 5 years
3. Complete quantitative composition of the product
4. Animal safety data
   - Individual active components
     —COnt rolled studies
     —Partial] y controlled or uncontrolled studies
   - Combinations of the individual active components
     –Controlled studies
     —Partially controlled or uncontrolled studies
   - Finished biological product
     —Controlled studies
     —Partially controlled or uncontrolled studies