

Product Development for Preventive Vaccines

**CT products regulated by
CBER: Strategies to assist in
product development**

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Preventive Vaccines Against Bio-T Agents

- **Disease Prevention**
 - “classical” vaccine role
- **Deterrence**
 - Discourage potential use of disease agent

Preventive Vaccines Against Bio-T Agents

- **Prevention of disease spread**
 - Ring vaccination
- **Pre-immunization against exposure**
 - Immunization of troops, health care workers

Preventive Vaccines Against Bio-T Agents

- **Agents pose significant risk**
 - High mortality, highly infectious
- **Long term protection**
 - single treatment

Preventive Vaccines Against Bio-T Agents

- **Government role in public health response**
 - “Orphan” drugs
 - Instrument of public policy

Challenges Associated with Preventive Vaccines

- **Manufacturing**
- **Efficacy measurements**
- **Stockpile and use**

Manufacturing

- **New substrate is a new product**
 - Tissue culture replacing old methods
 - Modern adventitious agent testing
- **New vaccines**
 - Limited experience

Manufacturing

- **Limited and rapid production**
 - Early development of manufacturing process
 - Inspection and GMPs
- **Maintaining manufacturing potential**
 - Changeover protocols

Cell Culture Smallpox Vaccine

- **Manufacturing issues for a new vaccine**
 - **Tissue culture instead of calf skin means new vaccine**
 - **Accelerated process development**
 - **Inspections early and often**

Efficacy

- **Surrogate assays for vaccine effectiveness in the absence of the disease**
 - Potency, immunogenicity
 - Modern assays
 - Animal models

Efficacy

- **Assay validation**
 - New assays for old measurements
 - New assays to measure immune response
- **Clinical decisions from efficacy measurements**
 - Duration of protection

Cell Culture Smallpox Vaccine

- **Efficacy issues for a new vaccine**
 - Human challenge/protection study, as well as field efficacy trial, not feasible
 - Immune correlate of protection unknown
 - Develop confidence in efficacy, not proof

Cell Culture Smallpox Vaccine

- **Efficacy issues for a new vaccine**
 - **Non-inferiority to product with proven effectiveness**
 - **Assays for comparison of immune response, potency**
 - **Humoral and cellular response important**

Stockpile

- **Store or use**
- **Instant availability**
 - **IND then license**
- **Storage conditions (NPS)**

Stockpile

- **Long-term stability studies**
 - Potency assays
 - Validation of assays
 - Product storage lifetime
- **Re-labeling of product**
 - Transition from IND to license

Stockpile

- **Transport and Use**
 - Retention of potency through distribution chain
- **Product shelf-life**
 - Extension of dating
 - Replenish stockpile

Smallpox Vaccine

- **Storage and potency of remaining calf skin vaccine**
- **Re-licensure of remaining calf skin vaccine**
- **Storage and re-labeling of tissue culture smallpox vaccine**

Summary

- Preventive vaccines against biological agents of terror provide a critical response to actual and potential acts of bio-terrorism
- The development of preventive vaccines against biological agents of terror pose unique problems in manufacturing, analysis and storage

