



The WHO Smallpox Vaccine Resource

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Post-eradication mandate to WHO

- Declaration of Eradication confirmed by World Health Assembly, 1980, Resolution WHA 33.3
- Program of post-eradication activities and policies
 - established Committee on Orthopox Infections to review and oversee implementation of post-eradication policy
 - WHO must be prepared to respond to a re-emergence of smallpox

Establishment of the stockpile

- At eradication, 200 million doses retained in case smallpox should reappear
- After several years saw no recurrence, stockpile reduced to 20 million doses, held in 2 sites
- Later, stockpile concentrated in one site, retaining 2.5 million doses

Concerns of Member States

Context of increasing global concern about the possibility of intentional release of biological agents

- Policy on mass immunization
- Availability of vaccine
- Vaccine strains
 - Which strains should be used?
 - Where and how to obtain seed virus?
 - GMP and standards
- Strategy and preparedness plans

Concerns of Member States

- **Policy on mass immunization reviewed by Orthopox Committee** - confirmed search and containment with ring vaccination as appropriate policy
- **Availability of vaccine** - to be augmented
- **Vaccine strains**
 - Which strains should be used? - Only strains proven effective in control of smallpox disease
 - Where and how to obtain seed virus? - Seed virus made available through standardized process
 - **GMP and standards** – updated to comply with modern practices for newly manufactured 1st and 2nd generation vaccines
- **Strategy and preparedness plans** – concept of a 2 component reserve and development of an operational framework for acquisition and release

Emergency response to an outbreak of smallpox

Challenges in planning

- The possibility of multifocal outbreaks
- Lack of familiarity with the signs and symptoms of smallpox, causing delay in identification, reporting, and consequent implementation of control measures
- Inadequate national public health surveillance mechanisms to rapidly detect and confirm suspected cases.

Other critical considerations

- Increased world population
- Increased population mobility and international travel
- Increased population density, especially in the developing countries
- Decrease in the proportion of the population with persisting immunity to smallpox
- Seven month time-lag for manufacturers to gear up mass production of second generation smallpox vaccines

Operational Framework

We cannot predict where such events may occur, how they might be distributed, and what disruption they might cause



Therefore we have selected an approach to allow maximum flexibility according to the context, but which has the advantages of pre-planning and coordination

Operational Framework

Two-Tier system:

- WHO-held Stockpile
- The Global Resource- includes stocks held in countries which have committed a specified amount or proportion of their national stocks, to be released if required

Target = 200 million doses

Components of the WHO Smallpox Vaccine Resource

WHO Stockpile

'physical stockpile'

- 32.6 million doses
- **Held by WHO**
- For immediate use in case of an emergency

National Smallpox Vaccine Stock

'virtual stockpile'

- 27 million doses (target 170)
- **Held by Member States in their National Stock or by vaccine manufacturers**
- Pledged to WHO
- Release through agreed protocols

THE WHO STOCKPILE

- 1st & 2nd generation vaccine
- Diluent, bifurcated needles
- Owned and held physically by WHO
- Stored under controlled conditions

THE WHO STOCKPILE (2)

- Use restricted to proven outbreak of smallpox
- Cover diverse scenarios, including multiple, large, urban outbreaks in a country or countries
- Rapid access for deployment with emergency response teams, or shipment

National stocks pledged to WHO

- Specified amount or proportion of national stocks can be committed
- Pledging country responsible for regular potency testing
 - Every 5 years (older vaccine) or following manufacturers' instructions (2nd generation vaccines)
- Need to ensure concomitant provision of ancillary supplies for safe administration

National stocks pledged to WHO (2)

- If required, countries would be asked to release some or all to WHO for emergency use
- Detailed protocols for request, release, transportation to outbreak sites being prepared with each pledging country
- Globally distributed stocks could facilitate more rapid access in some circumstances
- Requires attention to regular updating and continued reinforcement of protocols

Legal considerations

Concern about sending unlicensed vaccines or vaccine from non-prequalified manufacturers to third countries

- Both the WHO Geneva Stockpile and the pledged national stocks should not be subject to litigation for adverse events
- Vaccine from 'virtual' stockpile will become property of WHO before being used for response
- Vaccine offered to a country for smallpox emergency response will only be released on acceptance of a legal disclaimer

Management of an outbreak

- WHO currently follows up all rumours of smallpox outbreaks through its Alert and Response Operations
- SOPS for smallpox outbreak response have been developed
- Notification of smallpox is mandatory under the IHR(2005)

Management of an outbreak (2)

- Under the IHR, the DG may convene an Emergency Committee drawn from a roster of experts
- Based on epidemiological, logistic, laboratory, security, and infrastructural considerations, the Emergency Committee will advise on access to vaccine and wider international measures to contain spread

Management of an outbreak (3)

- Programmatic considerations - must assure that immunization is performed safely and monitored correctly
- WHO last reviewed its immunization strategy in 2001, and concluded that the best approach remained search and containment with ring vaccination
- The definition of the “ring” will depend on the circumstances

Remaining or unresolved issues for smallpox stockpile development

- Replacement of older vaccine stock
 - variable potency and not fully characterized for adventitious agents
- Adverse events profiles of 1st and 2nd generation smallpox vaccines
 - Safety/acceptability in many groups
 - Outbreak contexts with large numbers of immunocompromised persons pose very real constraints on use of current stockpile

Implications of current R&D into MCMs for the WHO Stockpile

- More highly attenuated vaccine candidates in development
- Offer prospect of smallpox vaccines with lower risks of adverse events
- Safer for use in immunocompromised individuals
- Greater flexibility for deployment in emergency conditions
- ? Different strategies or policies for use? (will depend on characteristics)

Implications of current R&D into MCMs for the WHO Stockpile

- Incorporation of [new] drugs if/when evidence indicates efficacy, and safety in humans
- Imminent new vaccines and drugs suggest need for continuing stockpile investment and enhancement – how to define needs and limits?

Thank you

<http://www.outbreak.who.int>