Review of the Centers for Disease Control and Prevention's Smallpox Vaccination Program Implementation: Letter Report #4

Committee on Smallpox Vaccination Program Implementation

ISBN: 0-309-55875-1, 54 pages, 8.5 x 11, (2003)

Review of the Centers for Disease Control and Prevention's Smallpox Vaccination Program Implementation

Letter Report # 4

Committee on Smallpox Vaccination Program Implementation
Board on Health Promotion and Disease Prevention

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

INSTITUTE OF MEDICINE • 500 FIFTH STREET, NW • Washington, DC 20001

Support for this project was provided by Centers for Disease Control and Prevention. The views presented in this report are those of the Institute of Medicine Committee on Smallpox Vaccination Program Implementation and are not necessarily those of the funding agencies.

Additional copies of this report are available in limited quantities from the Committee on Smallpox Vaccination Program Implementation; Board on Health Promotion and Disease Prevention; Institute of Medicine; 500 Fifth Street, NW; Washington, DC 20001. The full text of this report is available online at http://www.nap.edu.

Printed in the United States of America.

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Shaping the Future for Health

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Bruce M. Alberts is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Wm. A. Wulf is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Bruce M. Alberts and Dr. Wm. A. Wulf are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

.

COMMITTEE ON SMALLPOX VACCINATION PROGRAM IMPLEMENTATION

BRIAN STROM, M.D., M.P.H., *(Chair),* George S. Pepper Professor of Public Health and Preventive Medicine, Professor of Biostatistics and Epidemiology, Professor of Medicine and Professor of Pharmacology, University of Pennsylvania School of Medicine

KRISTINE GEBBIE, Dr.P.H., R.N., *(Vice Chair),* Elizabeth Standish Gill Associate Professor and Director of Center for Health Policy, Columbia University School of Nursing

ROBERT WALLACE, M.D., M.Sc., *(Vice Chair),* Professor of Epidemiology and Irene Ensminger Professorship in Cancer Research, University of Iowa

E. RUSSELL ALEXANDER, M.D., Professor Emeritus of Epidemiology, School of Public Health and Community Medicine, University of Washington

RONALD BAYER, Ph.D., Professor of Sociomedical Sciences, Mailman School of Public Health, Columbia University

R. ALTA CHARO, J.D., Associate Dean for Research and Faculty Development, University of Wisconsin Law School and Professor of Law and Bioethics, University of Wisconsin Law School and Medical School

THOMAS COATES, Ph.D., Professor of Medicine and Epidemiology, University of California, San Francisco

PENELOPE DENNEHY, M.D., Associate Director of Pediatric Infectious Diseases, Hasbro Children's Hospital and Professor of Pediatrics, Brown Medical School

VINCENT FULGINITI, M.D., M.S., Professor Emeritus of Pediatrics, University of Arizona Health Sciences Center

JAY HARPER, M.B.A., M.D., M.P.H., Clinical Assistant Professor of Environmental and Occupational Health, University of Pittsburgh Graduate School Public Health

COLEEN KIVLAHAN, M.D., M.S.P.H., Vice President of Medical Affairs, University of Missouri Health Sciences Center

JEFFREY LEVINE, M.A., Vice President/Group Manager, Ketchum Washington, DC

KENNETH MCINTOSH, M.D., Professor of Pediatrics, Harvard Medical School and Professor of Immunology and Infectious Diseases, Harvard School of Public Health

ELIZABETH MURANE, R.N., M.S., Public Health Nurse and Retired Director of Public Health Nursing for Shasta County, CA

PETER ROSEN, M.D., Attending Emergency Medical Physician, Beth Israel Deaconess Hospital (Boston, MA)

WILLIAM WESTON, M.D., Professor of Dermatology and Pediatrics, University of Colorado School of Medicine

ROBERT WOOLSON, Ph.D., Professor of Biometry and Epidemiology, Medical University of South Carolina

Health Promotion and Disease Prevention Board Liaison

GEORGE ISHAM, M.D., Medical Director and Chief Health Officer, HealthPartners, Inc. (Minneapolis, MN)

Consultant

WILLIAM H. FOEGE, M.D., M.P.H., Presidential Distinguished Professor, Department of International Health, Emory University and Health Advisor, Bill and Melinda Gates Foundation

Study Staff

KATHLEEN STRATTON, Ph.D., Study Director
ALINA BACIU, M.P.H., Program Officer
ANDREA PERNACK, M.P.H., Program Officer
NICOLE AMADO, M.P.H., Research Associate
AMBER CLOSE, Senior Project Assistant
ROSE MARIE MARTINEZ, Sc.D., Director, Board on Health Promotion and Disease Prevention

REVIEWERS

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

Bobbie Berkowitz, Ph.D., R.N., University of Washington
John Conte, M.D., University of California, San Francisco
Michael Katz, M.D., March of Dimes Birth Defects Foundation
John Lumpkin, M.D., M.P.H., Robert Wood Johnson Foundation
Nicole Lurie, M.D., M.S.P.H., The RAND Corporation
Hugh H. Tilson, M.D., Dr.P.H., University of North Carolina

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Ronald Estabrook, Ph.D.,** University of Texas Southwestern. Appointed by the National Research Council and Institute of Medicine, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

PREFACE

The Institute of Medicine (IOM) Committee on Smallpox Vaccination Program Implementation was convened in October 2002 to provide timely advice to the Centers for Disease Control and Prevention (CDC) in its implementation of the national smallpox vaccination program.

The committee's work differs in two respects from that of typical IOM committees. First, the evidence base used is somewhat different, because the committee is commenting on an ongoing government program as it evolves. The evidence reviewed by the committee is sometimes qualitative. The bulk of the evidence includes CDC presentations to the committee and reports on program status, articles about the program in the Morbidity and Mortality Weekly Report, CDC media telebriefing transcripts, national and local media coverage of the smallpox vaccination program, the policy statements and issue briefs of public health and health care organizations, and to a lesser extent the experiences, opinions, and perspectives of public health and health care leaders and workers expressed in presentations to or informal discussions with the committee. Second, most of the committee's products are brief, frequent "letter reports" addressed to the CDC Director. Letter reports offer an abbreviated version of the extensive background and documentation provided in more sizable IOM reports, and often focus on one or a few topics of immediate importance to a program's progress or to next steps in the program. Although they differ from typical IOM reports in size and nature, letter reports undergo the standard process of external peer review, conducted by reviewers anonymous to the committee until report is released, and monitored by the National Research Council.

The present letter report is fourth in a series. For the purpose of brevity, some background information about the program is generally not repeated in every report; only a reading of the entire report series would provide a complete overview of the committee's work to date. For ease of reference, every report includes a table of contents, a listing of key messages, and a summary of all recommendations made in the report. All the committee's reports to CDC are available for downloading at: www.iom.edu/smallpox.

TABLE OF CONTENTS

REVIEW OF THE CENTERS FOR DISEASE CONTROL AND PREVENTION'S SMALLPOX VACCINATION PROGRAM IMPLEMENTATION

Letter Report #4

August 12, 2003

Dr. Julie Gerberding
Director
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, GA 30333

Dear Dr. Gerberding:

The Committee on Smallpox Vaccination Program Implementation is pleased to offer you the fourth in a series of brief reports providing timely advice to assist Centers for Disease Control and Prevention (CDC) and its partners in their implementation of the vaccination program.[1] This report responds to issues raised by CDC at the committee's May 1, 2003 meeting. In particular, the report includes: (1) a discussion of smallpox preparedness and its integration into overall public health preparedness; (2) the committee's advice regarding offering vaccination to members of the general public who insist on receiving it; and (3) an examination of selected aspects of smallpox vaccination program implementation.

In a previous report (IOM, 2003c), the committee remarked on the importance of working to attain a level of smallpox preparedness, and not simply focusing on numbers of vaccinated individuals. Since then, CDC officials have remarked that the smallpox program is "not about a number, it is not about should we have 40,000 people or 400,000 or 4 million people…. It's about how do we get prepared" (CDC, 2003i). Furthermore, CDC plans to conduct an assessment of its smallpox preparedness efforts and recommend program adjustments to emphasize education and training, and ways to facilitate reporting and test readiness (Connolly, 2003b).

The report is organized into three main sections: (1) Integrating Smallpox Preparedness into Overall Public Health Preparedness; (2) Vaccination of Members of the General Public Who Insist on Receiving Smallpox Vaccine; and (3) Selected Aspects of Smallpox Vaccination Program Implementation.

[1] As of July 25, 2003, 38,004 civilian volunteers have been vaccinated against smallpox (CDC, 2003l), and as of June 13, 2003 2,125 hospitals have participated in the smallpox vaccination program (Strikas, 2003).

INTEGRATING SMALLPOX PREPAREDNESS INTO OVERALL PUBLIC HEALTH PREPAREDNESS

"State health departments have been actively involved in planning and preparing for the possibility of a bioterrorist event. We are now seeing that this level of preparation can also assist in unexpected natural outbreaks."

Tommy Thompson, Secretary of the Department of Health and Human Services, in reference to the monkeypox outbreak (CDC, 2003a)

The discussion of integration of smallpox preparedness into overall public health preparedness is organized around four main topics: (1) Challenges in Defining and Assessing Public Health Preparedness; (2) Elements of Preparedness; (3) Testing Preparedness; and (4) Sustaining Smallpox and Overall Public Health Preparedness.

Challenges in Defining and Assessing Public Health Preparedness

There is significant agreement about the difficulties and flaws that characterize the public health infrastructure, and in the last two years there has been considerable discussion about the need for public health preparedness. Public health system leaders know the system is not sufficiently prepared based on the way it has responded to a number of threats and crises in recent years. However, the public health system is still in the early stages of developing consensus on defining preparedness and identifying evidence-based standards for planning for and evaluating preparedness. At a minimum, public health preparedness requires adequate and sustained funding based on priorities supported by evidence, and a strong public health infrastructure, including surveillance, workforce, and communication (IOM, 2002).

Assessments of the public health infrastructure's capacity to respond to bioterrorism conducted after the events of September and October 2001 found a severe lack of financial resources, and a great deal of fragmentation within the public health system, from surveillance systems (which were multiple, overlapping and duplicative, and incompatible in various ways) to communication (which was limited, reliant on obsolete, inefficient channels, etc.) both internal and with other sectors (IOM and NRC, 1999; Heinrich, 2001; Peters et al., 2001; IOM, 2002; Salinsky, 2002). It is unclear at this time whether the recent influx of funding aimed at strengthening the public health infrastructure is being used to reinforce public health capacity in an integrated way, responsive to local needs and epidemiological evidence, or to simply create new funding and program categories, adding to existing fragmentation. The IOM Committee on Emerging Microbial Threats to Health in the 21st Century has described recent funding increases as opportunities for the nation to prepare to "protect against acts of bioterrorism and improve the U.S. public health response to all microbial threats" but expressed alarm that "some of these funds have been diverted from multipurpose infrastructure building to single-agent preparedness" (IOM, 2003a: 171). In fact, smallpox may have "received the lion's share of attention and … drawn attention away from the wide range of other agents that could be used" in a bioterror attack (Powers and Ban, 2002).

Vaccination: Only One Component of Smallpox Preparedness

In the early months of the smallpox preparedness program, preparations to respond to a potential smallpox attack have consisted largely of vaccination-related activities. These have been resource-intensive, giving rise to concerns about the opportunity costs (i.e., to essential public health services) of the smallpox vaccination program and about the optimal balance of investment of public health funds (e.g., are smallpox-related activities funded at the expense of a more wide-ranging kind of preparedness?) (APHA, 2002; Libbey, 2003; Madlock, 2003; NACCHO, 2003b; Nikolai, 2003). Surely, being prepared for a potential attack requires much more than just vaccination. It includes planning for a range of possible scenarios, including contingencies for crowd control, quarantine, and isolation; training, retraining, and management of response teams; education and training of health care providers, emergency responders, and many others to facilitate rapid surveillance, reporting, and notification; planning and coordination with many partners, including some at the state and federal level; and testing and continuous improvement of plans.

The smallpox vaccination program and associated activities implemented by CDC and its state and local partners have provided information and training about smallpox disease and vaccine to public health and health care workers, have probably improved clinician knowledge and rash illness diagnostic skills, and have led to vastly improved communication and collaboration among public health agencies, between the public health and clinician communities, and among public health, law enforcement, and emergency response agencies (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003; NACCHO, 2003b; Elliott, 2003). However, much more is necessary to strengthen and test smallpox preparedness, and to ensure that smallpox-related efforts are part of overall public health preparedness activities. The committee hopes that this report will provide some useful direction toward that end.

Smallpox Preparedness: Only One Component of Overall Public Health Preparedness

The national smallpox vaccination program may well be the first disease-specific test of implementing public health preparedness in a systematic and comprehensive manner, and with some public visibility. The smallpox vaccination program has taken the notion of preparedness beyond the realm of public health professionals and academics and has brought it to the attention of a broader audience of health care workers, emergency responders, and even the general public.

Implementing the smallpox vaccination program, however, has also highlighted the need to integrate smallpox preparedness into readiness to respond to a vast range of public health challenges, including bioterror agents and other weapons of mass destruction, emerging or reemerging infectious diseases, natural disasters, and the insidious and growing threat of chronic diseases and their predisposing conditions (e.g., obesity). Smallpox is just one of a multitude of actual and potential threats to the public's health.

The Continuation Guidance for Cooperative Agreement on Public Health Preparedness and Response for Bioterrorism (CDC, 2003b), describes the capacities needed for smallpox response in the context of all other bioterrorism threats, even calling for coordination with the National Public Health Performance Standards which guide public health activities in general. In practice, such integration has been lacking and has been difficult to accomplish, in part due to the intense emphasis on smallpox vaccination, which has been advanced perhaps at the expense of other aspects of smallpox preparedness, as well as overall public health preparedness to respond to any threat.

A Standard for Smallpox Preparedness

> *"The federal government should consider playing a more concerted role in providing resources and instituting unified standards for the common defense against the microbial threat, while giving state and local authorities the flexibility to implement programs in a manner that will best meet local needs."*
>
> *(Brower and Chalk, 2003: xvi)*

The question of what exactly is involved in preparedness to respond to a smallpox attack has been a recurrent theme at committee meetings and in presentations to the committee. Many of the requirements for smallpox preparedness apply to preparedness in general; there are necessary components of the public health infrastructure including workforce, surveillance and laboratory capacity, information technology, legal authority, and communication networks. What remains to be clarified at the state level, with the guidance of CDC, are the specifics (e.g., vaccination sites; numbers of responders, vaccinated or not; strategies for training, communicating with, and mobilizing responders, etc.) needed to act effectively in each state and jurisdiction.

Before the occurrence of a public health emergency, such as a smallpox release, planning, coordination, and communication among local, state, and federal public health agencies must take place in order to establish leadership and responsibility (ASTHO, 2002; Salinsky, 2002). In the event of a bioterror attack, final authority in the matter must reside somewhere.

Similarly, leadership is required to establish a minimum standard against which preparedness may be tested. Having 50 or more different standards for preparedness seems inconsistent with a coordinated, effective response; for example, one state might prepare enough to mass vaccinate all residents in 10 days, while a neighboring state could be prepared to accomplish this in 2 days. Such variation may cause confusion and weaken confidence in the public health system's handling of a crisis. In the pre-event setting, CDC has been flexible in its guidelines to states, and has advised states to define preparedness needs locally, in recognition of the fact that bioterrorism occurs at the local level. However, due to the infectiousness of certain agents, such as smallpox, the local quickly becomes national, and jurisdictional boundaries become less relevant. The regional planning required to prepare for a response to major fires is analogous to the preparedness planning required across jurisdictional boundaries for a response to a smallpox attack. Such circumstances would require stronger national (i.e., CDC) leadership to set some standards for preparedness while collaborating with state public health agencies in acknowledgement of the great variety in circumstances and resources across states and localities (ASTHO, 2002; Brower and Chalk, 2003; IOM, 2003c). **The committee recommends that**

CDC provide guidance to assist state public health agencies (and their partners[2], as appropriate) in establishing a baseline level or a minimum standard of preparedness for a smallpox attack, after which, each state could individually assess its priorities and further expand its preparedness against smallpox and other threats to the public's health as needed. The committee has been informed that CDC is developing metrics/indicators of preparedness to guide all state partners in implementing their cooperative agreements with CDC. The smallpox preparedness metrics/indicators will be the subject of the committee's meeting on September 4, 2003, and the committee hopes this effort will help to establish a minimum standard of smallpox preparedness.

Smallpox preparedness activities conducted in the first months of 2003 have enhanced the readiness of state and local public health agencies to respond to a potential smallpox attack (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003; NACCHO, 2003a), but as noted above, vaccination alone—the focus of most of these activities—is not sufficient for preparedness. In fact, many states are pausing in their smallpox vaccination activities before proceeding to a broader group of potential vaccinees to evaluate their progress and ensure safety, to address changing circumstances by updating forms, materials, and processes, and finally, to consider what level of vaccination is needed for preparedness (ASTHO, 2003; IOM, 2003c). The deliberate and cautious implementation of the vaccination program to date testifies to the impact of lessons learned from the Swine Flu vaccination program of 1976 (Hardy, 2002; Strikas, 2002).

Attaining a high level of preparedness may well be possible without vaccinating any personnel pre-event. For example, Virginia Commonwealth University Health System, that presented its hospital preparedness plans to the committee at the May 1, 2003 meeting, has chosen not to have health care workers vaccinated pre-event (Edmond, 2003).[3] The health system's decision was based on considerations of hospital patient safety. Although no vaccinated teams of responders were formed, a policy on smallpox vaccination was developed, with plans to revisit the policy as needed. Furthermore, a working group on smallpox preparedness was established, facilities were modified in accordance with requirements for treating smallpox victims, training on smallpox diagnosis, treatment, and infection control measures was conducted, and plans were put in place to rapidly vaccinate hospital staff in a post-event scenario. The committee believes that Virginia Commonwealth University Health System's smallpox preparedness activities provide a good example of how an organization or jurisdiction can be well-prepared to respond to a smallpox attack without necessarily having workers vaccinated pre-event.

CDC's initial attention to the numerical targets so well publicized in the media may have contributed to confusion and concern about goals and outcomes among the public health and health care communities, as well as in the general public (ASTHO, 2003; Connolly, 2003a; ENA, 2003; GAO, 2003; Russell, 2003; Solet, 2003). It has not been made completely clear to

[2] State partners may include, but not be limited to, emergency management agencies, law enforcement, fire and emergency medical services, hospital and other health care associations.

[3] The ACIP estimated approximately 5,100 acute care hospitals would be eligible to participate in the smallpox vaccination program (ACIP, 2002). As of June 13, 2003, 2,125 hospitals have participated, with whole or partial teams of vaccinated response personnel (Strikas, 2003).

most audiences how national estimates of numbers of vaccinees were derived, and how they relate to the publicly available threat assessment and to smallpox preparedness. Although the committee recognizes that the CDC has publicly acknowledged that preparedness is not about numbers (see page 1), it is clear that there is lingering confusion about the vaccination program's aims. This confusion is reflected in recent media reports that characterize the program as having fallen short of its goals (Connolly, 2003a; Snowbeck, 2003)—when comparing the fewer than 40,000 vaccinees in early July 2003 (CDC, 2003l) to the initially publicized target of vaccinating approximately 500,000 and 10 million individuals, in the first and in the second rounds of vaccination, respectively. There is also lingering confusion about how the 500,000 estimate described by CDC related to the 15,000 estimate cited by the ACIP in June 2002 (AAFP, 2002; CIDRAP News, 2002; Manning, 2002). Public confidence and clarity about preparedness efforts would likely be enhanced if the CDC explained how and why it came to view its earlier benchmarks as less than helpful (e.g., were early estimates of vaccinee numbers the upper bounds of what was needed for an effective response to a smallpox attack?). Given that CDC supports ongoing smallpox immunization (CDC, 2003m), there should be clarification about the goals and objectives being pursued (IOM, 2003c), to help reconcile the apparent incongruity between the claim that preparedness is "not about a number" and the stated intent to move forward with vaccination to ensure there are "enough people … immunized" (CDC, 2003i). What number of vaccinees is needed for preparedness? Vaccinating many more than the number needed may waste precious resources that could be utilized to prepare against other threats to the public's health. Vaccinating fewer than what is needed to respond effectively and rapidly may leave the public vulnerable and unprotected.

The recent SARS and monkeypox episodes have provided CDC the opportunity to once again demonstrate its authoritative voice and competence as the nation's public health leader. However, these serious infectious disease threats posed relatively straightforward public health challenges, without the national security issues that complicate the smallpox vaccination program. To maintain its credibility, CDC should demonstrate a sustained commitment to clarity and openness about its smallpox preparedness goals, by working toward a concrete description of what preparedness entails (despite the complexities and unknowns involved), communicating regularly with the public, and discussing any specific numbers of vaccinees only within this broader context.

Elements of Smallpox Preparedness

At the committee's May 2003 meeting, one presenter described the essentials for improving smallpox preparedness as planning, training to the plan, exercising to the plan, and revising the plan (Selecky, 2003). In presentations and conversations with several state and local health departments, the committee heard similar comments about what program administrators believe are the "ingredients" of smallpox preparedness (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003). Most programs remarked on the importance of:

- developing relationships with all relevant partners (might help enhance surveillance and reporting, as well as planning and implementation of smallpox response);

- engaging in regular communication with other local and state public health agencies;
- communicating openly, regularly, and consistently with the media and the public, to create a foundation of optimal communication before a potential smallpox event;
- having a core of set of workers to provide initial response and vaccinate others;
- having concrete plans, including job descriptions and locations; and
- educating and training all participants before an event.

These themes are consistent with the three elements of smallpox preparedness identified in Annex A of the DHHS/CDC Continuation Guidance for Cooperative Agreement on Public Health Preparedness and Response for Bioterrorism (CDC, 2003b) and discussed in greater detail below:

1. **Preparing key responders**—with a section devoted to health care responders and preparedness in the health care sector (includes the relationship-building, training, and planning described above);
2. **Rapid public health response**—rapid detection, identification, investigation and response—to suspected or confirmed cases of smallpox (also includes the training, communication and relationships noted above, in addition to infrastructure capacity for surveillance, prompt reporting by providers, etc.); and
3. **Protecting the public (e.g., through mass vaccination)—**all ingredients described above contribute to the ability of jurisdictions to operate orderly, efficient mass vaccination clinics.

Two additional elements are discussed briefly below, to address areas not directly covered by the three elements of preparedness listed above. These include the important role of the health care community in overall public health preparedness, and the role of public and media communication.

Preparing Key Responders

The first element of smallpox preparedness described in the CDC/DHHS guidance involves preparing key responders. As the committee noted before, this does not necessarily involve vaccinating workers, but it would ideally include training and education of key responders, and even prescreening for vaccination in the event of a smallpox attack. It is unclear what level of pre-event smallpox vaccination is needed, and how numbers of vaccinated personnel relate to the ability to respond effectively to a smallpox attack. This is a decision that must be made in the face of great uncertainty by each jurisdiction before deciding whether to vaccinate additional volunteers, and if so, the number and type of personnel to vaccinate. CDC and its partners have worked to strike a balance between vaccine risk and the benefit of having vaccinated health care and public health personnel pre-event, but it is difficult to determine when the line has been crossed between having insufficient people vaccinated to mount an effective and rapid response, and exposing more people than absolutely necessary to a vaccine that is not free of risk, in the absence of imminent threat of disease.

It appears that most jurisdictions have chosen to address this dilemma by cautiously vaccinating at least a small number of volunteers, having apparently concluded that smallpox preparedness is served by having a cadre of vaccinated individuals, typically organized into health care and public health response teams (based either institutionally or regionally), in accordance with Advisory Committee on Immunization Practices (ACIP) recommendations regarding the organization of smallpox response efforts (CDC, 2002d). However, having a number of personnel immune to smallpox and ready to vaccinate, conduct public health investigations, and treat victims is not the sum of preparedness, especially if responders are scattered across the jurisdiction in multiple facilities. Whether vaccinated before an event or not, effective mobilization of key responders requires prior preparation to ensure, at a minimum:

- adequate size and composition of health care and public health response teams;
- regularly tested and updated plans known to all participants and relevant agencies;
- initial and periodic training, including training about response plan(s) (as well as training of vaccinators, case investigators, etc.);
- job assignments and descriptions for all responders (e.g., vaccinators, public health investigators, crowd control, and security), and consideration of relevant licensure or practice privileges should teams need to cross jurisdictional, state, or even national borders; and
- reliable and efficient channels of communication among all relevant parties, including methods for contacting team members (e.g., pagers), and for the movement of information between health care organizations and public health agencies, and between the health sector and traditional first responder agencies such as law enforcement and emergency management (English et al., 1999).

Furthermore, having adequate workforce to respond to a smallpox (or other) event requires managing staff turnover (workers who leave or retire), and the ability to mobilize as many vaccinated personnel as possible. One recipient activity described in Annex A of the DHHS/CDC guidance is the development and maintenance by states and territories of a registry of all public health, health care, security and other personnel who may be occupationally at risk and should receive vaccination immediately in the event of a smallpox release.

In addition to having identified such priority occupational groups to be vaccinated post-event, programs should take necessary steps to maximize the use of any available vaccinated personnel. For example, the Department of Defense (DoD) has vaccinated over 400,000 military personnel, some of whom are reservists, and others who will complete military service. The committee hopes that CDC and DoD could collaborate to maintain contact with vaccinees, particularly those who enter civilian life, and to link them to any mechanism developed to include as many as possible in planning for preparedness. Contact should also be maintained with health care or public health workers who received a smallpox vaccine because of exposure to a case of monkeypox, so they could be utilized for response to a smallpox event. **The committee recommends that CDC support the establishment of state and/or local, and if appropriate, national, voluntary registries of individuals who have undergone vaccination to be mobilized, trained, and assigned as needed in the event of a smallpox attack. Such registries would include all willing vaccinated personnel not associated with a response team ranging from retired or relocated health care or public health workers to military**

reservists and former military personnel. Such registries might help supplement and enhance the personnel available to respond to public health crises (e.g., participating in the mass distribution of vaccines or other pharmaceuticals, caring for casualties, providing security, managing crowds). Establishing such registries will require consideration of issues related to confidentiality and privacy, among others. Ongoing efforts to organize volunteer personnel to help in emergencies (e.g., the USA Freedom Corps and the Public Health Service reserve corps) may serve as resources (Thompson, 2003).

Decisions should also be made about the vaccination activities needed to maintain a cadre of key responders immune to smallpox virus in the long-term, but the evidence on the level of long-term immunity proffered by smallpox vaccination is mixed. Older data suggested that smallpox immunity lasts 3 to 5 years after vaccination (CDC, 2002a), while more recent research suggests possibly longer duration of immunity (Frelinger and Garba, 2002; Slifka, 2003). More conclusive research would undoubtedly assist in future policy decision-making regarding smallpox preparedness. Given the 454,856 personnel vaccinated through the DoD smallpox vaccination program (Grabenstein, 2003), many of whom have had and will have a series of serum specimens included in the Department of Defense Serum Repository, CDC should work with DoD to explore how the DoD Serum Repository can support research on smallpox antibody levels at different periods of time post-vaccination.

Whether a jurisdiction vaccinates traditional emergency responders, from law enforcement to firefighters, these parties should be considered partners in overall public health preparedness. Previously, emergency management officials, police, and fire departments had not considered public health agencies to be emergency responders, and health departments typically have not counted emergency and fire personnel among the ranks of public health responders. The committee has heard at every meeting about the importance of building relationships with a wide range of partners in the community; a common outcome of the smallpox vaccination program has been the forging of linkages between the public health and health care communities, and between public health and traditional emergency response agencies. Communication between all relevant partners is essential, including mechanisms for notification and information sharing.

Rapid Public Health Response (Rapid Identification and Investigation of Suspect and Confirmed Cases of Smallpox)

The second element of smallpox preparedness, rapid public health response, is defined in Annex A of the Guidance (CDC, 2003b) as "disease surveillance for rash illnesses and laboratory analysis to rapidly detect a single case of smallpox and any subsequent cases." Building capacity for rapid response requires strengthening communication and information networks, training and education of public health, health care and other relevant personnel, and the review of legal authority and public health law.

Communication and information networks needed for rapid public health response require many components, including connectivity among levels of the public health infrastructure (agencies and laboratories), a system for rapid reporting by practicing clinicians, a means for rapid notification of all relevant parties in the event a case of smallpox is confirmed, and a way

to notify and mobilize all response team members. An additional aspect of communication that should not be overlooked is the provision of timely, clear, and accurate information to the media and public.

Because clinicians might well be the first to identify a potential smallpox case, training and education are needed to enable health care providers in all settings to assess and report rash illnesses. All clinicians, including primary care providers, infectious disease practitioners, emergency physicians, and those in other health care settings need to be familiar with the precautions to be taken and parties to be notified and consulted (local and state public health agency, CDC). At the public health agency level, public health response team members require regularly updated training and education about their agency's plans, about their roles, and about the knowledge and skills needed to rapidly identify and respond to suspected or confirmed smallpox cases.

Many aspects of public health surveillance and information systems and channels that operate both within and among states rely on public health law which defines types of authority during public health emergencies (quarantine, evacuation, etc.) (Fraser and Fisher, 2001). Although the variation in public health statutes across states is understandable and to some extent inevitable, the Turning Point Public Health Statute Modernization Collaborative has been working to achieve a level of consistency and uniformity through a draft Model State Public Health Act (IOM, 2002; Turning Point Public Health Statute Modernizing Collaborative, 2003). Following this and other resources, states could review the requirements of legal authority that will be needed to meet all contingencies in the event of smallpox attack or other public health threats and facilitate any changes needed to ensure effective response.

Protection of the Public (Through Mass Vaccination, etc.)

The third element of preparedness described in the CDC/DHHS guidance is the protection of the public, through means such as mass vaccination. To ensure the public is protected, the location of vaccine stocks and logistic plans must support the most efficient distribution of vaccine to all local jurisdictions involved in smallpox vaccination. The location and operation of vaccination clinics must also be established before a potential event. To apply this element of smallpox preparedness to comprehensive public health preparedness for all threats, the same sites could be used to distribute other vaccines or countermeasures, and provide other services in response to an outbreak or other threat. Furthermore, the circumstances of an attack and available resources may not allow the immediate vaccination of the entire population, so plans for prioritizing categories of vaccinees should be worked out pre-event, perhaps taking as guidelines the definition of essential personnel, the needs of medically at-risk groups, and those of groups at high risk of exposure (Fock et al., 2002). Furthermore, contraindications and screening criteria for smallpox vaccination in a post-event situation may be different, and these potential changes should be explored as soon as possible. Prospective vaccinees in a mass vaccination situation might also have different needs and rights for information and education, and they will require some degree of follow-up (e.g., vaccine take checks). Planning should include these and other considerations.

To facilitate rapid public health response and conduct efficient mass vaccinations, there are special subsets of the population that will require added consideration in the areas of planning, communication, and training of key responders. These include populations that have historically been negatively impacted by government policies or programs, populations with special needs, and other hard-to-reach populations, including, but not limited to, immigrants, particularly those with limited English proficiency. To help ensure that these populations are included in preparedness planning and programs, pre-event communication and plans for post-event communication (including vaccination clinic site informational and screening materials and procedures) should emphasize social, cultural, and linguistic competence, and wherever possible, should include the participation of opinion leaders and community leaders, including those representing special populations, in planning, implementation, and testing of response plans.

The Role of the Health Care Community in Public Health Preparedness

Good communication and information systems (within and among public health agencies, and at the interface with the health care sector) form the core of smallpox and overall public health preparedness (IOM, 2002; Fraser and Fisher, 2001). These include surveillance and reporting by health care providers (e.g., physicians, nurse practitioners, physician's assistants) who identify unusual symptoms or patterns. On the one hand, the West Nile virus experience underscored the value of alert and knowledgeable health care providers who can respond rapidly to suspicious symptoms, and of established and tested reporting mechanisms (GAO, 2000). On the other hand, analysis of the early response to the West Nile outbreaks showed that lines of communication between health care providers and public health agencies were unclear, and there was confusion about "what to report, when, and to whom" (GAO, 2000: 20). In a more recent example provided by the monkeypox outbreak, local health authorities and CDC were apparently only notified about the initial rash 13 days later (Mitchell, 2003). The "disconnect" between the health care and public health communities is a detriment to readiness to protect the population's health against threats. The health care sector, including private health care practices, hospitals, health care systems, health care organizations, and insurers, constitutes a major stakeholder in bioterrorism preparedness because it often serves as the first line of defense in a disease outbreak and it employs a substantial proportion of potential responders to a public health threat (including the majority of personnel vaccinated against smallpox) (GAO, 2000; Covert, 2001; Fraser and Fisher, 2001; IOM, 2002). This explains why communication and collaboration between the health care and public health communities are essential to bioterrorism preparedness. The Health Resources and Services Administration (HRSA) National Bioterrorism Hospital Preparedness Program Cooperative Agreement Guidance for FY 2003 describes areas where collaboration is needed between public health agencies and hospitals, as well as other health care partners. The crosscutting guidance provided in this document is also included in the CDC Guidance (CDC, 2003b).

It was not entirely clear from the HRSA and CDC crosscutting guidance whether all hospitals and health care providers in a jurisdiction are expected to participate in planning for preparedness, and in implementing and testing plans. Nevertheless, the preparedness efforts of state and local public health agencies should engage all hospitals and health care systems, not just those participating in vaccination program (IOM, 2003d). Hospitals and health care systems

that declined to participate in the vaccination program have cited valid reasons, such as concerns about liability and potential risk to patients. However, it is important that these organizations ensure that their emergency preparedness plans incorporate contingencies for responding to bioterrorism. It is necessary that the health care community (and any relevant partners), at a minimum, conduct or oversee the following activities:

- develop, implement, and exercise bioterrorism response plans as part of or in addition to their existing emergency preparedness plans;
- have clear protocols for interfacing with public health authorities (both routinely, such as common infectious disease reporting, and in emergencies, such as the first cases of a suspected outbreak) and for collaborating with other hospitals and health care systems;
- review and modify institutional policy as needed, and call for changes in state licensure and accreditation protocols (Blank et al., 2003);
- provide ongoing staff training on bioterror agents, including smallpox;
- develop guidelines for identifying and managing suspicious cases (including suspected smallpox) in their outpatient clinics, emergency departments, laboratories, and other facilities;
- link with the local or state jurisdiction's public health preparedness efforts (including the acquisition and distribution of Strategic National Stockpile drugs, vaccines, and supplies, including smallpox vaccine, regionally); and
- exercise, test, and revise plan(s) as needed.

Although it is essential that public health agencies reach out and collaborate with professional organizations and the hospital industry, such efforts might overlook the increasing number of health care providers in private practices or ambulatory care settings who are not affiliated with professional organizations, but with entities such as the American Medical Group Association or the Medical Group Management Association. The public health community is responsible for finding ways to communicate with and integrate the widest possible range of health care providers in the planning, training for, and testing of smallpox and overall public health preparedness.

Public health agencies are also responsible for strengthening and updating information systems to facilitate disease surveillance and reporting by health care providers, for making efforts to familiarize the health care community with surveillance and reporting procedures, and for providing timely feedback to such reporting and enhancing all communication channels with the health care community, with particular attention to infectious disease experts and primary care providers (Teutsch and Churchill, 1994; Thacker and Stroup, 1994; Baxter et al., 2000; Elliott, 2002). These activities should be coordinated with CDC's existing internet-based resources.

At the federal level, CDC has conducted many activities to inform and educate providers about smallpox and smallpox vaccination, and these efforts must be sustained over time, and must be enhanced to include the knowledge and skills required for a broader kind of preparedness. A range of training and education resources for clinicians are also available from the American Medical Association (AP, 2003b), the Agency for Health Research and Quality, the Association of Professionals in Infection Control, and from a number of university-based

centers that study bioterrorism and disaster preparedness (e.g., the Centers for Public Health Preparedness).

In addition to the efforts of public health agencies, accreditation systems could be used to further the engagement of hospitals and health care organizations in bioterrorism and overall public health preparedness. In the area of accreditation, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has been integrating bioterrorism and smallpox components into the requirements for emergency preparedness. The committee urges CDC to work with all health care accrediting bodies (JCAHO, National Commission for Quality Assurance, and URAC) to encourage the incorporation of emergency preparedness standards (i.e., for developing, implementing, and exercising plans for responding to a potential bioterrorist attack including, but not limited to, smallpox) into requirements for the accreditation of hospitals and healthcare organizations.

The Role of Public and Media Communication in Smallpox Preparedness

Public communication is an essential component of public health and smallpox preparedness. As detailed in the CDC guidance issued May 2, 2003, health departments should have communication plans in place and channels of communication tested to prepare for the possibility of an attack (CDC, 2003b). However, as with other aspects of preparedness, risk communication should be focused on all possible threats, including, but not limited to, smallpox. Public health officials and spokespersons should be familiar with all potential bioterror agents, and should also have a clear understanding of other major threats to the public health.

Practicing good communication would suggest that before a potential event and the intense sense of crisis it would create, public health authorities communicate to the public about what preparations are being made (e.g., rapidly accessible vaccine and other pharmaceutical stocks, mass vaccination or point of distribution sites), and about the availability of prepared key responders in their jurisdiction. Having information about what is in place and what will be done before a crisis occurs will help to ease the public's fears and concerns. This includes communicating about the smallpox vaccine, its risks and benefits, its availability, and plans for its rapid distribution when needed, as noted above.

The media would play a vital role in a potential bioterrorist event; journalists and other media specialists should be included in scenarios and exercises (DiGiovanni et al., 2003). This will help educate the media about the nature of infectious agents, the capacity of the public health and health care systems to respond, and plans to protect the public's health. Also, community leaders and opinion leaders have been shown to have an important role in communicating with the public in a crisis (DiGiovanni et al., 2003). Such individuals should be included in communication plans, and their roles well-described before a potential emergency

Testing Smallpox and Public Health Preparedness

Evaluating the readiness of public health and health care systems to mount an effective response is challenging, and requires a clear standard and indicators of preparedness to test against (as noted above), and tools with which to test preparedness. Helpful ways to examine and test preparedness systematically might include: (1) building hypothetical scenarios; and (2) analyzing the public health response to real-life situations such as recent outbreaks, as analogous, though perhaps on a different scale, to future potential threats.

Using Scenarios to Test Preparedness

Many types of smallpox attack scenarios could be developed to aid in exercising and testing preparedness. There are multiple variables to be considered, from ways in which the disease may be introduced, number of initial contacts, pattern of spread and number of geographical areas hit—just a few examples of the vast range of unknowns. What is the duty of the public health system in the face of such great unknowns, and what tools are available to help develop the capacity to respond to all or many possible scenarios?

Although no centralized collection or database of smallpox (or other public health threats) scenarios exists at this time, there are a number of related resources, including the Columbia University collaboration with the National Association of County and City Health Officials (NACCHO) in the Public Health Ready project (developing standards for planning and evaluating public health emergency scenarios), the NACCHO CD-ROM for scenario building, and expertise available from the Department of Defense (Columbia University School of Nursing, 2003; NACCHO, 2003a). **The committee recommends that CDC facilitate the development of a range of scenarios for potential smallpox attack(s), including one or more multi-threat scenarios, and urge states to use these to expand and continuously improve their plans to respond to a wide range of possibilities.** The committee offers its assistance in conceptualizing these scenarios, should such advice be needed.

For each scenario that is developed, state and local jurisdictions could assess their personnel and training needs, their infrastructure requirements (including legal authority), their communication plans and messages, the partners to be involved, etc. For example, local public health agencies could conduct their exercises in conjunction with local hospitals required to conduct exercises for JCAHO accreditation (Fraser and Fisher, 2001). Existing tools, such as the state and local assessment instruments developed by the National Public Health Performance Standards Program (CDC, 2003c) and the local and state Public Health Preparedness and Response Capacity Inventories (CDC, 2002b; CDC, 2002c), could be used as resources to develop a detailed and quantitative minimum standard (as recommended above) for assessing preparedness to respond to various scenarios. Resources are also available for specific components of preparedness capacity, such as a recently developed model for efficient mass smallpox vaccination campaigns (Hupert et al., 2003).

Using Lessons Learned to Test Preparedness

Another option for testing response capacity and processes, and for identifying gaps in preparedness might be to conduct state and/or local systematic reviews of public health and health system performance in response to recent outbreaks, natural disasters, and other public health crises. It is likely that many or most jurisdictions have had experience with at least one potential or actual public health crisis in recent years.

Many jurisdictions who responded to West Nile virus, or to the anthrax attacks described themselves as nearly overwhelmed; responding to a major public health threat left a slim margin of resources available for other essential public health services (GAO, 2000; NACCHO, 2001). More than one infectious agent may surface at the same time (e.g., the emergence of both SARS and monkeypox within weeks of each other), either through deliberate introduction or natural occurrence, and the public health system needs to be prepared to mobilize quickly and prioritize all its resources and respond as well as possible to more than one threat. A smallpox attack may occur in concert with other events, such as meningitis in a college population, a spike in West Nile infections, or a major food-borne disease outbreak. Health departments struggling with implementing smallpox preparedness report difficulties in conducting routine immunization activities, operating family planning clinics, or conducting other disease investigation (AP, 2003a; Cook, 2003). The added strain of SARS in some of these jurisdictions nearly overwhelmed their response capacity (Neergaard, 2003).

To test performance and identify lessons learned, a jurisdiction could examine, among other aspects of preparedness:

- the relationships and channels of communication between the public health and health care communities during the crisis, and in general;
- the speed and ease of health care provider referral, reporting, and request for technical assistance;
- the involvement of other parties when relevant (fire fighters, law enforcement);
- the training and education needs revealed by the incident, both in public health and health care communities;
- the public communication needs revealed by the incident;
- the gaps in the public health infrastructure uncovered by the incident, including in information systems, legal authority, surveillance, workforce deployment, and communication; and
- the implications of these findings for the jurisdiction's overall preparedness, and in particular, its ability to respond effectively to a smallpox attack.

Sustaining Smallpox and Overall Public Health Preparedness

The resurgence of tuberculosis (TB) as a public health threat in the last two decades strikingly illustrates the importance of sustaining public health capacity. In the early 1970s, funding for tuberculosis decreased dramatically, and tuberculosis control programs at the state

and local levels were dismantled (IOM, 2000). As the disease was considered a waning threat, capacity to deal with TB was allowed to diminish, and as a result, the re-emergence of TB exposed a public health system unprepared to respond effectively. Protecting the health of the public requires sustained readiness, and wherever possible, multi-purpose readiness. Although threats to the public's health evolve, the structures, skills, and resources needed to address them are often the same, or overlap significantly.

Sustaining general public health preparedness requires an array of capabilities and resources, and strategic planning at all levels is needed for long-term smallpox preparedness, if this is determined to be a necessity. Maintaining specific elements of smallpox preparedness includes, but is not limited to, the following activities:

For key responders:

- Vaccinating and revaccinating select key responders as appropriate to address turnover and decreasing immunity; and
- Providing training and education on an ongoing basis to all key responders on the subject of smallpox response plans and on their functional assignments or roles, on smallpox disease and vaccine, etc.

For public health response:

- Sustaining the public health infrastructure to facilitate effective rash surveillance, syndromic surveillance, reporting, laboratory capabilities, and communication; and
- Re-training and communicating with health care workers and providers on identifying and diagnosing suspicious symptoms, reporting requirements and contact information regularly.

For mass vaccination:

- Testing the readiness of key responders responsible for mass vaccination (vaccinators, security, etc.) regularly;
- Maintaining adequate vaccine stocks; and
- Testing capacity to set up clinic operations and rapidly process large numbers of people regularly.

The first two key messages of the report are:

* Smallpox is not the only threat to the public's health, and vaccination is not the only tool for smallpox preparedness.
* To improve smallpox preparedness, it is essential to "plan, train to the plan, exercise to the plan, and revise the plan" (Selecky, 2003).

VACCINATION OF MEMBERS OF THE GENERAL PUBLIC WHO INSIST ON RECEIVING SMALLPOX VACCINE

On December 13, 2002, President Bush announced his policy on pre-event vaccination against smallpox. In those remarks, the President stated, "Our government has no information that a smallpox attack is imminent… Given the current level of threat and the inherent health risks of the vaccine, we have decided not to initiate a broader vaccination program for all Americans at this time" (White House, 2002). Because of the possible threat, he said that "the military and other personnel who serve America in high-risk parts of the world" would be vaccinated and that "medical professionals and emergency personnel and response teams that would be the first on the scene in a smallpox emergency" could volunteer to receive the vaccine (White House, 2002).

During those remarks, the President also stated, "There may be some citizens, however, who insist on being vaccinated now. The public health agencies will work to accommodate them. But that is not our recommendation at this time" (White House, 2002). CDC has been charged with implementing this component of the President's policy, in addition to facilitating the vaccination of public health and health care response teams and vaccination of a broader group of health care, police, fire, and emergency response personnel. The committee appreciates the President's motivation to be responsive to the general public, particularly to those who are concerned for their personal and family's safety and who believe that a smallpox vaccination is the only way to ensure safety against the threat of smallpox introduction.

The committee notes, however, that public health programs do not proceed simply on the basis of an individual's request for medication, a vaccine, or any other intervention. The same is true of immunizations or prescription medications given by health care providers. Immunizations are not given unless the risk to the patient and population is believed to be outweighed by the benefit to be gained. In this case, smallpox vaccination not otherwise indicated by participation in smallpox preparedness efforts, exposure to monkeypox, or risk of disease from other orthopox viruses in the course of laboratory work and in the absence of identified risk for that individual of acquiring smallpox would be an extremely unusual circumstance outside of a clinical trial, as is discussed below.

CDC has asked the committee's advice on how to carry out this program (Henderson, 2003). The committee has several concerns about a vaccination program aimed at the general public at this time that need to be considered before determining how to launch such a program:

LOGISTICS: It is not clear how many members of the general public are seeking vaccination. As of early May, CDC's "hotlines have never been completely inundated by people from the public calling and wanting to know where to get the vaccine," but CDC also acknowledges that "there have been calls [about this issue] to some state and local health officials over time" (Henderson, 2003: 80). CDC has also stated that "there's been relatively little clamoring" for the vaccine by members of the general public (McNeil, 2003). If few are seeking vaccination, the burden on public health agencies might be slight, but this might be counteracted by a possibly broad geographic distribution of those seeking vaccine. In addition, sporadic requests for

vaccination from members of the general public, for whom different informational materials and medical oversight might be required, do not necessarily improve smallpox preparedness and could well be even more disruptive to public health agencies than a large-scale but concentrated set of requests. Other issues related to public or private insurance coverage for employment loss and medical care for adverse events or ensuing disability for members of the general public will have to be addressed.

RESOURCES: The committee has noted several times in previous reports that many public health agencies are stressed to their limits in trying to implement the smallpox vaccination program for the target professional populations, executing the other elements of preparedness, dealing with adverse events following vaccination, improving communication, enhancing the various vaccine surveillance programs, and addressing competing public health mandates, such as SARS. It is possible that the development and execution of a robust public vaccination program at this time would severely deplete human and fiscal resources from other high priority public health activities and even detract from the next expansion of the planned vaccination program or from a mass vaccination program in the event of an introduction of smallpox.

COMMUNICATION: Communicating about the public health system's readiness and ability to protect the public could greatly influence how many people feel it is necessary to receive the smallpox vaccine prior to any exposure or identified case. If the public is well-informed about the plans that CDC, states, and localities have in place to respond to a smallpox attack (e.g., an adequate vaccine supply, plans for mass vaccination clinics, and development of a newer smallpox vaccine), there may be less demand. The committee encourages CDC and their state and local partners to describe to the public how the public health system is enhancing preparedness to protect them from the consequences of a smallpox attack, and about the state of preparations. By learning about the range of preparations that are being made and the existence and distribution of prepared key responders in each jurisdiction, members of the general public will be better able to judge whether they want to pursue receiving the smallpox vaccine in a pre-event setting.

SAFETY: As with all smallpox vaccinees, vaccinated members of the general public would pose a risk to their families and other close contacts, due to the long period of time following vaccination when contact with the vaccination site can cause injury to third parties. Although the basic issues of potential spread to families and contacts are the same as among health care and public health workers, the level of vaccinee knowledge about adverse events and agency monitoring are likely to be substantially less when members of the general public are vaccinated. Thus, each new vaccinee poses additional risk to the general population without, in the absence of an actual outbreak of smallpox, any added benefit for the vaccinee or the general population. It will also be important to determine how much follow-up for short- and long-term clinical outcomes would be appropriate, and who would be responsible for submitting follow-up reports needed for surveillance, since no institutional aegis would be present.

RISK-BENEFIT: In the absence of any current benefit to individual vaccinees and the remote prospect of benefit in the future (as such benefit would be realized only in the event of a smallpox outbreak, and the outbreak occurred in the vaccinee's region), the balance of benefit to the individual and risk to others (through contact with the vaccinee or through disruption of other

public health initiatives) becomes unfavorable. This poor risk-benefit balance is particularly problematic here, where third parties have not consented to the risk of contact with a vaccinee. In the absence of other forms of benefit, therefore, offering vaccination to members of the general public is contrary to the basic precepts of public health ethics, which focus on a fair and reasonable balance of risks and benefits among individuals and for the population as a whole.

Two potential areas of benefit might alter this equation, however, in some circumstances. One is when, as with first responders, there is a possibility of greater personal need for the vaccination. In the general population, this may occur when individuals have been exposed to monkeypox or when they work with the smallpox virus (and other closely related viruses). For these individuals, their personal protection needs can appropriately be seen to outweigh the risk their vaccination would impose upon themselves and others.

A second circumstance would be one where vaccination of individuals offers a benefit to the general population, such as in a clinical trial, where participation facilitates scientific research that might lead to safer or more effective ways to guard against the disease. Clinical trials also offer a series of apparently effective techniques for minimizing risks to participants and third parties through careful attention to participant screening, education, and monitoring. Thus, here too, the combined benefits to the individual and society may outweigh the risks of proceeding with vaccination.

Given all of these concerns, **the committee recommends that CDC proceed with a deliberate and stepwise approach toward meeting the President's policy of offering vaccine to members of the general public who insist on receiving it by:**

1. **Conducting brief quantitative surveys to determine public interest and desire for smallpox vaccine. These surveys should include public and private health agencies as well as the general public, in order to understand the potential scope of public interest.**

2. **Determining the budgetary and other requirements that would meet the demand noted.**

3. **Identifying, monitoring, and referring people to existing or planned smallpox vaccine clinical research trials or other well-structured clinical arrangements that meet the basic requirements of medical and public health ethics, including assurances for safety of vaccinees and their contacts, acceptable balance between risk and benefit, and acceptable distribution of scarce public health resources to meet all preparedness as well as other public health goals. The committee encourages CDC to consider utilizing a pilot program or some other means of evaluating the initial experiences with this effort.**

The third key message of the report is:

* Vaccinating members of the general public beyond the key personnel states deem necessary for preparedness should proceed only under the aegis of smallpox vaccine clinical research trials or other well-structured clinical arrangements that meet the basic requirements of medical and public health ethics.

SELECTED ASPECTS OF SMALLPOX VACCINATION PROGRAM IMPLEMENTATION

In the following section of the report, the committee discusses several important components of the national smallpox vaccination program: (1) Communicating About and Coordinating the Response to Adverse Events; (2) Data Systems Used in Smallpox Vaccination Program; (3) Pregnancy Screening; (4) Advisory Committee on Immunization Practices Smallpox Vaccine Safety Working Group (ACIP SVS WG); (5) Evaluation and Safety Studies; and (6) Compensation Available for Smallpox Vaccine Injuries.

Communicating About and Coordinating the Response to Adverse Events

Communication among CDC, states, and local jurisdictions is extremely important for identifying every serious adverse event, conducting follow-up of the vaccinee who experiences the adverse event, and providing feedback to states and particularly local jurisdictions about how their reporting efforts help to ensure the overall safety of the national smallpox vaccination program. The committee heard that some local jurisdictions feel overburdened by the adverse event management and reporting requirements created by both the state and CDC (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003; Nikolai, 2003). In many jurisdictions, there also seems to be confusion among local health departments, hospitals and health care systems, and treating physicians about who is supposed to report which type of adverse event to which system (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003). The use of multiple data systems for the smallpox vaccination program has contributed to some of this confusion.

These observations highlight the need for greater communication and coordination among CDC, states, local health departments, hospitals, and health care providers with respect to adverse event reporting. Because state and local partners cite the need for improved coordination and reduction of the time burden for reporting and managing adverse events, the committee is concerned that partners in the smallpox vaccination program could be reluctant to report all adverse events or ill-informed about how to report them. **To help ensure that the adverse event reporting and follow-up procedures work as seamlessly as possible, the committee recommends that CDC coordinate better with their state partners and provide feedback to local partners who reported the adverse event.**

Data Systems Used in Smallpox Vaccination Program

With the rapid development of the national smallpox vaccination program, CDC has had to develop data systems for use during the program in a very short time frame. CDC should be congratulated for developing the Pre-Event Vaccination System (PVS), the Smallpox Vaccine Adverse Event Active Surveillance System (subsequently referred to as the "Active Surveillance System"), and the Hospital Smallpox Vaccination Monitoring System (HSVMS) so quickly. In conjunction with the Vaccine Adverse Event Reporting System (VAERS), these data systems have allowed adverse events following smallpox vaccination to be reported quickly, and helped identify new patterns of adverse events (e.g., myo/pericarditis, myocardial infarction), which ultimately may or may not be shown to be causally associated with the smallpox vaccine.

Streamlining Data Collection

Of the multiple data systems being used concurrently during the pre-event smallpox vaccination program, PVS, the Active Surveillance System, and HSVMS were all created uniquely for the pre-event smallpox vaccination program; VAERS is a data system that was previously established to collect reports of adverse events following any vaccination. For the purposes of the smallpox vaccination program, these data systems have been designed to work together. PVS and HSVMS provide a link to the Active Surveillance System, and VAERS supplements the data gathered through the Active Surveillance System. (More detailed descriptions of these data systems are available in the committee's second report [IOM, 2003c].)

In an ideal world, one data system would have been created specifically for the smallpox vaccination program that could have worked in conjunction with VAERS. However, the timing of the vaccination program and the different types of users that need to access each system necessitated that these data systems be created in the manner that they were. Even so, the committee believes that there may be ways to integrate these systems better, so the data-reporting burden on all vaccination partners is reduced. The data-reporting burden also includes the weekly data reports that states are required to send to CDC, which are sometimes redundant with the data that states have already entered into PVS. **The committee recommends that CDC pursue ways to streamline the data systems that are used in the smallpox vaccination program, improving user-friendliness and integrating the multiple systems to avoid duplicate data entry, especially considering that any future expansion of the vaccination program would require a larger number and greater diversity of data system users, some of whom may be using these systems for the first time.**

When the vaccination program expands to include new types of vaccinees (many of whom do not work in a health department or hospital setting), there potentially will be many new users of PVS, HSVMS, the Active Surveillance System, and VAERS. To ensure continued collection of data on all vaccinees, new users of these data systems will have to be educated about existing data systems, their purpose, and how they are linked together. The committee encourages CDC to provide greater outreach and communication about the data systems used in the smallpox vaccination program to all the potential users of these systems in the expanded program, as well as a redoubling of outreach and communication efforts to partners involved in the first phase of

the program who have not completely utilized these data systems. The committee also encourages CDC to plan for streamlining or limiting the data collected from vaccinees, should an outbreak occur, in order to keep things moving more efficiently.

Ease of Use and Value Gained from PVS

As effective as these data systems have been at helping to identify serious adverse events following smallpox vaccination, state and local vaccination programs appear to be experiencing continuing difficulty in using these systems. For example, the committee has heard during presentations at committee meetings and in discussions with state and local health departments that PVS is not user-friendly (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003; Madlock, 2003; Nikolai, 2003). State and local health departments have reported that it takes inordinate amounts of time to enter data into PVS, and that the CDC servers that host this system sometimes do not function properly. CDC has acknowledged these problems with PVS, and has stated that it is working to resolve them. The committee encourages CDC to resolve these problems as quickly as possible, since the cumbersomeness of PVS threatens broad use of this system by state and local vaccination programs, potentially leading to a loss of useful information.

The data entered into PVS provide great value to overall evaluation of the vaccination program's progress. It is this value that counterbalances the burden placed on state and local vaccination programs to enter data into PVS. However, the committee has heard that some state and local vaccination programs view the difficulty in entering data into PVS as outweighing the perceived benefits they receive from their participation (Committee on Smallpox Vaccination Program Implementation Study Staff, 2003). The committee encourages CDC to facilitate and support regular, timely data reports from PVS and other sources to its state and local partners so they can gain value from their participation in the range of data systems used for the pre-event smallpox vaccination program.

Utility of the Active Surveillance System

As described above, the data systems that CDC has utilized during the pre-event smallpox vaccination program seem to have been effective at identifying serious adverse events following smallpox vaccination. However, the committee cannot be completely certain of how effective the Active Surveillance System has been at identifying these serious adverse events until all vaccinees are entered into the system. An "active" surveillance system is effective when there is a confirmed outcome on virtually every vaccinee. As of June 11, 2003, only 10,835 (44%) of 24,781 PVS records of vaccinees that had at least 28 days elapse since the time of vaccination were included in the Active Surveillance System (Mootrey, 2003b). The recent reports of two cases of cardiomyopathy identified three months after smallpox vaccination (CDC, 2003n) also point to the need to continue active surveillance of all vaccinees, including follow-up of those vaccinees who report only mild symptoms in the weeks after vaccination. CDC conducted a survey of their grantees to gain a better understanding of their participation (or lack thereof) in the Active Surveillance System. The 48 grantees that responded to the survey identified four main reasons for data entry delay in the Active Surveillance System: (1) follow-up time is longer than anticipated; (2) data entry is slow because of general lack of personnel or

infrastructure resources; (3) technical difficulties related to digital certificates; and (4) problems with PVS (Mootrey, 2003a).

The committee understands that CDC has diligently encouraged every state and local vaccination program to create an Active Surveillance System entry for every vaccinee. **Because the civilian smallpox vaccination program is a true partnership between CDC, states, and local jurisdictions, the committee recommends that CDC continue and expand their communication with states and local jurisdictions about the imperativeness of their participation in the Active Surveillance System, stressing that the safety of the vaccination program cannot be guaranteed without their full participation and cooperation.** In these communications, CDC should stress that the number of people vaccinated in the expanded vaccination program could be many times larger than the number of response team members vaccinated so far. Therefore, the consistent use of the Active Surveillance System would provide a rich source of data for detecting trends in reported adverse events.

In its first letter report (IOM, 2003b: 17), the committee identified its reasons for recommending the creation and use of an active surveillance system:

> "Considering the anticipated risks of the vaccination program and the currently unknown benefit, it is extremely important that all adverse reactions from the smallpox vaccine (both known and suspected) be identified in a timely manner. Relying on passive systems that are dependent on vaccinees and their clinicians to bring the adverse reaction to the attention of the smallpox vaccination program managers will not capture all serious adverse reactions."

The committee still believes in the value of the Active Surveillance System, but recognizes the importance of doing an evaluation of the efficacy of the system so its role in the ongoing program can be assessed. Such an evaluation should involve getting data on every person vaccinated in the first phase of the program entered into the Active Surveillance System, and then evaluating the completeness, validity, and added value of the data gathered through the Active Surveillance System compared to other means (e.g., VAERS, the Clinician Information Line). Once such an evaluation is conducted (with as complete ascertainment as possible of data on all vaccinees, so reliable statistical analyses can be generated), the committee and CDC can have a better understanding of the relative value of the Active Surveillance System in the ongoing operation of the pre-event smallpox vaccination program. Regardless, such an evaluation would provide reassurance of the completeness of safety data, and correspondingly, the overall safety of the vaccination program.

It is important to recognize, however, that an evaluation of the Active Surveillance System during the first phase of the program may not necessarily be generalizable to the expanded program. In the expanded vaccination program, there may be a larger number of people vaccinated than in the first phase of the program. Because of this potentially larger number of vaccinees, there may also be a larger number of adverse events reported. The standardized data collection format used in the Active Surveillance System may make investigations easier for this potentially greater volume of reported adverse events and may allow determinations of probable causality to be made more quickly, potentially lessening the sense of alarm that would arise from

the sheer volume of adverse events that could be reported. Additionally, whereas the first phase of the program focused on public health and health care workers who already may have had knowledge of adverse event reporting mechanisms, workers vaccinated in the expanded vaccination program (and their fellow workers who may be entering data on this new pool of vaccinees) may not have the same knowledge about adverse event reporting mechanisms. Thus, the Active Surveillance System may have more value during the expansion of the vaccination program, especially if proactive communication about the specific data systems being used during the smallpox vaccination program, the purpose of each one, and how they are linked together is provided to those who will be responsible for data entry and management.

Pregnancy Screening

On May 2, 2003, CDC described women who had been exposed to smallpox vaccine during pregnancy and their enrollment in the National Smallpox Vaccine in Pregnancy Registry in an article appearing in the Morbidity and Mortality Weekly Report (CDC, 2003k). The registry includes women found to be pregnant when vaccinated, those who became pregnant within 28 days of vaccination, and those who, while pregnant, were in close contact with a person vaccinated within the previous 28 days. The registry will be used to monitor outcomes of pregnancy in these women. Women vaccinated through the military smallpox vaccination program, the civilian smallpox vaccination program, and recent clinical research studies are included in the registry.

In pregnant women, the smallpox vaccine can cause fetal vaccinia, a rare but serious condition that can lead to premature delivery, skin rash with scarring, stillbirth, or death of an infant after delivery (CDC, 2003o). Some infants who experience fetal vaccinia are born with skin scars, but are otherwise healthy (CDC, 2003o). Fewer than 50 cases of fetal vaccinia have ever been reported in the world, and only three of these cases occurred in the United States (CDC, 2003o). From 1967 to 1971, when smallpox vaccine was routinely given in the United States, only one case of fetal vaccinia was reported among an estimated 90,000 to 280,000 pregnant women who received the vaccine (CDC, 2003o). Smallpox vaccine has not been shown to cause an increased risk of birth defects (CDC, 2003o).

In the military program, from December 13, 2002 to April 22, 2003, a total of 62,222 women of reproductive age were screened for smallpox vaccination, and 52,185 were vaccinated; 85 were inadvertently exposed to smallpox vaccine during pregnancy. (As of June 11, 2003, 125 women from the military program were enrolled in the registry [Grabenstein, 2003].) The median age was 22 years. On the basis of the estimated date of conception, 62 women conceived before vaccination and 23 conceived during the 4 weeks after vaccination. In the civilian program, from January 24, 2003 to April 24, 2003, a total of 6,174 women of reproductive age were vaccinated; 6 were inadvertently exposed to smallpox vaccine during pregnancy. (As of June 18, 2003, 8 women from the civilian program were included in the registry [Mulinare et al., 2003].) The median age was 31 years. On the basis of estimated date of conception, 2 women conceived within 1 week before vaccination and 4 conceived during the 4 weeks after vaccination. Two of the civilian women had miscarriages during early pregnancy. In clinical studies of the smallpox vaccine, from November 2001 to April 24, 2003, a total of 12 women

were inadvertently exposed to smallpox vaccine during pregnancy. The denominator for women of reproductive age for this population is not available. The median age was 28 years. Each of the women had a negative pregnancy test on the day of vaccination (CDC, 2003k). In all of these populations, the actual number of pregnancies exposed to smallpox vaccine could be expected to be underreported, since not all women will report their pregnancies to the registry and some pregnancies may end before a woman recognizes that she is pregnant.

Because exposure to smallpox vaccine during pregnancy can cause fetal vaccinia, a rare but serious condition, CDC and the Department of Defense (DoD) have provided education about the risk of smallpox vaccine exposure during pregnancy and advised women not to receive the smallpox vaccine if they are pregnant, to take a pregnancy test if they think they might be pregnant, and avoid pregnancy for 4 weeks after vaccination, and advised close contacts of pregnant women not to receive the smallpox vaccine (CDC, 2003h; DoD, 2003).

CDC has estimated that the expected rate of unknown pregnancy (i.e., pregnancies of $\leq$4 weeks' gestation or $\leq$6 weeks based on obstetrical dating) and the expected rate of conception during a 4-week period would be 12 per 1,000 women in the general population and 8 per 1,000 women in a population comparable to the older, health-care workers vaccinated in the civilian program, in the absence of screening and counseling (CDC, 2003k). The reported rate of pregnancies exposed to smallpox vaccine during the first phase of the civilian and DoD programs is approximately 1 per 1,000, which is substantially lower than the expected rates of unknown pregnancy and conception during a four week period (in the absence of screening and education) of 8 per 1,000 women in the population comparable to the civilian health-care workers and 12 per 1,000 women in the general population (CDC, 2003k).

Even though some women have been inadvertently exposed to smallpox vaccine during the civilian vaccination program, the lower than expected rate of unknown pregnancies and conception in the four weeks after vaccination in women vaccinated in the civilian program reassures the committee that the pregnancy screening practices have been relatively effective thus far. Stronger advice about contraception during the four weeks after vaccination or greater emphasis on the need to conduct a pregnancy test on the morning of vaccination could help to reduce the rate of women inadvertently exposed to smallpox vaccine during pregnancy. It is impossible, however, to detect every pregnancy since pregnancy tests might miss very early pregnancies. Understanding this and recognizing that each woman has the right to decide for herself whether a pregnancy test is appropriate, the committee agrees with the October 2002 recommendation of the Advisory Committee on Immunization Practices that "Routine pregnancy testing of women of child-bearing age is not recommended" (CDC, 2002d).

CDC has stated that they are considering expanding the questions and advice about pregnancy and intention to become pregnant (included in the Vaccine Information Statement Supplement E) (Mulinare et al., 2003). The committee believes that additional public health interventions to screen for pregnancy and provide advice on avoiding pregnancy could probably be beneficial, if they do not detract from other important screening and programmatic activities. **Considering that the rate of inadvertent exposure to smallpox vaccine during pregnancy is lower than expected and it is impossible to detect all pregnancies at the time of vaccination, the committee does not recommend extra pregnancy screening efforts at this time.** Data on

the rate of pregnancies exposed to smallpox vaccine should be evaluated regularly, with the decision on whether to intensify pregnancy screening efforts also being reevaluated regularly.

On June 11, 2003, CDC recommended smallpox vaccination for persons investigating monkeypox outbreaks, involved in caring for infected individuals or animals, or who have had close or intimate contact with individuals or animals confirmed to have monkeypox (CDC, 2003a). Smallpox vaccination is recommended for persons who have contraindications to vaccination (e.g., pregnancy, eczema) if they have had close or intimate contact with a person with a rash illness, but CDC cautions that it is important to confirm suspected cases of monkeypox before recommending smallpox vaccination for a person with contraindications. Considering that there may be some pregnant women who will be advised to receive a smallpox vaccination because of their close personal contact with a confirmed case of monkeypox, the committee recognizes that it will be important for CDC to describe how such women will be incorporated into the National Smallpox Vaccine in Pregnancy Registry. These women will not have experienced an "inadvertent" smallpox vaccine exposure, because smallpox vaccination will have been recommended due to their contact with a monkeypox case. As these issues begin to be worked out, the committee encourages CDC to describe how data on them will be combined with or separated from the pregnancies exposed to smallpox vaccine stemming from the pre-event smallpox vaccination program, and how follow-up data on the pregnancies exposed to smallpox vaccine because of contact with monkeypox will contribute to evaluation of the other pregnancies included in the registry.

Advisory Committee on Immunization Practices Smallpox Vaccine Safety Working Group (ACIP SVS WG)

CDC and the Advisory Committee on Immunization Practices Smallpox Vaccine Safety Working Group (ACIP SVS WG; subsequently referred to in the text as "working group") have placed a high priority on safety in the national smallpox vaccination program. When safety concerns have arisen, CDC and the working group have responded promptly, as evidenced by the emergency meeting of the full Advisory Committee on Immunization Practices and the working group on March 28, 2003. The committee was reassured that CDC and the working group reported in a timely fashion and conducted further evaluation of the cardiac adverse events that came to light in March. The committee also commends CDC and the working group for modifying screening and education materials when it was recognized that there could possibly be an association between smallpox vaccination and the development of cardiac adverse events, and for communicating these changes to state and local partners in a rapid fashion. The committee notes that the working group has described CDC as being professional, timely with data, and responsive in their interactions with the working group (J. Neff, verbal presentation at ACIP meeting, 6/18/03).

As has been stated before, the charge of the working group is to (1) evaluate data on vaccine safety and the system for monitoring, treatment, and response and (2) monitor safety data for vaccinia immune globulin (VIG) and Cidofovir made available under oversight of the U.S. Food and Drug Administration (FDA) through investigational new drug (IND) protocols (ACIP SVS WG, 2003a).

The committee appreciated receiving information on the operating procedures of the working group (ACIP SVS WG, 2003b). This helped reduce some of the confusion about how the working group was organized and structured. The Summary of the March 20-21, 2003 meeting of the working group by the working group chairpersons (ACIP SVS WG, 2003a) helped address many of the committee's questions and concerns expressed in previous reports (IOM, 2003b; IOM, 2003c). The committee was heartened to see clear descriptions of the case definitions for specific adverse events, trigger points for action on specific events, and actions that should be taken in response to specific triggers.

In assessing trigger points, the working group is (1) identifying appropriate data sets for use in estimating expected incidence, (2) developing statistical reference rates, and (3) determining what action should occur in response to triggers (ACIP SVS WG, 2003a). The working group has developed case definitions, trigger events, trigger points, and responding actions for neurologic, dermatologic, and cardiac adverse events; they have also developed case definitions, trigger points, and responding actions for different types of inadvertent inoculation (e.g., resulting from pregnancy, immune suppression, contact transmission). The committee endorses the general approach that the working group is taking for all of these actions. The working group has developed detailed plans for assessing different disease endpoints. However, understanding that the committee has not been privy to all of the working group's discussions, the committee would like to obtain more information about the working group's deliberations about death as an endpoint (as compared to the disease endpoints that are being considered).

The working group noted in the summary of the March 20-21, 2003 meeting that they still needed to define a trigger point for further action with regard to inadvertent vaccination of HIV infected persons. The committee looks forward to seeing the working group's definition of this trigger point when it is finalized.

The committee also endorses the working group's proposal for animal studies that investigate the basic pathophysiology of cardiac disease in relation to smallpox vaccination, and the proposal to systematically observe and record how vaccine sites are managed and what outcomes result (ACIP SVS WG, 2003a).

As the working group has followed the safety data from the civilian and military smallpox vaccination programs, they have paid increased attention to the myo/pericarditis cases reported in both programs. In evaluating both the inflammatory (i.e., myo/pericarditis) and ischemic (e.g., myocardial infarction, angina) cardiac events, the working group was asked to evaluate a number of questions related to these events. Specific to the myo/pericarditis cases, the working group was asked, "Does a causal relationship exist between vaccination and inflammatory heart disease?" (Neff, 2003). The working group concluded, "DoD data support a risk for myocarditis after smallpox vaccination that is significantly higher than background rate, & suggest that a causal association is highly likely" (Neff, 2003).

This conclusion was one of the primary reasons that the majority (10 of 12) of the working group recommended that CDC "[c]ontinue with the current pre-event volunteer program, to vaccinate and maintain vaccination status of selected public health and first response health care

workers with careful screening for known risk factors with a goal of meeting and maintaining state and local health department readiness needs," in addition to the entire working group recommending, "No member favors beginning phase 2 of the vaccination program" (Neff, 2003). After being presented with these recommendations of the working group, the full ACIP unanimously approved a draft resolution and later released a final statement recommending to CDC that it would be "unwise to expand beyond its current, pre-event smallpox vaccination recommendations because of the new and unanticipated safety concerns, i.e. myo/pericarditis, whose extent and severity, particularly of long term sequelae, are not yet known. Any smallpox vaccination that occurs should be carried out only within the context of the currently recommended response teams and state and local response plans, and should be administered according to currently recommended vaccination procedures and protocols" (ACIP, 2003).[4] In their statement, the ACIP also reiterated "that it is critical for smallpox preparedness planning, within the context of broader terrorism and emergency response planning, to continue at the federal, state and local levels" (ACIP, 2003).

Evaluation and Safety Studies

The committee appreciated receiving the updated "Smallpox Vaccination Program Plans for Phase 1 Evaluation and Research" (CDC, 2003g) and found it very helpful to see all of the ongoing and planned evaluation and research activities in one document.

As CDC has acknowledged, evaluation of the cardiac adverse events reported following smallpox vaccination is very important to safely continue the smallpox vaccination program. CDC has been consulting with multiple experts in the field of cardiology and chronic disease epidemiology to investigate both the ischemic adverse events and the myo/pericarditis cases. To evaluate the cardiac adverse events, CDC's investigations have included: CDC-assisted epidemiologic field investigations ("epi-aids") in the states where deaths have occurred to obtain more comprehensive information on the cases; evaluation of case series data; collection of data on expected rates of cardiac events in comparable unvaccinated populations; and potential prospective studies that could provide information on biologic plausibility and rates of these events (CDC, 2003g).

Both CDC and the working group described considering the utility of animal studies that would investigate the basic pathophysiology of cardiac disease in relation to smallpox vaccination. CDC has stated that "studies to evaluate possible biologic mechanisms for cardiac adverse events following smallpox vaccination are being considered" (CDC, 2003j). As stated

[4] Less than a week after the ACIP released its statement on the national smallpox vaccination program, the National Vaccine Advisory Committee (NVAC) issued a letter to the Acting Assistant Secretary for Health and Director of the National Vaccine Program containing a resolution that was unanimously passed by the NVAC: "The National Vaccine Advisory Committee reaffirms the necessity for the nation's health system to be prepared for biological threats, man-made or natural, and encourages continued efforts in this regard. With respect to the smallpox vaccination, the Committee recommends that the Assistant Secretary for Health in consultation with the Department's Office of Public Health Emergency Preparedness consider the recommendations of ASTHO regarding the routine smallpox vaccination program and that further smallpox vaccinations, beyond those of public health response and vaccination teams, should be delayed until a national consensus is developed on appropriate next steps" (NVAC, 2003).

earlier, the committee endorses carrying out such studies, and any other studies that could help elucidate possible biological mechanisms for the cardiac adverse events seen following smallpox vaccination. The committee also endorses the working group's proposal that a prospective protocol-driven case-control study be conducted to assess the association between cardiac adverse events and smallpox vaccination (ACIP SVS WG, 2003a).

To supplement the studies being planned by CDC, the committee suggests that CDC consider collecting data on which states are using screening criteria for cardiac events that are more stringent than those recommended by ACIP on April 4, 2003 (CDC, 2003d). Subsequently, CDC may want to consider using these data to determine if states that are using more stringent cardiac screening criteria are experiencing lower rates of cardiac adverse events in people vaccinated after April 4, 2003 than states adhering to ACIP's recommendations.

The committee has heard that some states are screening for positive HIV status more stringently than what was deemed necessary by ACIP and CDC. For example, Rhode Island is requiring proof of a recent (in past 45 days) negative HIV test before someone can be vaccinated (A. Artenstein, personal communication, 6/13/03). As the committee noted in its first report, "Hospitals and health departments will implement the first phase of the pre-event vaccination program in slightly different ways, depending upon the circumstances and needs of their communities. Much could be learned from this differential administration of the program" (IOM, 2003b: 7). Knowing now that at least one state is using different screening criteria than what was recommended by CDC, the committee suggests that CDC collect data on the screening practices of other states, and use these data to supplement the overall evaluation of the implementation of the civilian smallpox vaccination program.

DoD has stated that they will conduct follow-up of the myo/pericarditis cases seen among people vaccinated through the DoD program at 6 weeks, 6 months, and 12 months. After review of the 12-month data, DoD will determine whether additional follow-up is warranted (J. Grabenstein, personal communication, 6/16/03). At the May 1, 2003 committee meeting, CDC said that they intend to have continuing follow-up of the myo/pericarditis cases (including a standardized protocol and guidelines for how to conduct follow-up of those cases that have been identified), but the specifics have yet to be finalized (Mootrey, 2003c). Recently, CDC has also stated that "guidelines for evaluation and follow-up of patients with myo/pericarditis have been drafted" (CDC, 2003j). When the follow-up procedures and guidelines have been finalized, the committee looks forward to receiving this information.

The committee has some additional general comments on CDC's approaches and planned efforts for evaluation and safety studies related to smallpox vaccination. These issues may need to be addressed in order to have reliable findings from all the evaluation and research efforts. By listing these guiding principles, the committee is not saying that CDC is not already implementing such measures, but rather, that these principles should be considered for every

evaluation or safety study undertaken by CDC to assess the smallpox vaccination program:

- Small, unrepresentative samples should be kept to a minimum. Small samples sizes could detract from the generalizability of the study.
- Sample sizes for many studies may be limiting for subgroup analyses. The majority of vaccinees in the first phase of the civilian program have been re-vaccinees. Considering the differential adverse reaction profile for primary vaccinees versus re-vaccinees, care should be taken to ensure that there are enough data on primary vaccinees.
- Since the vaccination program is moving to a more heterogeneous pool of vaccinees, evaluation efforts should focus on gathering data from people with less health knowledge than those vaccinated in the first phase.
- As with all studies, efforts should be taken to maximize participation rates in each study. Maximizing participation rates is not only important for generalizability, but also for the ability to validly compare rates (e.g., adverse event rates for the newer attenuated vaccines versus the old vaccines).
- CDC has made a specific effort to gather information from hospitals on their participation in first phase of the smallpox vaccination program. However, the issues that are relevant to hospitals often are also relevant to health care systems. A concomitant effort should be made to gather information from health care systems.
- As has been noted in previous reports, the committee has stressed the importance of concurrent control groups for many of the studies. Control groups and cases should be studied using the same methods. The committee again encourages CDC to develop concurrent control groups for as many of their studies as possible, given the current realities of the pace of the smallpox vaccination program. The use of such control groups would greatly aid the investigations of the recently reported cases of cardiomyopathy (CDC, 2003n) and myo/pericarditis.
- There is a general need for longer follow-up in some of the vaccinee studies. Particularly, there is a need to follow those who experienced serious adverse events in order to learn about long-term outcomes, especially for those who experienced cardiac adverse events. Right now, this involves a relatively small number of people, but the information gained from long-term follow-up will be extremely important. There may also be value in long-term follow-up of a sample of vaccinees who experienced no adverse events, as well as a sample of those vaccinees that experienced mild, less severe adverse events. This is particularly relevant now that two cases of dilated cardiomyopathy have been identified three months after vaccination (CDC, 2003n). (The DoD is planning on using the Millennium Cohort Study and the Defense Medical Surveillance System to compare and contrast people who have received the smallpox vaccine to people who have not received the vaccine [J. Grabenstein, personal communication, 6/15/03].) Plans should also be made to assemble enough information so that follow-up can be done easily in the future.
- Follow-up would also be valuable for the pregnancies inadvertently and intentionally (i.e., in response to contact with a case of monkeypox) exposed to smallpox vaccination. The committee notes that DoD has an ongoing birth defects registry (covering all dependants of military personnel) that could contribute information on any concerns that might arise.

The committee also suggests that CDC and the ACIP consider holding periodic invitational workshops on the science of smallpox vaccine safety and efficacy to update and disseminate new findings in these areas. The results of these workshops could be actively disseminated to CDC's state and local partners in the smallpox vaccination program to update them on the latest research.

The committee encourages CDC to think long-term about the research agenda for the smallpox vaccination program. CDC has stated that the pre-event smallpox vaccination program will be an ongoing program (CDC, 2003i; CDC, 2003m), specifically in terms of vaccinating new people for maintenance of response teams, and broadly in terms of planning for a smallpox response. There will be many policy and implementation questions that will have to be answered along the way. **The committee recommends that CDC begin developing a structured, prioritized research agenda that can aid decision-making as the smallpox preparedness program moves forward.** The committee offers its assistance in refining this research agenda as the program evolves. Considering the extent of evaluation and research efforts that CDC could propose for the smallpox vaccination program as it moves forward, and the limited resources available to support all needed evaluation efforts, the committee encourages CDC to consider requesting the use of Public Health Service 1% Evaluation funds for this purpose (if this approach has not been pursued already). [5]

CDC has asked for the committee's assistance in prioritizing research and evaluation efforts specific to the smallpox vaccination program, given the limited resources available for these activities (B. Gellin, personal communication at report briefing, 3/26/03). **The committee recommends that in the short-term, studies of the serious adverse events should receive the highest priority. For safety-related questions, in the longer-term, studies examining long-term outcomes for those who experienced both serious and mild adverse events and studies of how mild adverse events contributed to lost work or social function should be a high priority. For system-related questions, in the longer-term, studies of cost and opportunity costs should be a high priority.** Although still important, the committee believes that studies on the reasons why people declined vaccination, tracking rarer adverse events, improving adverse event classification, and tracking persons with missing data should be considered next-tier priorities.

Compensation Available for Smallpox Vaccine Injuries

As stated in the committee's third letter report, "the committee notes the need for additional clarification by CDC to the states on the provisions of the [Smallpox Emergency Personnel Protection Act of 2003 (P.L. 108-20)], and for fact sheets or other explanatory materials for potential vaccinees" (IOM, 2003d). CDC has since developed a summary of the Smallpox Emergency Personnel Protection Act of 2003 ("SEPPA") benefits and compensation for smallpox vaccine injuries that is posted to its website (CDC, 2003e). However, at the time of the writing of this report, the compensation language in the Smallpox Vaccine Information

[5] The Department of Health and Human Services is authorized under the Public Health Service Act to set-aside up to one percent of appropriations for Public Health Service (PHS) programs for evaluation (directly, or by grants of contracts) of the implementation and effectiveness of PHS programs (42 USC 238(j)).

Statement (VIS) (CDC, 2003f) had not yet been updated to reflect the newly enacted legislation. To ensure that potential vaccinees are aware of the compensation available to them for any adverse events that are determined to be connected to the smallpox vaccine, the committee encourages CDC to update the VIS as soon as possible, and publicize the existence of the fact sheet. When the interim final rule implementing SEPPA is published, this fact sheet should be expanded with further information on what types of compensation are available, how to apply for compensation, the statute of limitations and statute of repose, and any other relevant information. The issue of compensation for live born children who were exposed to the vaccine in utero should be clarified as well.

To help publicize the existence of these materials, the committee suggests that CDC notify states when these updated materials are available. The committee also encourages CDC to send a post-vaccination fact sheet or letter explaining the compensation available under SEPPA to every person who has been identified as experiencing an adverse event. CDC could also consider whether such information should also be sent to everyone who has already been vaccinated.

As of June 20, 2003, 17 suspected cases of myo/pericarditis and 4 probable cases of myo/pericarditis following smallpox vaccination were reported in the civilian population (CDC, 2003n). Because of the probable association of smallpox vaccination with increased incidence of myo/pericarditis, CDC is now including myo/pericarditis in the tables of "selected adverse events associated with smallpox vaccination among civilians" appearing weekly in the Morbidity and Mortality Weekly Report. The ACIP Smallpox Vaccine Safety Working Group has concluded that "Smallpox vaccination increases risk of myo-pericarditis" (Neff, 2003). The DoD has stated, "the observed rate of myopericarditis among primary vaccinees is 3.6-fold higher than the expected rate among personnel on active duty who were not vaccinated" (Halsell et al., 2003).

Research in non-smallpox vaccine settings suggests that some people who experience myocarditis may develop long-term sequelae such as left ventricular dysfunction (Hiroe et al, 1985) and cardiomyopathy (Hayakawa et al, 1984; Das et al, 1985; Drucker and Newburger, 1997). As of June 20, 2003, two cases of dilated cardiomyopathy were diagnosed in civilian smallpox vaccinees three months after vaccination (CDC, 2003n). CDC is now advising, "Because smallpox vaccination appears to be associated causally with myocarditis, which can cause [dilated cardiomyopathy], further evaluation is warranted" (CDC, 2003n). In one study, one fourth of patients reporting to a major medical center with symptomatic dilated cardiomyopathy died within a year, and half died within five years (Dec and Fuster, 1994).

The possibility of long-term sequelae from the smallpox vaccine must be acknowledged. Whereas the acute smallpox vaccine injuries are relatively well understood, less is known about smallpox vaccine injuries that occur on a longer-term basis. SEPPA specifies that an individual who was administered the vaccine who is requesting a benefit under the law must file an initial request for benefits or compensation "not later than one year after the date of administration of the vaccine" (108th U.S. Congress, 2003). (Individuals who experienced accidental vaccinia inoculation, however, have up to "two years after the date of the first symptom or manifestation of onset of the adverse effect" [108th U.S. Congress, 2003] to file an initial request.) For

individuals who received the smallpox vaccine, it currently is unclear to the committee how, if at all, any injuries that manifest themselves more than one year after vaccination will be addressed. It also is unclear how longer-term sequelae that result from an acute smallpox vaccine injury (e.g. cardiomyopathy that results from a "silent" case of myocarditis, with no initial request for benefits filed in the year after vaccination) will be handled. Also, in SEPPA, a 'covered injury' is covered if it is "determined…to have been sustained by an individual the direct result of administration to the individual of a covered countermeasure during the effective period of the Declaration" (108th U.S. Congress, 2003). (The term 'Declaration' refers to the Declaration Regarding Administration of Smallpox Countermeasures issued by the Secretary on January 24, 2003, and published in the Federal Register on January 28, 2003.) The committee believes that it will be important to clarify and explain in the interim final rule the interpretation of "a direct result of…a covered countermeasure" (i.e. smallpox vaccine), since this will affect the level of evidence required for an injury to be covered. The committee encourages CDC to work with those who are developing the interim final rule for the smallpox vaccine injury table to clarify the conditions under which longer-term sequelae from the smallpox vaccine will be considered to be a direct result of smallpox vaccination.

The last two key messages of the report are:

* The safety system appears to be working well to date, but CDC and its partners should remain vigilant to ensure the continuing safe implementation of the program.
* The development of a research agenda for the smallpox vaccination program is important to ensuring the long-term success of smallpox preparedness efforts, as well as providing useful information for overall public health preparedness.

CONCLUDING REMARKS

The committee offers its assistance in the future in any areas that would prove useful to CDC. Two possible areas include developing a research agenda to support and evaluate the implementation of the smallpox preparedness program, and exploring how to better integrate smallpox preparedness into overall public health preparedness.

In closing, the committee summarizes several of the key messages set forth in this report:

- First, smallpox is not the only threat to the public's health, and vaccination is not the only tool for smallpox preparedness.
- Second, to improve smallpox preparedness, it is essential to "plan, train to the plan, exercise to the plan, and revise the plan" (Selecky, 2003).
- Third, vaccinating members of the general public beyond the key personnel states deem necessary for preparedness should proceed only under the aegis of smallpox vaccine clinical research trials or other well-structured clinical arrangements that meet the basic requirements of medical and public health ethics.
- Fourth, the safety system appears to be working well to date, but CDC and its partners should remain vigilant to ensure the continuing safe implementation of the program.

- Fifth, the development of a research agenda for the smallpox vaccination program is important to ensuring the long-term success of smallpox preparedness efforts, as well as providing useful information for overall public health preparedness.

The committee wishes to thank you for the continuing opportunity to be of assistance to the Centers for Disease Control and Prevention and its partners as they work to protect the nation's health.

Brian L. Strom, *Committee Chair*
Kristine M. Gebbie, *Committee Vice Chair*
Robert B. Wallace, *Committee Vice Chair*
Committee on Smallpox Vaccination Program Implementation

REFERENCES

108th U.S. Congress. 2003. Smallpox Emergency Personnel Protection Act of 2003 (Public Law 108-20). Accessed July 11, 2003. Web page available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_cong_public_laws&docid=f:publ020.108.pdf

AAFP (American Academy of Family Physicians). 2002. Panel calls for limited smallpox vaccination. FP Report 8(8).

ACIP (Advisory Committee to Immunization Practices). 2002. Record of the Meeting of the Advisory Committee on Immunization Practices -- June 19-20, 2002. Accessed July 30, 2003. Web page available at: http://www.cdc.gov/nip/acip/minutes/acip-min-jun02.rtf.

ACIP (Advisory Committee on Immunization Practices). 2003. Advisory Committee on Immunization Practices (ACIP) Statement on Smallpox Preparedness and Vaccination. Accessed July 17, 2003. Web page available at: http://www.bt.cdc.gov/agent/smallpox/vaccination/pdf/acipjun2003.pdf.

ACIP SVS WG (Advisory Committee on Immunization Practices Smallpox Vaccine Safety Working Group). 2003a. March 20-21, 2003 Meeting of the Advisory Committee on Immunization Practices (ACIP) Smallpox Vaccine Safety Working Group, Chicago, Illinois: Summary of the Chairs.

ACIP SVS WG (Advisory Committee on Immunization Practices Smallpox Vaccine Safety Working Group). 2003b. Operating Procedures of the ACIP Smallpox Vaccine Safety Working Group (ACIP SVS WG).

APHA (American Public Health Association). 2002. APHA Policy Statement on Smallpox Vaccination. Accessed June 17, 2003. Web page available at: http://www.apha.org/legislative/policy/smallpox.pdf.

AP (Associated Press). 2003a, May 13. SARS battle strains U.S. health system. FOX News Channel.

AP (Associated Press). 2003b, June 16. AMA seeks to standardize training for bioterrorism. The Wall Street Journal.

ASTHO (Association of State and Territorial Health Officials). 2002. Nature's Terrorist Attack: Pandemic Influenza. Accessed July 15, 2003. Web page available at: http://www.astho.org/pubs/Pandemic%20Influenza.pdf.

ASTHO (Association of State and Territorial Health Officials). 2003. ASTHO Smallpox Preparedness Survey Results (April 25, 2003). Accessed July 7, 2003. Web page available at: http://www.astho.org/pubs/spxsummaryb2.pdf.

Baxter R, Rubin R, Steinberg C, Carroll C, Shapiro J, and Yang A. 2000. Assessing Core Capacity for Infectious Diseases Surveillance. Final Report Prepared for the Office of the Assistant Secretary for Planning and Evaluation. Falls Church, VA: The Lewin Group, Inc.

Blank S, Moskin LC, and Zucker JR. 2003. An ounce of prevention is a ton of work: mass antibiotic prophylaxis for anthrax, New York City, 2001. Emerging Infectious Diseases 9(6):615-622.

Brower J and Chalk P. 2003. The Global Threat of New and Reemerging Infectious Diseases: Reconciling U.S. National Security and Public Health Policy. Arlington, VA: RAND.

CDC. 2002a. About the Vaccine: Immunity Against Smallpox. Accessed July 1, 2003. Web page available at: http://www.bt.cdc.gov/training/smallpoxvaccine/reactionss/about_vac_Immunity.html.

CDC. 2002b. Local Public Health Preparedness and Response Capacity Inventory. Accessed May 30, 2003. Web page available at: http://www.phppo.cdc.gov/od/inventory/docs/Local%20Inventory%20version%201_1_FINAL. pdf.

CDC. 2002c. State Public Health Preparedness and Response Capacity Inventory. Accessed May 30, 2003. Web page available at: http://www.phppo.cdc.gov/od/inventory/docs/State%20Inventory%20version%201_1_FINAL.pdf.

CDC. 2002d. Summary of October 2002 ACIP Smallpox Vaccination Recommendations. Accessed January 9, 2003. Web page available at: http://www.bt.cdc.gov/agent/smallpox/vaccination/acip-recs-oct2002.asp.

CDC. 2003a. CDC Recommends Smallpox Vaccination to Protect Persons Exposed to Monkeypox. Accessed June 16, 2003. Web page available at: http://www.cdc.gov/od/oc/media/pressrel/r030611.htm.

CDC. 2003b. Continuation Guidance - Budget Year Four - Annex A: Summary of Smallpox Preparedness Activities. Accessed July 7, 2003. Web page available at: http://www.bt.cdc.gov/planning/continuationguidance/pdf/annex_a.pdf.

CDC. 2003c. National Public Health Performance Standards Program. Accessed June 20, 2003. Web page available at: http://www.phppo.cdc.gov/nphpsp/.

CDC. 2003d. Notice to readers: supplemental recommendations on adverse events following smallpox vaccine in the pre-event vaccination program: recommendations of the Advisory Committee on Immunization Practices. MMWR 52(13):282-284.

CDC. 2003e. Smallpox Emergency Personnel Protection Act of 2003: Benefits and Compensation for Smallpox Vaccine Injuries. Accessed June 16, 2003. Web page available at: http://www.bt.cdc.gov/agent/smallpox/vaccination/bene-comp.asp.

CDC. 2003f. Smallpox Vaccine Vaccine Information Statement (VIS). Accessed August 6, 2003. Web page available at: http://www.bt.cdc.gov/agent/smallpox/vaccination/pdf/smallpox-vis.pdf.

CDC. 2003g. Smallpox Vaccination Program Plans for Phase 1 Evaluation and Research. Unpublished document.

CDC. 2003h. Smallpox Vaccine Information Statement (VIS) Supplement E: Pregnancy and Breastfeeding Mean You Should Not Get Smallpox Vaccine. Accessed June 17, 2003. Web page available at: http://www.bt.cdc.gov/agent/smallpox/vaccination/preg-contra.asp.

CDC. 2003i. CDC Telebriefing Transcript: Update on Monkeypox and Severe Acute Respiratory Syndrome (SARS) Investigations. Accessed July 5, 2003. Web page available at: http://www.cdc.gov/od/oc/media/transcripts/t030619.htm.

CDC. 2003j. Update: cardiac-related events during the civilian smallpox vaccination program--United States, 2003. MMWR 52(21):492-496.

CDC. 2003k. Women with smallpox vaccine exposure during pregnancy reported to the national smallpox vaccine in pregnancy registry--United States, 2003. MMWR 52(17):386-388.

CDC. 2003l. Smallpox Vaccination Program Status by State, July 25, 2003. Accessed July 31, 2003. Web page available at http://www.cdc.gov/od/oc/media/spvaccin.htm.

CDC. 2003m. CDC Telebriefing Transcript: Safer, Healthier Summer. Accessed July 6, 2003. Web page available at: http://www.cdc.gov/od/oc/media/transcripts/t030626.htm.

CDC. 2003n. Update: cardiac and other adverse events following civilian smallpox vaccination--United States, 2003. MMWR 52(27):639-642.

CDC. 2003o. Smallpox Vaccination Information for Women Who Are Pregnant or Breastfeeding. Accessed July 17, 2003. Web page available at: http://www.bt.cdc.gov/agent/smallpox/vaccination/pdf/preg-factsheet.pdf.

CIDRAP (Center for Infectious Disease Research and Policy) News. 2002. Scope of smallpox vaccination program not yet decided, HHS official say. Accessed August 1, 2003. Web page available at: http://www.cidrap.umn.edu/cidrap/content/bt/smallpox/news/pox2shots.html.

Columbia University School of Nursing. 2003. Project Public Health Ready. Accessed July 1, 2003. Web page available at: http://www.nursing.hs.columbia.edu/institute-centers/chphsr/phready.html.

Committee on Smallpox Vaccination Program Implementation Study Staff. 2003. Conversations with Public Health Agencies About the Smallpox Vaccination Program and Smallpox Preparedness: Synthesis and Detailed Notes. Unpublished Document.

Connolly C. 2003a, April 15. Smallpox vaccine on verge of spoiling. The Washington Post.

Connolly C. 2003b, June 20. Panel urges caution on smallpox inoculation. The Washington Post. A09.

Cook R. 2003, April 5. Smallpox planning detracts from core public health, officials say. Associated Press.

Covert MH. 2001. Public Health System's Capacity to Respond to Bioterrorism. Testimony on behalf of AHA (American Hospital Association) before the Subcommittee on Technology and Procurement Policy, Committee on Government Reform, U.S. House of Representatives.

Das SK, Colfer HT, and Pitt B. 1985. Long-term follow-up of patients with previous myocarditis using radionuclide ventriculography. Heart Vessels Suppl 1:195-8.

Dec GW and Fuster V. 1994. Idiopathic dilated cardiomyopathy. N Engl J Med 331(23):1564-75.

DiGiovanni Jr. C, Reynolds B, Harwell R, Stonecipher EB, and Burkle Jr. F. 2003. Community reaction to bioterrorism: prospective study of stimulated outbreak. Emerging Infectious Diseases 9(6):708-712.

DoD (Department of Defense). 2003. Smallpox Information. Accessed June 17, 2003. Web page available at: http://www.smallpox.army.mil/media/pdf/Smallpoxinfo.pdf.

Drucker NA and Newburger JW. 1997. Viral myocarditis: diagnosis and management. Adv Pediatr 44:141-71.

Edmond M. 2003. Transcript from the IOM's Committee on Smallpox Vaccination Program Implementation Meeting Three on May 1, 2003 in Washington, DC:231-251.

Elliott VS. 2002, April 22/29. Public health reporting flaws spell trouble: doctors complain about requirements that appear to lack follow-through. American Medical News.

Elliott VS. 2003, February 24. Public health's main fear over bioterrorism: surge capacity. American Medical News.

ENA (Emergency Nurses Association). 2003. Status: U.S. Smallpox Vaccination Program. ENA Washington Update. May 2003.

English JF, Cundiff MY, Malone JD, Pfeiffer JA, Bell M, Steele L, and Miller JM. 1999. Bioterrorism Readiness Plan: A Template for Healthcare Facilities. Accessed July 7, 2003. Web page available at: http://www.ntis.gov/search/product.asp?ABBR=PB2002108954.

Fock R, Bergmann H, Bussmann H, Fell G, Finke EJ, Koch U, Niedrig M, Peters M, Riedmann K, Scholz D, and Wirtz A. 2002. Influenza pandemic: preparedness planning in Germany. Euro Surveill 7(1):1-5.

Fraser MR and Fisher VS. 2001. Elements of Effective Bioterrorism Preparedness: A Planning Primer for Local Public Health Agencies. Washington, DC: NACCHO.

Frelinger JA and Garba ML. 2002. Responses to smallpox vaccine. New England Journal of Medicine 347(9):689-90.

GAO (U.S. General Accounting Office). 2000. West Nile Virus Outbreak: Lessons for Public Health Preparedness. GAO/HEHS-00-180. Washington, DC: Health, Education, and Human Services Division.

GAO (U.S. General Accounting Office). 2003. Bioterrorism: Preparedness Varied Across State and Local Jurisdiction. GAO-03-373. Washington, DC: Health, Education, and Human Services Division.

Grabenstein JD. 2003. U.S. Military Smallpox Vaccination Program. Presented to the CDC Advisory Committee on Immunization Practices Meeting on June 18, 2003.

Halsell JS, Riddle JR, Atwood JE, Gardner P, Shope R, Poland GA, Gray GC, Ostroff S, Eckart RE, Hospenthal DR, Gibson RL, Grabenstein JD, Arness MK, and Tornberg DN. 2003. Myopericarditis following smallpox vaccination among vaccinia-naive U.S. military personnel. JAMA 289(24):3283-3289.

Hardy G. 2002. Transcript From the IOM's Committee on Smallpox Vaccination Program Implementation Meeting One on December 19, 2002 in Washington, DC:284-291.

Hayakawa M, Inoh T, Yokota Y, Kawanishi H, Kumaki T, Takarada A, Seo T, and Fukuzaki H. 1984. A long-term follow-up study of acute myocarditis: an electrocardiographic and echocardiographic study. Jpn Circ J 48(12):1362-1367.

Heinrich J. 2001. Bioterrorism: Public Health and Medical Preparedness. Testimony on behalf of GAO (United States General Accounting Office) before the Subcommittee on Public Health, Committee on Health, Education, Labor, and Pensions, U.S. Senate on October 9, 2001.

Henderson J. 2003. Transcript from the IOM's Committee on Smallpox Vaccination Program Implementation Meeting Three on May 1, 2003 in Washington, DC:54-82.

Hiroe M, Sekiguchi M, Take M, Kusakabe K, Shigeta A, and Hirosawa K. 1985. Long follow-up study in patients with prior myocarditis by radionuclide methods. Heart Vessels Suppl 1:199-203.

Hupert N, Cuomo J, Callahan MA, and Mushlin AL. 2003. Modeling efficient mass vaccination campaigns. Paper presented June 26, 2003, at AcademyHealth’s Public Health Systems Research Meeting in Nashville, TN.

IOM (Institute of Medicine). 2000. Ending Neglect: The Elimination of Tuberculosis in the United States. Washington, DC: National Academy Press.

IOM (Institute of Medicine). 2002. The Future of the Public's Health in the 21st Century. Washington, DC: National Academy Press.

IOM (Institute of Medicine). 2003a. Microbial Threats to Health: Emergence, Detection, and Response. Washington, DC: National Academy Press.

IOM (Institute of Medicine). 2003b. Review of the Centers for Disease Control and Prevention's Smallpox Vaccination Program Implementation: Letter Report #1. Washington, DC: National Academy Press.

IOM (Institute of Medicine). 2003c. Review of the Centers for Disease Control and Prevention's Smallpox Vaccination Program Implementation: Letter Report #2. Washington, DC: National Academy Press.

IOM (Institute of Medicine). 2003d. Review of the Centers for Disease Control and Prevention's Smallpox Vaccination Program Implementation: Letter Report #3. Washington, DC: National Academy Press.

IOM (Institute of Medicine) and NRC (National Research Council). 1999. Chemical and Biological Terrorism: Research and Development to Improve Civilian Medical Response. Washington, DC: National Academy Press.

Libbey PM. 2003. Testimony on behalf of NACCHO (National Association of County and City Health Officials) before the Subcommittee on Labor, Health, and Human Services, Education and Related Agencies, Committee on Appropriations, U.S. Senate on January 29, 2003.

Madlock Y. 2003. Transcript from the IOM's Committee on Smallpox Vaccination Program Implementation Meeting Three on May 1, 2003 in Washington, DC:152-173.

Manning A. 2002, October 16. Advisory panel expands smallpox vaccine plan. USA Today.

McNeil Jr. DG. 2003, June 18. After the War: Biological Defenses; 2 Programs to Vaccinate for Smallpox Come to a Halt. The New York Times. Section A; Page 13.

Mitchell S. 2003, June 12. Monkeypox shows gap in bioterror readiness. United Press International.

Mootrey G. 2003a. Adverse events following smallpox vaccination in civilians. Presented to the IOM's Committee on Smallpox Vaccination Program Implementation on May 1, 2003.

Mootrey G. 2003b. Adverse Events (non-cardiac) Following Smallpox Vaccination in Civilians. Presented to the CDC Advisory Committee on Immunization Practices Meeting on June 18, 2003.

Mootrey G. 2003c. Transcript From the IOM's Committee on Smallpox Vaccination Program Implementation Meeting Three on May 1, 2003 in Washington, DC:72-73.

Mulinare J, Broder K, Cano M, and Seward J. 2003. Preventing inadvertent exposure of pregnant women to smallpox vaccine. Presented to the CDC Advisory Committee on Immunization Practices Meeting on June 18, 2003.

NACCHO (National Association of County and City Health Officials). 2001. West Nile Virus: Lessons Learned for State and Local Planning. Accessed June 17, 2003. Web page available at: http://archive.naccho.org/documents/WestNileVirus.pdf.

NACCHO (National Association of County and City Health Officials). 2003a. Bt CREATE: A Customizable Bioterrorism Tabletop Exercise Builder.

NACCHO (National Association of County and City Health Officials). 2003b. Impact of smallpox vaccination program on local public health services. Research Brief. (9).

Neergaard L. 2003, May 12. SARS battle strains U.S. health system. The Kansas City Star.

Neff J. 2003. Report for the Work Group on Smallpox Vaccine Safety. Presented to the CDC Advisory Committee on Immunization Practices Meeting on June 18, 2003.

Nikolai K. 2003. Transcript from the IOM's Committee on Smallpox Vaccination Program Implementation Meeting Three on May 1, 2003 in Washington, DC:173-189.

NVAC (National Vaccine Advisory Committee). 2003. Letter from NVAC Chairman to Acting Assistant Secretary for Health and Director, National Vaccine Program. Accessed July 30, 2003. Web page available at: http://www.cdc.gov/od/nvpo/meetings/ jun2003/letter.pdf.

Peters KE, Drabant E, Elster AB, Tierney M, and Hatcher B. 2001. Cooperative Actions for Health Program: Lessons Learned in Medicine and Public Health Collaboration. Chicago, IL: American Medical Association and Washington, DC: American Public Health Association.

Powers MJ and Ban J. 2002. Bioterrorism: threat and preparedness. The Bridge. 32(1).

Russell S. 2003, January 18. Smallpox vaccine plan starts Tuesday, despite concerns; Some health workers may opt out over risks, compensation issues. San Francisco Chronicle.

Salinsky E. 2002. Will the Nation be ready for the next bioterrorism attack? mending gaps in the public health infrastructure. NHPF Issue Brief. (776).

Selecky MC. 2003. Transcript from the IOM's Committee on Smallpox Vaccination Program Implementation Meeting Three on May 1, 2003 in Washington, DC:82-106.

Slifka, M. 2003. Is there still immunity to smallpox? Accessed June 26, 2003. Web page available at: http://www.asm.org/Media/index.asp?bid=17304.

Snowbeck C. 2003, July 4. Thousands of smallpox shots unused. Pittsburgh Post-Gazette.

Solet D. 2003, February 19. Smallpox pre-vaccinations misdirect resources. Seattle Post-Intelligencer.

Strikas R. 2002. Transcript From the IOM's Committee on Smallpox Vaccination Program Implementation Meeting One on December 19, 2002 in Washington, DC:65-67.

Strikas R. 2003. National Smallpox Vaccination Program Update. Presented to the CDC Advisory Committee on Immunization Practices Meeting on June 18, 2003.

Teutsch SM and Churchill RE (Eds.). 1994. Principles and Practices of Public Health Surveillance. New York: Oxford University Press.

Thacker SB and Stroup DF. 1994. Future directions for comprehensive public health surveillance and health information systems in the United States. American Journal of Epidemiology 140:383-397.

Thompson T. 2003. Medical Reserve Corps (MRC): A Message from HHS Secretary Tommy G. Thompson. Accessed August 6, 2003. Web page available at http://www.medicalreservecorps.gov/.

Turning Point Public Health Statute Modernizing Collaborative. 2003. The Turning Point National Excellence Collaboratives - Draft Document. Accessed June 17, 2003. Web page available at: http://www.turningpointprogram.org/Pages/MSPHA013103.pdf.

White House. 2002. President Delivers Remarks on Smallpox. Accessed January 8, 2003. Web page available at: http://www.whitehouse.gov/news/releases/2002/12/20021213-7.html.

APPENDIX

Committee on Smallpox Vaccination Program Implementation

SUMMARY OF RECOMMENDATIONS

REVIEW OF THE CENTERS FOR DISEASE CONTROL AND PREVENTION'S SMALLPOX VACCINATION PROGRAM IMPLEMENTATION

Letter Report #4

INTEGRATING SMALLPOX PREPAREDNESS INTO OVERALL PUBLIC HEALTH PREPAREDNESS

A Standard for Smallpox Preparedness

The committee recommends that CDC provide guidance to assist state public health agencies (and their partners[6], as appropriate) in establishing a baseline level or a minimum standard of preparedness for a smallpox attack, after which, each state could individually assess its priorities and further expand its preparedness against smallpox and other threats to the public's health as needed.

Preparing Key Responders

The committee recommends that CDC support the establishment of state and/or local, and if appropriate, national, voluntary registries of individuals who have undergone vaccination to be mobilized, trained, and assigned as needed in the event of a smallpox attack. Such registries would include all willing vaccinated personnel not associated with a response team ranging from retired or relocated health care or public health workers to military reservists and former military personnel.

Using Scenarios to Test Preparedness

The committee recommends that CDC facilitate the development of a range of scenarios for potential smallpox attack(s), including one or more multi-threat scenarios, and urge states to use these to expand and continuously improve their plans to respond to a wide range of possibilities.

[6] State partners may include, but not be limited to, emergency management agencies, law enforcement, fire and emergency medical services, hospital and other health care associations.

VACCINATION OF MEMBERS OF THE GENERAL PUBLIC WHO INSIST ON RECEIVING SMALLPOX VACCINE

The committee recommends that CDC proceed with a deliberate and stepwise approach toward meeting the President's policy of offering vaccine to members of the general public who insist on receiving it by:

1. Conducting brief quantitative surveys to determine public interest and desire for smallpox vaccine. These surveys should include public and private health agencies as well as the general public, in order to understand the potential scope of public interest.

2. Determining the budgetary and other requirements that would meet the demand noted.

3. Identifying, monitoring, and referring people to existing or planned smallpox vaccine clinical research trials or other well-structured clinical arrangements that meet the basic requirements of medical and public health ethics, including assurances for safety of vaccinees and their contacts, acceptable balance between risk and benefit, and acceptable distribution of scarce public health resources to meet all preparedness as well as other public health goals. The committee encourages CDC to consider utilizing a pilot program or some other means of evaluating the initial experiences with this effort.

SELECTED ASPECTS OF SMALLPOX VACCINATION PROGRAM IMPLEMENTATION

Communicating About and Coordinating the Response to Adverse Events

To help ensure that the adverse event reporting and follow-up procedures work as seamlessly as possible, the committee recommends that CDC coordinate better with their state partners and provide feedback to local partners who reported the adverse event.

Streamlining Data Collection

The committee recommends that CDC pursue ways to streamline the data systems that are used in the smallpox vaccination program, improving user-friendliness and integrating the multiple systems to avoid duplicate data entry, especially considering that any future expansion of the vaccination program would require a larger number and greater diversity of data system users, some of whom may be using these systems for the first time.

Utility of the Active Surveillance System

Because the civilian smallpox vaccination program is a true partnership between CDC, states, and local jurisdictions, the committee recommends that CDC continue and expand their communication with states and local jurisdictions about the imperativeness of their participation in the Active Surveillance System, stressing that the safety of the vaccination program cannot be guaranteed without their full participation and cooperation.

Pregnancy Screening

Considering that the rate of inadvertent exposure to smallpox vaccine during pregnancy is lower than expected and it is impossible to detect all pregnancies at the time of vaccination, the committee does not recommend extra pregnancy screening efforts at this time.

Evaluation and Safety Studies

The committee recommends that CDC begin developing a structured, prioritized research agenda that can aid decision-making as the smallpox preparedness program moves forward.

The committee recommends that in the short-term, studies of the serious adverse events should receive the highest priority. For safety-related questions, in the longer-term, studies examining long-term outcomes for those who experienced both serious and mild adverse events and studies of how mild adverse events contributed to lost work or social function should be a high priority. For system-related questions, in the longer-term, studies of cost and opportunity costs should be a high priority.