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

Letter Report # 1

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

INSTITUTE OF MEDICINE
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Willing is not enough; we must do."

—Goethe

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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:

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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.

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

Letter Report #1

January 16, 2003

Dr. Julie Gerberding
Director
Centers for Disease Control and Prevention
1600 Clifton Road, NE
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Dear Dr. Gerberding:

The Centers for Disease Control and Prevention (CDC) asked the Institute of Medicine (IOM) to convene an expert committee to advise it and its public health colleagues on the implementation of a pre-event smallpox vaccination program. The IOM agreed to provide this advice through a series of timely reports. We are pleased to communicate to CDC observations, conclusions, and recommendations from the first meeting of the committee of volunteer experts who have agreed to serve the IOM in this effort. The committee's areas of expertise include internal medicine, infectious diseases (including smallpox), dermatology, pediatrics, nursing, epidemiology, public health law and ethics, public health practice, emergency medicine, and pharmacology.

CDC charged the IOM committee with providing guidance on how to best implement the President's policy regarding pre-event smallpox vaccination, addressing the following eight areas:

1. the informed consent process;
2. contraindications screening;
3. the system in place to assess the safety profile of the smallpox vaccine;
4. guidance for the treatment of vaccine complications;
5. professional training programs CDC is developing;
6. the communications efforts;
7. guidance CDC offers to states in developing their implementation plans; and
8. overall progress at achieving the goals of the program.

Given the rapid pace of planning for the smallpox vaccination program, the committee realizes that while it has been working on this report, CDC has been moving ahead, and at the time of the report's release, it is possible that CDC has already accomplished some of the components the committee is recommending.

In addition to CDC's partners, many in the general public will be interested in this communication. Moreover, all reports of IOM committees are released to the public. We thus

provide some background information directed at readers less familiar with the issue. This letter is divided into general statements about implementing the recently announced pre-event smallpox vaccination program, followed by targeted recommendations on the specific components of the committee's charge.

Our intent is to help CDC and its partners across the country implement President Bush's pre-event smallpox vaccination policy as safely as possible. We begin by offering our professional admiration for the hard work of CDC staff and their public health partners in our states and territories, major metropolitan areas, counties, and local communities who have been working under conditions of many uncertainties to prepare for this program. We hope we can help make these efforts even more successful.

BACKGROUND INFORMATION AND COMMITTEE PROCESS

On September 30, 2002, the Centers for Disease Control and Prevention (CDC) entered into a contract with the Institute of Medicine (IOM) of the National Academies to provide targeted advice on the implementation of a "pre-event" or precautionary smallpox vaccination program. An independent, non-governmental, non-profit organization operating under the 1863 congressional charter to the National Academy of Sciences, the IOM has provided advice on matters of health and medicine for over 30 years. The IOM often tackles issues of importance to CDC's public health mission, including matters of vaccine financing, supply, development, and—perhaps most relevant to this project—safety. The IOM operates by convening ad hoc committees of the nation's experts, invoking policies and procedures developed over many years to assure the advice is free from sponsor or other interested-party influence, unbiased with respect to the questions at hand, and based on evidence.

The last case of smallpox in the U.S. occurred in 1949. General vaccination against smallpox—accomplished with cutaneous administration of a closely-related virus, vaccinia virus—ceased in the United States in 1972, when the threat of smallpox disease disappeared due to eradication efforts, which were declared complete by the World Health Organization on May 8, 1980. Only two official stocks of smallpox (variola) virus remained—under the auspices of the governments of the United States and the Soviet Union. It has often been rumored and suggested that some of the virus possessed by the Soviet Union could have been given illegally to people attempting to use the virus as a biological weapon, though factual evidence to support this concern has not been made public. The events of September and October 2001 increased U.S. concerns about all types of possible terrorism, including the potential for biological terrorism. Thus, attention turned to considerations of initiating vaccination against smallpox. CDC has been concurrently developing "post-event" vaccination plans (mass vaccinations after a smallpox release) and—the focus of this committee—"pre-event" plans (precautionary vaccination of smallpox response teams, first responders, and the general public).

On December 13, 2002, President Bush announced his policy on pre-event vaccination against smallpox (White House, 2002). Vaccination of select military personnel, including the President in his role as Commander-In-Chief, began immediately thereafter. At the time of this writing, voluntary vaccination of state-based teams of public health disease investigators and of

hospital-based teams of health care workers (who would respond to the first case of smallpox, should it ever appear) is scheduled to begin in late January 2003. The President has asked that this round of vaccinations be completed as quickly as possible and that a broader vaccination effort commence thereafter. As currently understood, the subsequent vaccinations will encompass the voluntary vaccination of all health care workers and those commonly defined as first responders, such as firefighters, police, and emergency medical personnel. Vaccination of the general public is specifically not recommended, but the President also announced the intent to provide vaccinations to those members of the public who request the intervention. The IOM's Committee on Smallpox Vaccination Program Implementation met for the first time December 18-20, 2002 to begin addressing their charge, stated most succinctly as providing advice on how best to implement the policy as announced by President Bush.

The committee has not been asked to, and will not, comment on the President's policy decision to recommend voluntary smallpox vaccination to health care, public health, and emergency personnel under a precautionary program, and to allow but not recommend access to the vaccine by people not included within those groups. The extensive expertise the committee brings to this issue will focus on program implementation.

The committee realizes that this is an atypical vaccination campaign, and that it is neither a research study nor an ideal public health program. Rather, it is a public health component of bioterrorism preparedness. The committee was constituted to help CDC and its partners at state and local health departments, hospitals, health clinics, and private medical offices throughout the country implement a program with inherent serious risks and with publicly unknown and unstated benefits, and to do so rapidly, within a timeline that has not been explicitly outlined. Thus, the committee has chosen to address to the best of its ability at this time questions specifically posed to it by CDC and, when evidence or time does not permit a reasoned answer, to pose questions that, if answered, might allow for better and more evidence-based advice. Due to the time pressures inherent in this vaccination campaign, this report presents the committee's recommendations on the first set of vaccinations described in the President's policy announcement. Subsequent reports will provide recommendations relevant to further vaccination efforts, hopefully informed by experience gained from the initial effort.

For practical reasons, the committee uses the term "phase I" to describe the planned vaccination of 500,000 public health and health care workers who volunteer to be part of smallpox response teams, and "phase II" to refer to the subsequent vaccination of 10 million health care and public health workers and other emergency responders. However, it is unclear what the rounds of vaccination are being called by CDC ("phases" seems most frequently used) and clarification is also needed about the target population for later vaccination efforts.

Much of the evidence on which the committee bases its conclusions derives from two sources—the historical medical literature on the effects of smallpox vaccine (vaccinia virus) and presentations from and material prepared by CDC at the time of the first committee meeting (noting that the committee has not received updated drafts of materials, such as consent forms). In addition, these sources are supplemented by material presented to the committee by interested partners in the vaccination program and anecdotal information about state, local, and hospital-level response around the country available in recent print media. A list of all materials

reviewed by the committee is available to the general public through the National Academies' Public Access and Records Office (http://www4.nationalacademies.org/onpi/paro.nsf; phone: (202) 334-3543; e-mail: publicac@nas.edu). Before addressing the specific items in its charge, the committee summarizes its key messages and then addresses some general considerations.

SUMMARY OF KEY MESSAGES

The committee urges CDC to:

1. Highlight the unique nature of the smallpox vaccination program as a public health component of a national bioterrorism preparedness policy, focusing on the delivery of clear, consistent, science-based information.
2. Proceed cautiously, allowing continuous opportunity for adequate and thoughtful deliberation, analysis, and evaluation. Embark on phase II only after adequate evaluation of phase I has occurred.
3. Use a wide range of methods for proactive communication, training, and education, and customize it to reach diverse audiences, including potential vaccinees, all health care providers, and the general public.
4. Designate one credible, trusted scientist as key national spokesperson for the campaign and sharpen and expand communication plans and strategies to ensure rapid, transparent, and sustained contact with the media throughout implementation.

GENERAL CONSIDERATIONS

National Security Concerns and the Unknown Balance of Risks and Benefits

The smallpox vaccination program has been competently planned by public health authorities, and decades of experience in vaccination programs and in clinical medicine have been brought to bear on this process. The planning of public health interventions, particularly immunization programs, includes cautioned and deliberate consideration of the risks of the intervention compared to its benefit. The benefit of this public health program is the likelihood that the vaccine will prevent morbidity and mortality from smallpox viral infection, if smallpox reappears. Nevertheless, there is evidence that the risks of the intervention are significant (Neff et al., 1967; Lane et al., 1969, 1970)—citation used by CDC to explain adverse reaction rates); the smallpox vaccine may be the least safe vaccine ever used on a wide scale.

Although the vaccine to be used in the first two phases of the program is the same calf lymph-derived vaccine stored since the 1970s, the host characteristics on a population level have changed significantly. First, a high proportion of the population has not been immunized against smallpox, and there is evidence that primary vaccinees are more likely to experience serious adverse reactions compared to those being revaccinated (Lane et al., 1969). The vaccine also carries significant risks for some members of the population—those with various types of immune suppression, such as HIV infection or due to cancer chemotherapy, those with certain diseases such as eczema and atopic dermatitis, and close personal contacts of vaccinees who

have such contraindications. The U.S. population has many more people at high risk for serious adverse reactions now compared to the 1960s, when most data concerning the safety profile of the vaccine was collected. Furthermore, it is assumed that with rigorous efforts at screening those at risk and with intensive efforts at educating vaccinees about caring for the vaccination site, accidental inoculation of high-risk contacts of vaccinees can be minimized. However, the actual risks will only be known after the vaccination program is operative.

The benefit of the vaccine is also unknown at this time. There is no reason to believe that the efficacy of the vaccine at preventing smallpox infection has changed, both in its protection of individual vaccinees, and the additional protection it offers to others by blocking smallpox transmission to the unvaccinated, although there is no way to ascertain whether the vaccine would be effective against bioengineered smallpox. However, the assumed benefit of the vaccine includes an estimate of the risk of encountering smallpox virus; this estimate was derived by the President and his advisors with a view to national security issues—facts and considerations not communicated to the committee.

Based on the administration's statement that the risk of a smallpox attack is indeterminate (not zero but currently assumed to be very low) (White House, 2002), the benefit of the vaccination program to the public also is not zero but is assumed to be very low. The benefit to any individual might indeed be zero if the individual never encounters the smallpox virus. However, in the event of exposure to smallpox virus, the benefit to individuals may be very high. Given this profile of high vaccination risk and likely very low to zero benefit, the administration's policy to offer vaccination to public health, medical, and emergency workers must be implemented in a most prudent and cautious manner.

In general, public health interventions are undertaken with recognition of some benefit to some individuals, no effect on others, and the possibility of some risk to a small percentage of the population (e.g., folic acid supplementation of the food supply), with expectation of overall benefit to the population receiving the intervention. This precautionary program is a public health component of national bioterrorism preparedness, and those who assume the vaccine's risks may have a small likelihood of individually benefiting from it.

In this context, it is imperative to highlight the voluntary nature of this vaccination campaign, and the paramount importance of safety, to protect the volunteers assuming this risk. The sense of urgency required by national security considerations should be kept in balance with the President's stated goal of safety. Therefore, learning from experience, making mid-course corrections on every aspect of the program, and maintaining constant and consistent communications with the public are integral to developing the safest program possible. Like all Americans, the committee hopes that the risk of smallpox disease reappearing approaches zero and that an abundance of caution can prevail. Therefore, information on the progress and outcomes of implementation—including but not limited to safety concerns and the experience of states and local communities—needs to be shared, analyzed, and discussed at every step before proceeding further. If the risk of smallpox disease (and thus the benefit of the vaccine) is truly very low, deliberation is key to assuring the safest program possible.

Issues of Timing

The pre-event smallpox vaccination program is a complicated and enormous task. Given the presidential directive for rapid implementation, the states, major metropolitan areas, and territories charged with developing plans for implementing the first phase of the program had very little time to respond to the guidance CDC issued for developing a program. At the time of the committee's December 2002 meeting and in subsequent media accounts, several states expressed concern that the original ambitious timeframe was not realistic (Young, 2003). Concurrently, CDC revealed that it would relax the 30-day timeline for the first phase of vaccination, but without providing specifics about the changed timeline (CDC, 2002a; Orenstein, 2002; Strikas, 2002). At the time of writing this report, the committee had not received written confirmation of this change.

The committee hopes that local health department and hospital readiness will dictate the launch date for phase I in each state or community, and duration of each state vaccination program. Furthermore, sufficient time should be allowed between the two phases to ensure adequate assessment and plan revision by CDC and its partners at the state and local levels.

Although advising deliberate and careful planning and implementation, the committee recognizes that the unique context of this program may change at any time, as new information about the nature and extent of threats to the public's health may become available to public health authorities. For example, the confirmation of a suspected smallpox case would immediately signal a change in policy and mandate the rapid implementation of vaccination plans.

As phase I, and ultimately, phase II are completed, it is advisable that CDC evaluate the long-term sustainability of the vaccinated smallpox response teams. There will be some turnover among the first vaccinated cohort of response team members, and CDC would need to determine how it can ensure that public health and health care smallpox response teams maintain an adequate number of vaccinated members with the necessary expertise for each team. The commencement of phase II vaccinations may help eliminate the concern over the immediate sustainability of response teams vaccinated during phase I, but the need for new rounds of vaccinations for newly designated members of response teams should be considered once phase I and phase II vaccinations have been completed.

An important task for CDC and its medical and public health partners will be to develop an agreed-upon set of questions that must be answered satisfactorily throughout phase I and before phase II can begin. The questions, borrowed from analyses of the Swine Flu program of the late 1970s (GAO, 1977), are "What evidence on which things, when and why, would make us change the course we now propose, and to what?" (Neustadt and Fineberg, 1978).

Should a deliberation about the fundamental nature of the policy not be possible, at a minimum **the committee recommends that CDC develop and communicate the criteria (e.g., types and rates of adverse reactions) that would trigger a reconsideration of the current systems in place to protect vaccinees and their contacts (e.g., the October 2002 Advisory Committee on Immunization Practices (ACIP) recommendations on contraindications,**

screening, care of the vaccination site, and administrative leave). For example, CDC might wish to consider from how many vaccinees it will require data and at what rate of specific serious adverse reactions (in vaccinees or their contacts) CDC would consider the program riskier than currently expected and the contraindication screening less adequate than needed (or safer than currently expected).

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. Since this program is a very unusual public health intervention, it will be important to gather data on which practices and techniques are most effective in different types of settings. **To most effectively evaluate the progress and outcomes of the first phase, the committee recommends that CDC utilize the variation in implementation by hospitals and health departments (e.g., differences in granting administrative leave, types of bandages used, different site care instructions, degree of patient contact, adverse reaction investigation) to obtain safety data, and to analyze these data before embarking on subsequent phases of the vaccination program.**

Clarity

The committee urges that CDC and the Department of Health and Human Services (DHHS) proceed in their public discussions and program guidance with attention to clarity, focusing on issues such as timelines and terminology.

First, there has been confusion on the part of the committee, and likely others as indicated by media reports on the subject (Altman and O'Connor, 2003; Young, 2003), about the characteristics of program phases, the numbers of people estimated to be vaccinated, when vaccinations will begin, and the estimated duration of each phase. Specific wording should be chosen (e.g., waves, phases, stages), clearly defined, and then used consistently in all communications from CDC and DHHS. In addition, all communications should be clear about whether particular guidance refers to pre-event (precautionary) smallpox vaccination or to post-event (response and control) vaccination. This is particularly important for any discussion of contraindications, which are very different under the situation of post-exposure vaccination. In this regard, the pre-event program must be explained as part of a general program of public health preparedness for bioterrorism and other threats to the public's health.

It is clear to the committee and other interested parties that the stated policy of the President is an absolutely voluntary vaccination program for hospitals that may choose whether to have a smallpox response team and for public health and health care workers who may volunteer to be members of a response team, but this matter bears continual emphasis in communications and planning.

Finally, some administration and other policy statements about the early part of vaccination implementation have described the group to be vaccinated as "first responders" or "response teams." The committee believes there is a need to more clearly explain in policy and

planning materials that in the event of a smallpox release, the first responders (i.e., those who are likely to first encounter or identify smallpox) will be public health and health care teams. Fire, police, and emergency personnel commonly described as first responders may have a role to play in mass vaccination, in addition to law enforcement's role in investigating the criminal aspects of a smallpox virus release.

Compensation for Adverse Reactions to the Smallpox Vaccine

Although not a specific "line-item" within its contractual charge, the committee interprets general issues of compensation for adverse reactions as integral to its stated charge to assess the overall progress at achieving the goals of the program. [The committee will use the term "adverse reactions" to describe both the common (i.e., local and systemic reactions) and serious adverse reactions (e.g., generalized vaccinia, serious cases of accidental inoculation, eczema vaccinatum, progressive vaccinia, vaccinia keratitis, and encephalitis). There may be some suspected adverse reactions that are not yet recognized as being causally associated with the vaccine. If these suspected adverse reactions are determined to be causally associated with the smallpox vaccine, then compensation should address these reactions as well.] It does so because it believes that the currently stated plans for compensation for adverse reactions could seriously affect achievement of the stated goal of the program—to increase the nation's bioterrorism preparedness. A number of hospitals have said that they will not participate in the pre-event vaccination program until these issues are resolved (McKenna, 2002; Price, 2002). The committee believes that resolution of the adverse reaction compensation issues is important for the informed consent process, clearly a part of the committee's charge. Concerns about lifelong disability resulting from the vaccine (particularly neurological disability from postvaccinal encephalitis) may also arise, and the committee encourages consideration of how to address disability issues. Implications of the pre-event vaccination program for issues related to health insurance, disability insurance, and life insurance should also be considered.

The committee notes that the Homeland Security Act of 2002 (Public Law No. 107-296) provides a federal mechanism to compensate vaccinees who are injured due to negligent manufacture or administration of the smallpox vaccine (but does not cover adverse reactions that occur despite non-negligent manufacture and administration). This has encouraged manufacturers and vaccine administration sites to participate in the pre-event vaccination program, as it reduces their liability exposure for adverse reactions. The Homeland Security Act does not, however, provide reimbursement to vaccinees for costs associated with participating in the program when there are no instances of negligence. These costs may include administrative leave (with possible loss of salary) in order to avoid accidental infection of vulnerable patients in their workplace; lost income due to time away from work while recuperating from adverse reactions that occur despite non-negligent manufacture and administration of the vaccine, particularly for non-salaried workers; and unreimbursed medical expenses associated with treating adverse reactions that occur despite non-negligent manufacture and administration of the vaccine. In addition, the committee notes with concern that there may be some people, such as patients and family members, who are infected accidentally by contact with a vaccinee, despite efforts to care for the vaccination site appropriately. Recognizing this, contacts should be considered part of the population that is vulnerable to adverse reactions, and thus, losses from the

vaccine. This is not unlike the policy of vaccine-associated paralytic polio in contacts of people who received the oral polio vaccine in the National Vaccine Injury Compensation Program. Without reimbursement for these losses, the committee fears that some, perhaps many, public health and health care workers will decline vaccination, thus undermining the effectiveness of the program's implementation.

Some of these adverse reactions may be covered by state worker's compensation programs. However, there is much uncertainty surrounding the types of vaccine adverse reactions and circumstances leading to those vaccine adverse reactions that would be coverable under each state's worker's compensation law. Public health and health care workers who are considering vaccination need accurate information about the rights and protections that are available to them under their state's worker's compensation law. **The committee recommends that CDC and its state and local public health partners immediately work to clarify each state's worker's compensation program's position on coverage for smallpox vaccine-related injuries and illnesses for workers covered under their programs.**

At the time of the issuance of this report, the implications of the Homeland Security Act were not fully understood by many of the state and local public health and health care partners in the smallpox vaccination program. This led to confusion and concern that individuals who have volunteered to be part of the nation's defense against bioterrorism—the public health and health care workers who participate in precautionary vaccination and their family members who are at risk of accidental inoculation—are inadequately protected financially from liability, compared to the much smaller group of public health and health care workers who agree to administer the vaccine (AHA, 2002; McDonough, 2003).

The committee heard during discussion that these concerns have been raised with Department of Health and Human Services and other administration officials (SEIU, 2002). These concerns may change as more is learned about the adverse reaction rates during phase I of the vaccination program. The committee also understands that the 108th Congress might address these issues. The committee urges timely attention and communication about the progress of these deliberations. Without this, concerns about the financial burden for caring for the adverse reactions of the smallpox vaccine (and the sobering consideration that some small but real number of vaccinees or their contacts could die or suffer permanent disability subsequent to vaccination) could greatly decrease the number of people who volunteer for smallpox vaccination. This could seriously impact the program's achievement of its overall goals of increasing United States terrorism preparedness. **The committee recommends that CDC and the Department of Health and Human Services support all efforts, some of which might be administratively or legislatively bold and creative, to bring this issue of compensation for smallpox vaccine adverse reactions—including those reactions that occur despite non-negligent manufacture and administration of the vaccine—to speedy resolution.**

Workforce Issues Resulting from Vaccination

Recognizing that this first phase of smallpox vaccination will only involve public health and health care response teams, the committee encourages CDC to consider some additional

issues that may affect the willingness of health care workers to participate in the pre-event smallpox vaccination program.

As phase I vaccinations begin, hospital patients could be adversely affected by the absence of health care workers from patient care duties because of adverse reactions or possible administrative leave (Altman, 2002). Most hospitals are not staffed with sufficient redundancy to absorb such staff losses safely (AHA, 2002). Depending upon the size of response teams at individual hospitals, staggering vaccinations may be a prudent step for ensuring the safety of not only the vaccinees, but also the patients. This may extend the time period originally anticipated for the first phase of vaccinations. However, this will help ensure that hospitals proceed with vaccinations only as quickly as safety will allow.

It should be noted that in the Department of Defense's initial experience vaccinating approximately 170 military personnel, there were no cases of secondary infections in contacts (Vogel, 2003). However, the committee notes that the controlled conditions of the military setting cannot always be replicated in a civilian setting.

The same concerns regarding absence of workers from hospitals during the period of phase I vaccinations also applies to state and local public health departments. Considering that the median size of a local public health department in the U.S. is 14 staff (NACCHO, 2001), having even a small number of staff unable to perform their duties for a few days because of adverse reactions to the vaccine could have a detrimental effect on the ability of the local public health departments to keep their standard public health programs operating sufficiently. These concerns become of even greater importance to public health departments that have even fewer staff. In terms of timing of smallpox response team vaccinations, the committee agrees with the ACIP recommendation that hospitals and health departments stagger vaccinations within individual institutions if this is deemed desirable by the individual programs (CDC, 2002e). The committee recognizes that staggering vaccinations might prove incompatible in some instances with the necessity of minimizing vaccine wastage.

In addition to concerns about potential absenteeism and its effects on hospital functioning and patient care, there are questions about the possible need for or usefulness of administrative leave as a way to support health care worker decision-making and perhaps to ensure patient safety. When the Advisory Committee on Immunization Practices (ACIP) met in October 2002, members discussed the issue of administrative leave for health care workers who would receive the vaccine in the pre-event vaccination program. In their recommendation, they stated, "With respect to administrative leave for health care workers, the ACIP does not believe that health care workers need to be placed on leave because they received a smallpox vaccination. Administrative leave is not required routinely for newly vaccinated healthcare workers unless they are physically unable to work due to systemic signs and symptoms of illness, extensive skin lesions which cannot be adequately covered, or if they do not adhere to the recommended infection control precautions. It is important to realize that the very close contact required for transmission of vaccinia to household contacts is unlikely to occur in the healthcare setting" (CDC, 2002e).

The issue of administrative leave is complicated. CDC has no authority to resolve the issue of costs for administrative leave; it can only provide guidance based on ACIP recommendations as stated above. Nevertheless, the committee is sympathetic to the concerns of workers who might not participate in the program without adequate accommodation, but also to the financial and staffing problems that hospitals or health departments would have in offering administrative or other paid leave. Ideally, any individual or institution that wished to use an administrative or other paid leave policy would be able to do so. However, this may not be feasible to resolve for phase I of the program, given the short time period until vaccinations begin and the reportedly short duration of phase I. Therefore, **the committee recommends that during phase I, CDC assess the effects of the current situation regarding administrative leave, disseminate the analysis widely, and before phase II begins, decide whether the ACIP recommendation needs to be reassessed. Any evidence of transmission of vaccinia virus to a patient from an immunized health care worker should lead to an active case investigation or to an immediate reassessment of policy.** In order to provide an appropriate evidence base for such a reassessment, CDC might wish to:

- Develop preliminary standards of care for the types and extent of contact recently vaccinated health care workers should have with patients, taking into account that hospitals care for different spectra of patients with respect to age, disease types, and disease severity;
- Survey and analyze the impact of the vaccine on absenteeism; and
- Analyze how the cost of offering administrative leave with pay compares with the cost of not offering administrative leave with pay (e.g., accidental inoculations in patients, medical errors due to health care workers not functioning at the proper level due to adverse reactions), using data from hospitals and health departments that decide on their own to offer administrative leave with pay.

Opportunity Costs

The committee is concerned, and heard concerns from CDC's state and local partners that the smallpox vaccination program will incur great costs that are hard to document (AHA, 2002; Altman and O'Connor, 2002; ANA, 2002; Burstein, 2002; Connoly, 2002a; Connoly, 2002b; Hardy, 2002; NACCHO, 2002; Associated Press, 2003; Mitchell, 2003; Richmond, 2003)—these costs include items such as:

- fewer resources (e.g., time, staffing, money, public service announcements, etc.) for public health programs than planned, due to the needs of the smallpox program, which could delay the development of plans for dealing with a smallpox release;
- hospitals' costs to enhance bioterrorism preparedness and response capabilities, often with limited financial assistance from the federal, state, or local governments;
- negative impacts on the public's perceptions of inoculations in general due to misunderstanding of the special characteristics of the smallpox vaccine; and
- medical errors that occur because of short-staffing due to absenteeism subsequent to vaccine-related illness (Nakamura and Weiss, 2002).

The committee recommends that CDC work with their public health partners to document as well as possible the true costs of the smallpox program. The committee has no specific recommendations at this time on how to do this, but a concerted effort to assess these costs is important and could help in shaping the smallpox immunization program as it expands.

SPECIFIC CONSIDERATIONS

Informed Consent Process

As noted above, the committee believes that it should be recognized that the pre-event smallpox vaccination program is not a typical public health program, but rather, a matter of national public health preparedness against a national security threat. Given the difficulty in characterizing or quantifying the actual threat, the benefit to vaccinees is unknown, and this reality should be recognized and communicated to potential vaccinees to enable an informed decision regarding vaccination. Health care workers who are volunteering to be a part of smallpox response teams are making a decision for the public good, as well as for personal protection. Some data, as well as reports from media sources, indicate that the potential personal benefit (i.e., protection) is an important factor in health care worker decisions to receive the vaccine (Everett et al., 2002). A further consideration in ensuring truly informed consent is the administration's responsibility to communicate promptly changes in the threat assessment to all health care workers considering vaccination, as well as the general public.

With regard to the consent documents and all other communications, the committee urges continued attention to the tensions inherent in assuring appropriate participation in the program. That is, there is a tension between maximizing participation of those appropriate for and consenting to vaccination—those with appropriate medical and public health responsibilities who are at risk for infection (should it appear) and without true contraindications themselves or in close personal contacts—and minimizing participation by those at high risk for adverse reactions (or in contact with those at high risk for adverse reactions), or those who for whatever reasons do not wish to be vaccinated.

The committee has two specific concerns about the informed consent aspects of this program. President Bush stressed in his announcement of December 13, 2002 that this is a voluntary program for public health and health care workers (White House, 2002). The committee is pleased with the emphasis on the voluntary nature of the program but stresses that consent is not a simple matter. It is easy to imagine situations whereby a potential vaccinee will not feel free to decline vaccination. A potential vaccinee might not wish to disclose fears about the risk of the vaccine, particularly in regard to one's own or a personal contact's HIV or pregnancy status, or even the fear of treating a smallpox victim. While in large hospitals or public health departments, other vaccinees might be available to volunteer for service, in small hospitals, a potential vaccinee might be the only worker with a specific, essential expertise and to decline could put the hospital or clinic at risk of incomplete coverage in the case of a smallpox outbreak. To decline vaccination could lead to rumors about the health status of decliners or their family members. Thus, a vaccinee who would otherwise decline to volunteer for vaccination might feel coerced into participation.

A second concern is more fundamental. It is standard practice to request consent to an intervention, such as vaccination, but highly unusual for an intervention, other than in clinical trials, to have known risks but unknown benefits. Yet, that is the nature of this program, within the broader context of national security. The committee suggests explicitly stating that the benefit of the vaccination program is to increase the nation's public health preparedness, but that the benefit of vaccination to any one individual might be very low (given the current threat assessment). Vaccinees must have a clear understanding of the real risks of the vaccine and of the consequences of developing smallpox, tempered by the best estimate of the risk of a smallpox release. The informed consent materials that are given to vaccinees must clearly lay out the risks and benefits to receiving the vaccine. Vaccinees should be quizzed verbally and in writing to assess their knowledge and understanding about the vaccine, and should be asked in a structured and standard way about their decision to be vaccinated. Communication and materials designed to obtain and ensure informed consent should avoid "Yes/No" questions, offering ample opportunity for potential vaccinees to make a thoughtful, well-informed decision. Furthermore, the screening process should include questions about household contacts and other close personal and professional contacts, and vaccinees should be provided with educational material for their contacts. To be certain that the consent is truly voluntary, **the committee recommends that all consent documents include a statement that the risks of the smallpox vaccine, while very low, are predictably higher than the risks associated with most other vaccines, but that the benefit is presently unknown—possibly very low (absent exposure to smallpox) or very high (in the event of exposure).**

The committee further recommends that informed consent forms include explicit notification of the availability, or lack thereof, of compensation for adverse reactions. The prototype information sheets provided by CDC for the post-event vaccination program guidance clearly state that CDC will NOT cover the costs of treating adverse reactions, other than the cost of vaccinia immune globulin (VIG) or cidofovir (Vistide), and that other medical costs must be borne by insurance or the vaccinee. A similar bold statement should be included in information and consent materials for the pre-event program as well. Many potential vaccinees may falsely assume that the provisions of the Homeland Security Act of 2002 or the federal Vaccine Injury Compensation Program would provide compensation for medical expenses or income loss experienced as a result of receiving or being exposed to the smallpox vaccine. This information may be an important factor that will weigh on a potential vaccinee's decision about whether to receive the vaccine. Understanding that the issues surrounding compensation for adverse reactions to the vaccine will most likely not be resolved before vaccinations are scheduled to begin, health care workers need to know this information before making a decision about whether or not to be vaccinated. If there are any developments in the availability of adverse reaction compensation for recipients of the smallpox vaccine (or their contacts), then the informed consent materials should be updated to reflect this change.

Given the many contraindications to receiving the smallpox vaccine, it is important to ensure that potential vaccinees have read and have thoroughly understood all of the material in the informed consent form. The committee suggests that the first page of the informed consent form contain a line for the vaccinee's signature, to acknowledge that the vaccinee has read all the

forms and has had all questions answered. Subsequent pages of the informed consent form should contain a space for the vaccinee's initials.

The committee also encourages CDC to pre-test the informed consent materials in populations with different educational, socioeconomic, and cultural backgrounds before these materials are used for the first phase of the pre-event smallpox vaccination program, if this is possible given the time frame. If not, then material should be evaluated after phase I and modified before phase II.

Screening Potential Vaccinees

The committee would like to commend CDC on all the hard work and planning that have already gone into developing effective, efficient, and equitable screening methods and guidelines for pre-event clinic operations. Much has already been accomplished, and everyone involved recognizes that additional issues need to be considered before vaccination of response teams begins.

CDC has stated that they will err on the side of caution in determining who should be vaccinated. The committee agrees that this is the correct approach, and encourages practicing continued and enhanced caution in screening vaccinees.

Consistency in Screening Materials

The committee understands that CDC had to develop all of the screening materials and guidance on a very accelerated basis, and thus had limited time to compare all documents for overall consistency. Since screening will be the first aspect of the vaccination program that response team volunteers will encounter, any confusion over screening guidelines could have a detrimental effect on the overall communications effort of the pre-event smallpox vaccination program. Consistent screening guidance will be paramount to ensuring the American public's trust in the vaccination program. The committee believes that it is very important to take the necessary time to ensure consistent guidance on contraindications and screening advice before the first member of a public health or health care smallpox response team is vaccinated. The chapter on smallpox that will be added to CDC's *Epidemiology and Prevention of Vaccine-Preventable Diseases* (CDC, 2002b), as well as all screening materials and guidance, should be examined for consistency.

Comprehension of Screening Materials

How successfully this first phase of vaccination is conducted will depend in part on how well potential vaccinees comprehend the educational and screening materials that are provided to them. **Understanding that different populations may interpret the educational and screening materials somewhat differently, the committee recommends that CDC pre-test the educational and screening materials in populations with different educational, socioeconomic, and cultural backgrounds before these materials are used for the first phase**

of the pre-event smallpox vaccination program, if this is possible given the time frame. If not, then material should be evaluated after phase I, and modified before phase II.

The committee encourages CDC to evaluate the educational and screening materials on an ongoing basis, and evaluate them as formally as possible following implementation of the first phase of the program. CDC should determine whether the educational and screening materials used for the first phase of the program would also be appropriate for the second phase. If revisions are indicated, the committee encourages CDC also to pre-test these revised materials on different populations.

Educating Household Contacts

Because the smallpox vaccine provides an increased risk of adverse events to household members of vaccinees (Neff et al., 2002), every effort must be made to screen out potential vaccinees whose household members have contraindications to the vaccine. The potential for household members to not disclose certain contraindications (e.g., pregnancy, HIV status) must be acknowledged. Therefore, it can be assumed that some potential vaccinees will not know if there is a contraindication in their household. **The committee recommends that CDC develop specific educational materials for household contacts of potential vaccinees.**

Potential vaccinees should be given such educational materials at the first visit to the vaccination clinic, and instructed to give them to all their household members. The educational materials should urge household members to disclose to the potential vaccinee any condition that could be considered a contraindication. It is important to develop such materials (like all the educational materials given to vaccinees) in languages other than English, to test them for comprehension and readability at different literacy levels, and to target them to specific user populations. When vaccinees return to the clinic to receive their vaccine, the informed consent materials should double-check whether the vaccinee discussed all of the contraindications with all members of his household, and determine that no contraindication in a household member was identified. **The committee recommends that the materials also include instructions about how household members can avoid accidental infection with vaccinia, should the household member choose not to disclose the contraindication to the vaccinee.**

The committee heard preliminary data that a significant proportion of those with contraindications were intending to take the vaccine (Everett et al., 2002). In so far as it is possible, this should be avoided . The committee thus spent considerable effort considering alternative means of screening, which might be more effective than simple provision of information. Ideally, the vaccine would not be administered at the place of work, to avoid peer pressure, and peer knowledge, about the decision made by a potential vaccinee, though this may be unavoidable in phase I.

Commonly used blood donation forms provide multiple confidential opportunities for donors to opt-out of the blood donation process if they believe that their blood is not safe to be given to someone else. The committee believes this model could be considered for the pre-event smallpox vaccination program. Vaccinees should not feel any pressure to receive the vaccine, for fear that a medical condition that they do not want to disclose may be discovered by the

vaccination clinic or potentially, by their employer. By offering multiple opportunities to opt-out of vaccination, CDC can help ensure that the program is carried out in the most ethical manner possible. **The committee recommends that CDC consider using the blood-donation opt-out and informed consent processes as models for the pre-event smallpox vaccination program.**

Reasons for Declining Vaccine

Potential vaccinees will have different reasons for declining the vaccine, ranging from personal contraindications, contraindications in household and other close contacts, fear about adverse reactions of the vaccine, or apprehension about the benefit of receiving the vaccine. **The committee recommends that CDC collect data on the reasons why potential vaccinees choose not to be vaccinated.**

One way of doing this would be to provide a form to all potential vaccinees at the first visit to the vaccination clinic asking permission to follow-up with them at a later date for a survey. A survey that could contain data from both vaccinees that chose to be vaccinated and potential vaccinees that decided against vaccination would be extremely valuable. Such a survey would be able to have a representative cohort of potential vaccinees as its study population, assuming that the non-response rate is similar in both populations. Being able to survey potential vaccinees who decided against receiving the vaccine will provide a representative control group (if non-response rates are similar) for any study of phase I vaccinees.

Another method for gathering data would be to add a carbon copy to the form that potential vaccinees complete regarding reasons for not receiving the vaccine. This method for gathering data would not offer representative cohort information (because it would not include the people who decided between the first and second visit to the vaccination clinic not to receive the vaccine, and never returned to the clinic for the second time), but it would at least provide detailed information on the reasons why some vaccinees decided against receiving the smallpox vaccine. Though not representative, these data could be used to inform revisions to educational materials for subsequent phases of the vaccination program. The carbon should only be included in the area of the page that collects data on the reasons for not receiving the vaccine, and not in the area of the page that would include personally identifiable information. Potential vaccinees should be informed that completing the form is entirely voluntary, and should be told that this information will be used for contrast group purposes.

Should either of these methods be employed, the committee encourages CDC to pre-test the survey and response materials in populations with different educational, socioeconomic, and cultural backgrounds.

Assessment of Safety Profile

CDC has obviously spent much time and effort in designing and planning for the comprehensive Smallpox Immunization Safety System (SISS). Ensuring that adverse reactions are identified, treated, quantified, and evaluated will be critical to the success of the pre-event

smallpox vaccination program. The committee offers a few recommendations to help ensure that the SISS is as comprehensive, efficient, and effective as possible.

Early recognition, evaluation, and appropriate treatment of adverse reactions to the smallpox vaccine will be critical to limiting the adverse consequences of the smallpox vaccination program, and to ensuring the public's continued acceptance of the program. Detecting adverse reactions and evaluating them early will be the first step in this process.

The committee has had limited time to explore the interaction between CDC and FDA, but hopes to turn to this important matter subsequently. CDC has capably assembled the necessary expertise to design the Smallpox Immunization Safety System and the other components of the vaccination program. However, the committee believes that it is necessary to have the Food and Drug Administration (FDA) fully engaged (to the extent which it is not already), and as quickly as possible, in all aspects of the program, and the SISS in particular. FDA involvement is important for ensuring that the requirements for the Investigational New Drug (IND) protocols for use of VIG and cidofovir are met. FDA's involvement is also critical to ensuring that FDA's surveillance systems become fully integrated into the overall surveillance for smallpox vaccine adverse reactions. CDC has been working extensively with FDA in determining how Vaccine Adverse Event Reporting System (VAERS) reports related to the smallpox vaccine will be shared with CDC and their state and local partners. The committee urges continued and enhanced CDC collaboration with FDA.

Identifying Adverse Reactions

The committee encourages CDC to work with the personnel who are already in place to provide local vaccination care, since they can be an important component of the evaluation of adverse reactions. Since the personnel who will be changing bandages will see vaccinees on a daily or very frequent basis, they should also be trained to recognize serious adverse reactions and advised on how to report these reactions to the appropriate data system. CDC should provide specific definitions for each serious adverse reaction to facilitate accurate data collection. Having these health care personnel trained to evaluate serious adverse reactions would also permit evaluation of vaccinees' rates of common adverse reactions (e.g., fever, malaise, sore arm). To facilitate this process, CDC should distribute widely information distinguishing between common adverse reactions and serious adverse reactions (e.g., generalized vaccinia, progressive vaccinia, encephalitis) that require further clinical evaluation.

Using the Pre-Event Vaccination System (PVS) to Collect Data on Adverse Reactions

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 current guidance from CDC states that all adverse events (i.e., known serious adverse reactions and serious adverse reactions that are suspected to be related to the vaccine) should be reported

to VAERS (CDC, 2002d). Relying primarily on a passive surveillance system (i.e., VAERS) is useful for identifying adverse reactions, but creates the possibility that many smallpox vaccine adverse reactions may not be reported. The committee believes it is important to confirm the response of every vaccinee to the vaccine (i.e., determining whether there is an adverse reaction and gathering data on common adverse reactions), rather than relying solely on VAERS and other passive surveillance systems, which will underestimate the incidence of adverse reactions.

When all Dryvax vaccine was still unlicensed, detailed adverse reactions reporting was part of the IND requirement and would have been captured in a standardized manner to support the IND (CDC, 2002c). However, since licensed Dryvax vaccine is available for use in the pre-event vaccination program, it is expected that VAERS will now be used to capture adverse reactions data. The VAERS report will ask for the Patient Vaccination Number (PVN), a unique identifier assigned to each vaccinee, which will allow the VAERS report to be linked to the patient's record in the Pre-Event Vaccination System (PVS). The PVS is a secure data exchange Internet-based system designed to collect information on those being vaccinated against smallpox. The PVS will only capture adverse reactions as descriptive text. Considering that the smallpox vaccine has not been routinely used in the last thirty years, and there is uncertainty as to whether the adverse reaction profile for today's population will be similar to what it was in the past, the committee believes that active surveillance must be employed.

The committee believes that active surveillance should be accomplished through the planned Pre-Event Vaccination System. The states and CDC plan to use the information contained in the PVS to monitor vaccine coverage, vaccine immunogenicity, complications, and reports of adverse reactions. States can either use the Internet-based PVS, or can choose to send the same data to CDC using a certified data exchange process. The PVS (and uploaded data from states that use the certified data exchange process) will contain demographic data on each vaccinee, the vaccine and diluent lot information of the reconstituted vaccine given to the recipient, the "take" reading, and limited information on adverse reactions. It would take but minor modification for PVS to be used to more fully record adverse reactions as well, so the presence or absence of adverse outcomes can be confirmed. **The committee strongly recommends that active surveillance for adverse reactions be employed, rather than relying exclusively on the passive surveillance systems that already exist (e.g., VAERS). The committee recommends that CDC use the Pre-Event Vaccination System (PVS) as the primary data collection system for adverse reactions.** Enhanced in this way, PVS could provide accurate and rapidly ascertained quantification of known adverse reactions, in approximately 500,000 vaccinated individuals. It will be important for CDC to be the entity that compiles all surveillance data on adverse reactions that are possibly related to the smallpox vaccine. Furthermore, however the Pre-Event Vaccination System is used in the end, it should be pre-tested to the extent possible before the first phase of vaccinations begin.

The PVS also may be useful in accomplishing other functions. Analysis of where the vaccine is distributed, how much is distributed, and how much vaccine is wasted will be intrinsic to making mid-course revisions to the implementation plan. The committee encourages CDC to use PVS for detailed monitoring of vaccine distribution, since this will be important for evaluating the overall implementation of the vaccination program. The committee suggests adding a field to PVS that would identify whether the vaccinee accidentally transmitted the

vaccinia virus to a contact. The committee encourages full analysis of "take" rate data, especially considering that this may be the only measure of efficacy of the vaccine for the time being.

PVS data should be analyzed regularly during phase I, and the full set of PVS data should be evaluated at the end of the first phase and prior to the commencement of the second phase. This information will help the transition from phase I to subsequent phases of the vaccination campaign. The committee also encourages CDC to provide additional training on the PVS to state and local partners so that the quality of data contained in PVS can be maximized.

The committee also was asked to provide advice on whether the proposed telephone survey of 10,000–20,000 vaccinees is an appropriate mechanism to obtain data on common adverse reactions, vaccinee satisfaction with the vaccination program, and the effect of vaccination on time lost from work. The committee suggests that if CDC decides to modify the PVS to make it an active surveillance system and utilize it as the primary mode of gathering data on adverse reactions, then the previously planned survey would become redundant. **The committee recommends a follow-up on a subset of individuals in PVS rather than a telephone survey of vaccine recipients. The follow-up survey could be used to gather information on long-term effects from the vaccine, as well as information on cases of accidental vaccinia infection in household members of vaccinees, rather than focusing on obtaining data on common adverse reactions.**

Evaluation of Risk Factors for Known Adverse Reactions

Data from the cohort of 500,000 vaccinated individuals who would be included in the PVS could be used to conduct a series of nested case-control studies, comparing those suffering from each serious adverse reaction to a random sample of unaffected patients who also had received the vaccine, in order to determine the risk factors associated with serious adverse reactions. This would be critically important information to have before embarking on phase II of the vaccination campaign, in order to be certain that those at risk of serious adverse reactions would not be given the vaccine. Thus, **the committee strongly recommends analysis of the phase I PVS data as a series of nested case-control studies, with results available before moving on to phase II of the vaccination program.**

Monitoring for Rare Adverse Reactions

Although the committee would like to see PVS used as the primary system for gathering data on adverse reactions, the committee recognizes that VAERS is an extremely useful tool, when used the way it was designed (i.e., for hypothesis generating for unusual and unexpected adverse reactions) rather than for quantification of expected adverse reactions. As such, VAERS should not be eliminated from the safety system. Rather, the committee suggests that VAERS be used as a back-up system and a system for generating hypotheses.

To help identify the combination of VAERS, PVS, and other surveillance systems that offers the best opportunity for identifying all possible adverse reactions, the committee encourages CDC to continue consulting state epidemiologists, vaccine program managers

familiar with tracking other vaccine-associated adverse reactions, and clinicians to address these issues.

Quickly identifying adverse reactions in vulnerable contact populations will be important for ensuring the safest vaccination program possible. The committee encourages CDC to explore the benefit and feasibility of using data from surveillance systems for vulnerable contact populations (e.g., Medicaid data, cancer registries) as an ancillary approach to monitoring adverse reactions.

The committee suggests that CDC consider using mortality surveillance to supplement the adverse reaction surveillance occurring through VAERS and PVS. To reach this end, the committee encourages CDC to reach out to and coordinate with medical examiners and coroners to educate them about the pre-event smallpox vaccination program and to provide guidelines that can be used for determining whether a death was the result of a serious adverse reaction from the smallpox vaccine or from a random unconnected cause. Mortality surveillance might also help identify an otherwise unrecognized actual smallpox case.

CDC mentioned plans to develop a pregnancy registry, to track the outcomes of any pregnancies in recent vaccinees. The committee agrees that the development of a pregnancy registry would be a prudent step, and could add to the limited body of knowledge that currently exists on the risk of spontaneous abortions to recent smallpox vaccinees and the incidence of fetal vaccinia.

Gathering Data on Background Rates of Conditions That Could Be Confused with Adverse Reactions

The nature of any large population experience is that there will be substantial numbers of unusual adverse reactions that, in fact, do not relate to vaccine administration, but simply represent background rates of disease. Thus, of the approximately 500,000 vaccine recipients in phase I, it is likely that there will be reports of acute diseases such as influenza or local outbreaks of viral gastroenteritis. Surveillance would be useful in identifying illnesses in vaccinees that may be misattributed as vaccine adverse reactions. It is also possible that unproven associations will be suggested as long-term adverse reactions of the smallpox vaccine, as has occurred with other vaccines. When it comes to the more difficult long-term problem of diseases such as multiple sclerosis and Guillain-Barré syndrome being potentially misattributed to the smallpox vaccine, there are currently no data systems to use for comparison. As with the swine influenza studies, observations of any long-term sequelae from individual observations of alert practitioners, or from VAERS, should be treated as signals and prompt more formal epidemiological studies to refute or validate them. There is also the possibility, if and when the vaccination program is expanded in phase II, that cohort studies could be set up in the sites using the Vaccine Safety Datalink, a CDC system already in place to evaluate adverse results of childhood immunizations. The committee encourages CDC to utilize surveillance systems that already exist (e.g., health care utilization rates from the National Hospital Discharge Survey and the National Ambulatory Medical Care Survey) to determine baseline rates of disease, and place the data that will be obtained from PVS and VAERS into perspective.

Establishment of a Data and Safety Monitoring Board (DSMB)

The committee also considered CDC's plans for monitoring the safety of the smallpox vaccine. The committee briefly heard about plans for the establishment of a smallpox vaccine data and safety monitoring board, jointly operated between CDC and the Department of Defense (DoD) (Winkenwerder and Grabenstein, 2002). Since military vaccinations commenced soon after the President's smallpox policy announcement on Dec. 13, 2002, the military should already have some safety data available. Where possible, the committee encourages CDC to share with their state and local partners any data or lessons learned from the DoD smallpox vaccination experience thus far. The committee first describes what it perceives to be the special considerations for such a board involved in the pre-event smallpox vaccination program.

Such boards are most commonly referred to as data and safety monitoring boards (DSMBs) or data safety and quality monitoring boards (DSQMBs), although data monitoring committee is also a term of reference. DSMBs are defined in essence by their membership, their relationship to the clinical intervention being monitored, their rules of operation, and the scope of their responsibilities. There are, in fact, no hard and fast rules for these entities, but a standard of practice exists and is codified in particular by the rules used by the National Institutes of Health for their DSMBs. The common feature of all DSMBs is independence—real and perceived—sufficient to protect the privacy and safety of the participants.

Many fine details of DSMB organization and function relate to their most common and important use—oversight of double-blinded research-oriented clinical trials. The smallpox vaccination program is neither blinded, research-oriented, nor a trial. It is a public health program. Given the risk of the vaccine and the nation's lack of familiarity with the vaccine and its adverse reactions, the committee applauds CDC's plans nonetheless to establish a monitoring committee in the spirit of a DSMB. It also applauds the intent to have the board jointly oversee the data emerging from the military vaccination program and the civilian program. This sharing of information and pooling of scientific resources can only improve the success of the vaccination program and increase the chances of the safest smallpox vaccination program possible.

The committee has concerns about the organizational arrangements proposed for the DSMB and their impact on independence. Currently it appears that the DSMB will operate as a working group of the Advisory Committee on Immunization Practices, a CDC advisory committee. This concern is in no way a reflection on either the competence or integrity of the ACIP members, its chair or Executive Secretary, the members of the military, or military advisory committees suggested for inclusion on the smallpox vaccine DSMB. Nevertheless, this close organizational tie to the government entities (DoD and CDC) responsible for the program violates one of the key attributes of all DSMBs—both real and perceived independence from the organizing group. A perception that the scientists overseeing the actual data on safety (who will have a responsibility for advising CDC whether the vaccinations are as safe as possible and for advising CDC whether to request the administration to halt an unsafe program) are not truly independent of those setting or overseeing policy could quickly imperil the smallpox vaccination program, not to mention the unintended consequences of eroding trust in all vaccination

programs or all public health programs. The DSMB's purpose should be perceived first and foremost as protection of vaccinees. If there are plans that could assure independent function, this should be communicated in detail to this committee immediately. **If CDC is unable to assure this independent functioning of the DSMB, the committee recommends that the proposed organizational arrangement be reconsidered.**

Given that there will likely be serious adverse reactions, including death, from the vaccine, the committee believes that public trust in the management of the program is essential. It is important to preserve another key attribute of a traditional DSMB—the ability of the board to review data and deliberate in private. This is important for assuring that the DSMB works in the best interest of the vaccinee, protected from any possible undue influence of the sponsoring agency. However, there will be great interest on the part of program managers, vaccinees, and the public in the safety assessments made by the DSMB. CDC has a responsibility for regular communication to the public about the findings from the DSMB.

Treatment of Vaccine Complications

CDC asked the committee for advice on whether the proposed safety system provides timely access to vaccinia immune globulin (VIG). The system that CDC is currently proposing instructs the treating physician to contact the designated state official; the state would inform CDC of a request for VIG and/or cidofovir (Vistide); the CDC clinical team would assess the request with the state and treating physician; CDC Drug Services and the National Pharmaceutical Stockpile would coordinate release of VIG and/or cidofovir; and the treating physician would be designated as a co-investigator on the Investigational New Drug (IND) protocol. The committee generally believes that the currently proposed system is adequate in this regard, although the potential variability of cases requires case-by-case consideration and treatment. The committee encourages CDC to assemble a group of national experts that could be consulted on serious vaccinia adverse reactions and could provide individualized treatment regimens where necessary. The committee would like to gain more information about the details of the VIG and cidofovir distribution plans, in particular, the criteria for distribution. CDC should carefully monitor the characteristics of the requests for VIG and cidofovir, and use these data as a form of passive surveillance.

CDC Safety System Guidance to States

CDC asked the committee to provide advice on whether the proposed safety system will provide for the development of state capacity, such that states will be able to manage smallpox vaccine adverse events if smallpox vaccination becomes routine. The committee felt that they did not have enough detailed information about the state plans to adequately address this question. Without more specific information on the state plans, it is unclear to the committee if the states are sufficiently prepared to manage adverse reactions in phase I or phase II. But based on the perspectives of state and local public health organizations (Hardy, 2002; NACCHO, 2002), **the committee recommends CDC evaluate each state's capacity for managing adverse reactions before indicating that a state is ready to begin vaccinations.** Evaluation of

states' experiences with management of adverse reactions during phase I should shed more light on their level of preparedness to implement phase II. Should routine vaccination of the general population commence, states' preparedness will have to be evaluated again.

Training and Education

CDC's five training focus areas in preparation for the first phase include smallpox vaccination clinics processing, adverse events training for designated physician experts, data management for safety/VAERS, laboratory diagnostics for rash illness and smallpox, and surveillance for rash illness (Quick et al., 2002). Based on its review of planning material, the committee noted a need to broaden the audiences for certain training, expand the range of material covered, and most importantly, extend the timeline of training itself. The committee's overriding concern is that the preparation and implementation of training (of vaccinators and health care providers) and education (of vaccinees and the general public) appear to require a more generous time frame than what is permitted by the late January planned start date (Young, 2003). The readiness of vaccination sites and staff should be among the primary criteria for initiating implementation. A hasty launch may mean insufficiently trained vaccinators and uninformed vaccinees, leading perhaps to an increased likelihood of poor outcomes.

Focus Areas of Training and Education

Recommendations made in the screening and safety discussion in preceding pages of the report are relevant to the first training area identified by CDC—smallpox vaccination clinics processing. It is hoped that training will include more than just county health officers and nurses, or will strongly emphasize the training of trainers, potentially to include health educators and others. During phase I, vaccination clinic workers need the knowledge and resources to educate the entire range of vaccinees, from professional to non-professional hospital workers of various cultural, linguistic, and educational backgrounds, about adequate hand washing technique and proper site care. Local health department trainees (health officers and nurses) will probably benefit from CDC assistance in the form of structured and detailed training modules for local vaccination clinic staff, focused educational materials for vaccinees, educational materials for all local health care providers, and plans to reinforce the learning of vaccinators and vaccinees.

In the area of educational materials, additional work is needed to ensure such items are highly effective. For example, the committee believes that the draft Vaccine Information Statement on smallpox is not sufficient as a tool for vaccinee education, and additional training and informational material should be customized, well-designed, and when possible, pre-tested to ensure functional relevance (to a vaccinee's work duties), readability, and cultural competence. Training standards should include the development of training material appropriate for the functional status (e.g., emergency department nurse), literacy level, and culturally diverse needs of vaccinees. Also, both vaccination clinics and the workplaces of vaccinees might contribute to supporting vaccinee site care knowledge and practices by making plans to reinforce information, given that repeated exposure to educational messages may be more successful in ensuring protective behaviors, like hand washing and site care. Both health care workers who

are vaccinees and the public health personnel vaccinating them may be engaged in training and re-training efforts.

The second training focus area refers to adverse reactions training for physician experts. Rapid and accurate identification of adverse reactions depends upon the ability of all clinicians—infectious disease specialists, primary care physicians, nurse practitioners, and others—to identify common and serious adverse reactions to the smallpox vaccine in their patients. **The committee recommends that CDC expand the scope of their training and education regarding the identification, treatment, and reporting of serious adverse reactions to all clinicians.** Education and training should also provide clear guidance about how adverse reactions should be reported and what resources are available to aid in their management and treatment. Webcasts for clinicians are not enough; outreach must be conducted through multiple modes. The committee commends CDC on the development of the 16-page color brochure providing information on smallpox vaccination and common and serious adverse reactions to the vaccine, and encourages CDC to distribute this brochure as widely as possible. Furthermore, if guidance has not been developed already, the committee encourages CDC to develop guidance for vaccination clinics (some of which may not be located in hospitals) on how to respond to anaphylactic reactions immediately following vaccination.

The committee was also asked to provide advice on what smallpox vaccine safety information practicing physicians need and how this can be most efficiently transmitted. The committee would first like to encourage CDC to think more broadly about who needs this information, and any plan to accomplish this should include sufficient reiteration to answer the problems of busy clinicians being able to attend single sessions. Rather than just focusing on "practicing physicians," this information should be provided to all types of health care providers—physicians, physician assistants, nurse practitioners, nurses. **The committee recommends that the first communication clinicians should receive is basic information about the details of the pre-event smallpox vaccination program.**

Although CDC has recognized a need to reach out to clinicians throughout the country and develop specific training materials for them, the committee believes that CDC has possibly underestimated the importance of the primary care system in the implementation of the pre-event smallpox vaccination program. The committee has limited information of plans to provide training about the vaccine to all primary health care providers (e.g., physicians and nurse practitioners), in addition to specialists and others. Given that CDC is encouraging health care workers contemplating vaccination to discuss their questions and concerns with their own health care providers (Rotz, 2002), the committee notes the need to provide some basic training and education to all providers, not just to those selected to address serious adverse reactions. The committee encourages CDC to expand their consideration of how the primary care system may become involved in the vaccination program, and the variety of modes (in addition to website-based) that can be used to provide training to the primary care community.

Much confusion and misinformation exist in both the general public (Blendon et al., 2003) and the health care community (Everett et al., 2002) about multiple components of the smallpox vaccination program. The committee encourages CDC to provide more consistent and

comprehensive information to as wide a distribution of clinicians as possible, enabling them, at a minimum, to:

- Counsel potential vaccinees when they are seeking information and assistance in deciding whether to be vaccinated;
- Effectively and sufficiently screen potential vaccinees (or their household contacts) who have contraindications to vaccination;
- Recognize adverse reactions, both common and serious;
- Report serious adverse reactions;
- Seek assistance with managing serious adverse reactions;
- Identify types of dressings to use on the vaccination site (and effectively educate their patients); and
- Care for the vaccination site, including proper hand washing technique (and effectively educate their patients).

Methods for training and communicating with providers may include, but not be limited to: communiques to all health care providers (e.g., state-based fax rapid delivery systems); take-home video and audio cassettes; website and telephone-based information as a backup to brochures and other written materials; and training trainers at the local level to conduct workshops on components of local implementation. Frequently asked questions (FAQs) or similar tools may also be useful for practicing clinicians, and such material may be disseminated electronically and in print.

Data management for safety, the third training focus area is discussed in an earlier section of this report. The fourth and fifth focus areas of the CDC training plan refer to laboratory diagnostics for smallpox and rash illness, and training for rash illness surveillance. The committee was unable to address these areas directly at this time, but believes that they are of great importance, and that the training principles outlined by CDC, and the guidance provided in this report should be applied to these components of the training plan.

Additional Training Areas and Training-Related Planning Activities

The committee expressed concern that many aspects of smallpox vaccination planning seem to have occurred in isolation from broader public health activity, reinforcing the programmatic separation characteristic of much public health planning and funding (Boufford and Lee, 2001; IOM, 2002). Although this is an atypical program, similar preparedness and large-scale implementation would be expected to characterize local public health readiness to respond to other public health crises, such as other bioterror threats and emerging infectious diseases. Ideally, smallpox activities would be integrated into overall bioterrorism preparedness, and as much as possible, measures taken to strengthen surveillance, staff training, and communication would be more broadly conceived as dually applicable to smallpox and other public health efforts. A possible strategy to optimize resources and broaden the impact of smallpox vaccination preparations may be collaboration with Centers for Public Health Preparedness to enhance various dimensions of the smallpox program, an opportunity not explicitly considered by CDC planners at the time of the committee's first meeting (Strikas, 2002).

Over the next 2–6 months, in anticipation of phase II of training and education, CDC should provide additional guidance and models/templates for training and education materials to be used at the state and local levels, and should develop a database of findings and evaluation materials. This may require activities such as conducting a survey or maintaining an evaluation site to assess the experience of vaccination clinics, hospitals, and health departments around the country. Furthermore, the committee hopes that CDC has been reviewing lessons learned from other mass events with public health implications (e.g., local governments' experience with mass campaigns, the expertise of organizations that routinely plan large events and the movement of large numbers of people).

The first phase of smallpox vaccination will provide unprecedented information about the training and education needs of vaccinators, public health and health care workers, prospective vaccinees and their close contacts. CDC may benefit from establishing mechanisms to collect such information throughout phase I that would be useful in the planning and implementation of expanded vaccination efforts.

Communication

Communication Planning

The Committee agrees with the assumptions behind CDC's pre-event communication planning, and has noted that CDC has provided a substantial outline of the communication objectives to be met and activities to be conducted prior to beginning vaccination. However, the Committee has noted the need for a more comprehensive, detailed, and strategic communications plan, and in the following pages, identifies some additional broad areas or issues that should be considered in communication planning, including:

- Timing;
- A single, expert voice to represent CDC in presenting science-based public health messages regarding smallpox;
- Audience specificity; and
- Clarity, appropriateness, and mode of delivery of messages (e.g., literacy level, pre-testing, Internet).

First, communicating to the public about the vaccine, its benefits and risks should occur before vaccination of health care workers begins. Now is the time to shape messages and influence perceptions with honest answers and scientific evidence; once a serious adverse reaction occurs, attempts to control information or change public opinion will likely be too little, too late. The next steps in the development of a pre-event communication plan require greater clarity and more specific details about the methods and channels to be used, and the outcomes expected.

Second, the committee believes it is important that the CDC communications effort strictly address the public health aspects of the smallpox vaccination policy, and focus on

providing public health and health care workers and the general public with the most complete and scientifically accurate information, while supporting informed decision-making regarding vaccination. Also, **the committee recommends that CDC's communication efforts about smallpox vaccination clearly separate public health issues from national security matters. The latter are best addressed by representatives of the administration more directly involved in such matters, and not by representatives of scientific agencies. Therefore, the responsibility of CDC is to deliver clear, consistent, and science-based public health communications.**

There is evidence from the risk-perception literature that the public expresses less fear when it receives its information from people it trusts (Gray and Ropeik, 2002) and trust is facilitated by honesty, transparency, and the transmission of consistently accurate, science-based information. **The committee recommends that CDC identify a single "voice" for the national vaccination program, a credible individual with a strong scientific background and an experienced communicator who can serve as the key CDC spokesperson. Additionally, the agency should develop several back-up sources for the media who can offer the same level of informed comment and thoughtful observation as the program's primary "voice."** Such spokespersons should be trained in media techniques, as necessary, to respond to the wide variety of difficult questions that are going to arise during this challenging enterprise. Since the media will also refer to many well-informed critics of the vaccination effort, it is crucial that CDC's communications are based in strong science and communicated with authority. These are essential ingredients to foster public confidence in the program's direction and ultimate outcome. This cadre of health communicators must be able to speak authoritatively to both members of the general public and to health care providers who have anxieties and concerns that must be addressed. To safeguard the separation between political and public health communications, the key spokesperson should not be a politician. This spokesperson (and other key public health communicators) should address the public and be available for the media immediately and regularly after the occurrence of a serious adverse reaction or smallpox release crisis. Such a spokesperson may gain the public's confidence by constituting a credible and consistent source of information, and reflecting the expert management of a public health crisis.

Third, if CDC has not done so already, its communication planning may be enhanced by developing specific objectives and strategies targeting each of the audiences that have been identified. As an example, the media, which itself informs the public and needs access to the best, science-based evidence, requires information and transparency that will enable their reporting on program status. Based on their enormous influence in shaping public opinion and disseminating information to the public, the committee believes that state and local efforts would be benefited by CDC-prepared communication objectives focused specifically on communicating with media professionals at the national, state, and local levels, with strategies intended to increase communication between the media and health officials at all levels. The nation's ability to prepare and respond to a smallpox attack or other potential bioterror threat, depends heavily on the content and influence of media outputs before an outbreak occurs. A well-informed public is also essential to the success of the smallpox vaccination program, and to public health preparedness in general. Community leaders, community-based organizations, and local civic associations possess human and communications resources that can prove invaluable

in assisting the CDC to develop, evaluate, and disseminate targeted public health information to the public.

The objectives outlined in CDC's Smallpox Response Plan and Guidelines (2002d, p. E-6) appear to combine the information needs of the general public, policy makers, and media, and the communication standards needed by health care workers. Some of the broad communication areas mentioned pertain to the knowledge and understanding of smallpox and immunizations concepts among health care workers and the public; ability of health care worker, public, media and policy maker audiences to respond appropriately to a smallpox case or outbreak; and protocols for surveillance and the communication of data needed after a smallpox case or outbreak. The first two areas are too broad, requiring much more detailed discussion of individual audiences and approaches, and the third is more accurately described as a matter of health informatics (e.g., surveillance, VAERS), discussed to some extent in this report.

A fourth area of great importance to communicating about smallpox has to do with message development and the delivery of information to the public. Methods for communicating to and with the public seem overly reliant on the Internet. Not all health care workers, and certainly not all members of the public, obtain their information on-line. Print materials should be made available through a variety of outlets, including professional associations, community organizations, and others. Information should be disseminated to the public broadly through a variety of methods, ranging from print materials tested for readability and cultural appropriateness, to public service announcements on television and radio. Given the public's limited and often incorrect knowledge about vaccines, communicating well and early about the smallpox vaccine is essential to support public confidence in the public health system. The public should be provided with pre-tested, targeted information about vaccines in general (how they are developed, how they work, their benefits and potential side effects), and about the smallpox vaccinia immunization in particular (i.e., the reality that the smallpox vaccine is different from other vaccines in its greater risk of adverse reactions and even death, though such risk is relatively low, and may be minimized if appropriate screening, site care, and other precautions are taken). Primary care providers and nurses should be well-informed through communication activities since they are trusted sources of information for individuals and communities. Transparent, culturally competent, accessible and understandable presentation of what is known and unknown is needed.

In general, CDC's communication plans reflect a greater focus on crisis management than on broader communication strategies. More emphasis should be placed on communications to help frame the public's initial awareness and knowledge and to build trust, which will be essential in dealing with a potential crisis. CDC has outlined four communication principles: (1) consistency and consensus; (2) acknowledgement of and tolerance for uncertainty; (3) communication research; and (4) importance of addressing diversity of communication needs. In addition to these principles, and as previously noted, the committee finds a need to differentiate between political and public health communications, and to position CDC firmly in the realm of evidence-based public health communications. Finally, but perhaps most importantly, there is the principle of informed consent, mentioned above. All communication materials and strategies targeting potential vaccinees and the general public should emphasize the voluntary nature of the vaccination program.

The second through fourth communication principles are addressed to some extent throughout the report. In regards to the first communication principle of consensus and consistency, the committee was unclear about how communication between CDC communicators and their state and local health communicators will occur. What strategies will be employed to ensure standard language is used and that local, state, and national decisions and plans are well-aligned?

The committee has concluded that CDC's communication strategy seems well-developed in two broad areas: passive information (e.g., training materials, fact sheets) about the disease, the vaccine, and the vaccination campaign, available on the website; and crisis material, prepared to respond to a news event/vaccine crisis or smallpox release. Although the first phase of the vaccination program involves only health care workers, it is never too soon to begin educating the general public, therefore, **the committee recommends that more attention be given to developing a variety of materials and channels to inform and educate the public about the immunization program before vaccinations begin.** Furthermore, communication planning and tools should differentiate between pre- and post-event information needs. Current training needs and news events are different from potential crisis response, and planning must take place to address each area individually.

A wide range of channels should be used to communicate to and with various audiences, from the media to the general public, from health care workers to policy makers. As the time to make the vaccine available to the general public nears, CDC may wish to consider a mass mailing to every U.S. household, in the style of former Surgeon General Koop's mailing on HIV/AIDS.

Some of the communications questions submitted by CDC to the committee were not answered, as they require empirical and formative communications research (e.g., message development, literacy-level testing). Other than recommending a candid, transparent communications approach that is sensitive to and appropriate for the range of literacy levels and cultural backgrounds among potential vaccinees and the general public, the committee hopes that CDC will seek other types of expert advice and resources.

The committee advises CDC to communicate frequently with the public focusing on consistency, transparency, and a balanced representation of what is known and not known. CDC should be very clear about its jurisdiction—questions about the likelihood of attack are national security issues that CDC is not able/qualified to answer. If asked about the risk of the smallpox vaccine, however, the agency should answer with the facts—that the risk of serious adverse reactions is relatively low, but still higher than any other vaccine in routine and mass use.

Guidance to States

With the exception of guidance on safety system issues, the committee is unable to comment on CDC's guidance to states due to lack of access to certain materials. The committee hopes to provide comments on other components of guidance to states in a future report, when it has received further information.

Overall Progress at Achieving the Goals of the Program

CDC's overall goal seems to be the successful implementation of an immunization program that is truly voluntary and as safe as possible, but that establishes the response capacity necessary to protect the public's health in the event of a smallpox attack. Success would mean securing an adequate set of vaccinated teams of health care workers willing to participate in responding to such an attack. The committee is unable to assess CDC's progress at this time, but will do so as program implementation experience allows.

Areas of Potential Future Inquiry

There are a number of important matters the committee recognized, but was unable to address in this report, and some additional areas on which CDC may wish to request guidance as the implementation of the vaccination program begins and progresses. These matters and areas include, but are not limited to:

- Discussion of the optimal response to an immediate change in the determination of smallpox threat, with a focus on state and local preparedness;
- A review of local readiness for implementation and an assessment of opportunity costs and resource allocation issues;
- Assessment of the adequacy of the screening materials, based on experiences during the first phase;
- Assessment of the adequacy of the informed consent materials (particularly the information provided to vaccinees on the relation of risks to benefits and the range of possibilities for adverse reactions), based on experiences during the first phase;
- Assessment of secondary transmission to contacts, including an assessment of site care guidance and vaccinee's adherence to that guidance;
- Occupational safety issues, particularly related to bifurcated needles;
- A review of the organization and function of the DSMB; and
- Prioritization of recommendations, recognizing that multiple demands may be necessary and some of the committee's recommendations require resources.

CLOSING REMARKS

In closing, the committee wishes to thank you for the opportunity to be of assistance to the Centers for Disease Control and Prevention as it implements this important vaccination program. We look forward to finding out how the committee can help CDC address other program components as it works with state and local partners to move forward with implementation.

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

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APPENDIXA

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 #1

GENERAL CONSIDERATIONS

Issues of Timing

The committee recommends that CDC develop and communicate the criteria (e.g., types and rates of adverse reactions) that would trigger a reconsideration of the current systems in place to protect vaccinees and their contacts (e.g., the October 2002 Advisory Committee on Immunization Practices (ACIP) recommendations on contraindications, screening, care of the vaccination site, and administrative leave).

To most effectively evaluate the progress and outcomes of the first phase, the committee recommends that CDC utilize the variation in implementation by hospitals and health departments (e.g., differences in granting administrative leave, types of bandages used, different site care instructions, degree of patient contact, adverse reaction investigation) to obtain safety data, and to analyze these data before embarking on subsequent phases of the vaccination program.

Compensation for Adverse Reactions to the Smallpox Vaccine

The committee recommends that CDC and its state and local public health partners immediately work to clarify each state's worker's compensation program's position on coverage for smallpox vaccine-related injuries and illnesses for workers covered under their programs.

The committee recommends that CDC and the Department of Health and Human Services support all efforts, some of which might be administratively or legislatively bold and creative, to bring this issue of compensation for smallpox vaccine adverse reactions—including those reactions that occur despite non-negligent manufacture and administration of the vaccine—to speedy resolution.

Workforce Issues Resulting from Vaccination

The committee recommends that during phase I, CDC assess the effects of the current situation regarding administrative leave, disseminate the analysis widely, and before phase II begins, decide whether the ACIP recommendation needs to be reassessed. Any evidence of transmission of vaccinia virus to a patient from an immunized health care worker should lead to an active case investigation or to an immediate reassessment of policy.

(continued)

Opportunity Costs

The committee recommends that CDC work with their public health partners to document as well as possible the true costs of the smallpox program.

SPECIFIC CONSIDERATIONS

Informed Consent Process

The committee recommends that all consent documents include a statement that the risks of the smallpox vaccine, while very low, are predictably higher than the risks associated with most other vaccines, but that the benefit is presently unknown—possibly very low (absent exposure to smallpox) or very high (in the event of exposure).

The committee further recommends that informed consent forms include explicit notification of the availability, or lack thereof, of compensation for adverse reactions.

Comprehension of Screening Materials

Understanding that different populations may interpret the educational and screening materials somewhat differently, the committee recommends that CDC pre-test the educational and screening materials in populations with different educational, socioeconomic, and cultural backgrounds before these materials are used for the first phase of the pre-event smallpox vaccination program, if this is possible given the time frame. If not, then material should be evaluated after phase I, and modified before phase II.

Educating Household Contacts

The committee recommends that CDC develop specific educational materials for household contacts of potential vaccinees.

The committee recommends that the materials also include instructions about how household members can avoid accidental infection with vaccinia, should the household member choose not to disclose the contraindication to the vaccinee.

The committee recommends that CDC consider using the blood-donation opt-out and informed consent processes as models for the pre-event smallpox vaccination program.

Reasons for Declining Vaccine

The committee recommends that CDC collect data on the reasons why potential vaccinees choose not to be vaccinated.

(continued)

Using the Pre-Event Vaccination System (PVS)
to Collect Data on Adverse Reactions

The committee strongly recommends that active surveillance for adverse reactions be employed, rather than relying exclusively on the passive surveillance systems that already exist (e.g., VAERS). The committee recommends that CDC use the Pre-Event Vaccination System (PVS) as the primary data collection system for adverse reactions.

The committee recommends a follow-up on a subset of individuals in PVS rather than a telephone survey of vaccine recipients. The follow-up survey could be used to gather information on long-term effects from the vaccine, as well as information on cases of accidental vaccinia infection in household members of vaccinees, rather than focusing on obtaining data on common adverse reactions.

Evaluation of Risk Factors for Known Adverse Reactions

The committee strongly recommends analysis of the phase I PVS data as a series of nested case-control studies, with results available before moving on to phase II of the vaccination program.

Establishment of a Data Safety and Monitoring Board (DSMB)

If CDC is unable to assure this independent functioning of the DSMB, the committee recommends that the proposed organizational arrangement be reconsidered.

CDC Safety System Guidance to States

The committee recommends CDC evaluate each state's capacity for managing adverse reactions before indicating that a state is ready to begin vaccinations.

Focus Areas of Training and Education

The committee recommends that CDC expand the scope of their training and education regarding the identification, treatment, and reporting of serious adverse reactions to all clinicians.

The committee recommends that the first communication clinicians should receive is basic information about the details of the pre-event smallpox vaccination program.

(continued)

Communication Planning

The committee recommends that CDC's communication efforts about smallpox vaccination clearly separate public health issues from national security matters. The latter are best addressed by representatives of the administration more directly involved in such matters, and not by representatives of scientific agencies. Therefore, the responsibility of CDC is to deliver clear, consistent, and science-based public health communications.

The committee recommends that CDC identify a single "voice" for the national vaccination program, a credible individual with a strong scientific background and an experienced communicator who can serve as the key CDC spokesperson. Additionally, the agency should develop several back-up sources for the media who can offer the same level of informed comment and thoughtful observation as the program's primary "voice."

The committee recommends that more attention be given to developing a variety of materials and channels to inform and educate the public about the immunization program before vaccinations begin.

APPENDIX B

Summary of October 2002 ACIP Smallpox Vaccination Recommendations

Background

In June 2001, the Advisory Committee on Immunization Practices (ACIP) made recommendations for the use of smallpox (vaccinia) vaccine to protect persons who work with orthopoxviruses, to prepare for a possible bioterrorism attack, and to respond to an attack involving smallpox. This recommendation was followed in June 2002 with draft supplemental recommendations that extended the ACIP's smallpox vaccination recommendation to include people designated to respond or care for a suspected or confirmed case of smallpox. Specifically, the ACIP recommended voluntary vaccination of people serving on what subsequently have been designated as

1. "Smallpox Public Health Response Teams" and
2. "Smallpox Health Care Teams"

The June 2002 draft supplemental smallpox vaccine recommendations also clarified and expanded the primary strategy for control and containment of smallpox in the event of an outbreak.

In September, the Centers for Disease Control and Prevention (CDC) asked the ACIP to provide additional guidance on eight smallpox vaccination implementation issues, including the scope and composition of the Smallpox Health Care Teams. The eight issues were:

1. types of healthcare workers that should be included in Smallpox Health Care Teams;
2. care of the smallpox vaccination site;
3. need for administrative leave for vaccinated healthcare workers;
4. screening for atopic dermatitits as a contraindication for vaccination;
5. screening for pregnanacy as a contraindication for smallpox vaccination;
6. screening for HIV infection as a contraindication for smallpox vaccination;
7. simultaneous administration of smallpox vaccines with other vaccines;
8. vaccination of smallpox vaccinators.

The ACIP's recommendations reflect consultation with CDC's Hospital Infection Control Practices Advisory Committee (HICPAC) and DHHS's National Vaccine Advisory Committee (NVAC). The ACIP recommendations are being forwarded to HICPAC for their review and consideration on October 22 and 23, 2002. The Healthcare Infection Control Practices Advisory Committee provides advice and guidance to CDC and DHHS regarding infection control practices and strategies for surveillance,

prevention, and control of health care- associated infections (e.g., nosocomial infections), antimicrobial resistance and related events in settings where healthcare is provided (e.g., hospitals, long-term care facilities, and home health agencies).

In the coming weeks, the joint ACIP-HICPAC recommendations will be forwarded to CDC and DHHS for their review and consideration.

Opportunity to Establish Smallpox Health Care Teams

The June 2002 Draft Supplemental Smallpox Recommendations recommended that states should designate initial smallpox isolation care facilities (type C facilities) and these facilities, in turn, should pre-designate individuals who would care for smallpox patients for vaccination. However, further discussions with state health officials and hospital administrators identified problems with this approach. It was problematic to designate type C hospitals since suspected smallpox patients are likely to present at the hospitals and health care facilities which are their usual source of care, and not only at designated hospitals. Therefore, health and bio-terrorism officials indicated it was preferable to offer all acute care hospitals the opportunity to establish Smallpox Health Care Teams.

1. Smallpox Health Care Teams

The ACIP recommends that in the first stages of a pre-event smallpox vaccination program, each acute care hospital identify a group of healthcare workers who would be vaccinated and trained to provide in-room medical care for the first few smallpox patients requiring hospital admission and to evaluate and manage patients who present to the Emergency Department with suspected smallpox. For the first 7-10 days after patients with smallpox have been identified, this team would be hospital-based and provide care 24 hours a day, using 8-12 hour shifts. Non-essential workers would be restricted from entering into the rooms of patients with smallpox.

The ACIP recommends that Smallpox Health Care Teams include:

1. Emergency Room Staff, including both physicians and nurses
2. Intensive Care Unit staff, including physicians, nurses, and in hospitals that care for infants and children, this encompass pediatricians, pediatric intensivists, and pediatric emergency room physicians and nurses
3. General Medical Unit staff, including physicians, internists, pediatricians, obstetricians, and family physicians in institutions where these individuals are the essential providers of primary medical care
4. Medical house staff (i.e., selected medical, pediatric, obstetric, and family physicians)
5. Medical subspecialists, including infectious disease specialists [this may also involve the creation of Regional teams of subspecialists (e.g., local medical consultants with smallpox experience, dermatologists, ophthalmologists, pathologists, surgeons, anesthesiologists in facilities where intensivists are not trained in anesthesia) to deliver consultative services
6. Infection control professionals (ICPs)
7. Respiratory therapists

8. Radiology technicians
9. Security personnel
10. Housekeeping staff (e.g., those staff involved in maintaining the health care environment and decreasing the risk of fomite transmission).

Overall, each Smallpox Health Care Team might include about 15 emergency room doctors and nurses, 15 intensive care unit doctors and nurses, and a total of 10-15 personnel from the other areas. It is anticipated that the size and composition of a smallpox medical care team will vary according to the individual institutions and their patient populations. Each hospital should have enough teams to ensure continuity of care. Smallpox vaccination would be voluntary.

Clinical laboratory workers are not included in the initial phase of pre-event smallpox vaccination because the quantity of virus likely to be in clinical specimens of blood and body fluids is low. Consistent adherence to standard precautions and ASM/CDC protocols will prevent exposure to virus in clinical specimens. Although it is not recommended that emergency medical technicians (EMTs), as a group, be vaccinated in this first phase, individual hospitals may identify and include hospital-based EMTs (i.e., personnel who would be dispatched to transport patients with suspected smallpox) on their Smallpox Health Care Teams.

2. Smallpox Vaccination Site Care

Following smallpox vaccination, the ACIP recommends that health-care workers involved in direct patient care should keep their vaccination sites covered with gauze or a similar absorbent material in order to absorb exudates that would develop. This dressing should, in turn, be covered with a semi-permeable dressing to provide a barrier to vaccinia virus. Use of a semi-permeable dressing alone could cause 1) maceration of the vaccination site and 2) increased prolonged irritation and itching at the site, thereby increasing touching, scratching and contamination of the hands. Products combining an absorbent base with an overlying semi-permeable layer can be used to cover the vaccination site. The vaccination site should be covered during direct patient care until the scab separates.

Vaccinia is generally transmitted by direct person-to-person and close contact (within 6 feet), and infection control precautions should be taken to reduce this likelihood. The most critical measure in preventing inadvertent implantation and contact transmission from the vaccinia vaccination site is thorough hand-hygiene after changing the bandage or after any other contact with the vaccination site. Hospitals should include a site-care component to their smallpox vaccination programs in which designated, vaccinated staff would assess dressings for all vaccinated health-care workers daily (whether involved in direct patient care or in other duties), determine if dressings needed changing, and then change the dressing if indicated. This designated staff would assess the vaccination site for local reactions and for vaccine take. They should also use the opportunity to reinforce messages to vaccinees about the need for meticulous hand-hygiene.

Transmission of vaccinia is also a concern in other settings when close personal contact with children or other persons is likely—for example, parenting of infants and young children. In these situations, the vaccination site should be covered with gauze or a similar absorbent material, and a shirt or other clothing should be worn, and careful attention to hand hygiene (hand washing) practiced.

3. Administrative Leave for Vaccinated Health Care Workers

With respect to administrative leave for health care workers, the ACIP does not believe that health care workers need to be placed on leave because they received a smallpox vaccination. Administrative leave is not required routinely for newly vaccinated healthcare workers unless they are physically unable to work due to systemic signs and symptoms of illness, extensive skin lesions which cannot be adequately covered, or if they do not adhere to the recommended infection control precautions. It is important to realize that the very close contact required for transmission of vaccinia to household contacts is unlikely to occur in the healthcare setting.

However, it is also recommended that vaccination of Smallpox Health Care Team members be phased in, starting with a small number of hospitals. Within a single institution, it would be prudent to designate a small proportion, e.g. 20-30% of the candidate healthcare workers, for the first phase of vaccinations to allow institutions to gain experience in post-vaccination management. The ACIP recognizes that the incidence of adverse events following vaccination of previously vaccinated persons is substantially less than in primary vaccinees, and therefore recommends that when feasible, previously vaccinated health care workers be included in this stage 1 vaccination program. It is also advisable to stagger vaccination of healthcare workers within an individual patient care unit by three weeks in order to minimize the number of vaccinated individuals who would be on sick leave concurrently in association with systemic effects of the vaccine, which usually occur at days 8-10 after inoculation.

4. Screening for Atopic Dermatitis as a Contraindication for Vaccination

Atopic dermatitis, irrespective of disease severity or activity, is a risk factor for developing eczema vaccinatum following smallpox vaccination in either vaccinees or in their close contacts. The majority of providers do not routinely make the distinction between eczema and atopic dermatitis, particularly when describing chronic exfoliative skin conditions in infants and young children. Due to the increased risk for eczema vaccinatum, smallpox (vaccinia) vaccine should not be administered to persons with a history of eczema **or** atopic dermatitis, irrespective of disease severity or activity. Additionally, persons with household contacts that have a history of eczema or atopic dermatitis, irrespective of disease severity or activity, are not eligible for smallpox (vaccinia) vaccination because of the increased risk that their household contacts may develop eczema vaccinatum.

Persons with other acute, chronic, or exfoliative conditions (e.g., burns, impetigo, varicella zoster, herpes, severe acne, or psoriasis) are at higher risk for inadvertent inoculation and should not be vaccinated until the condition resolves. The literature also reports that persons with Darier's disease can develop eczema vaccinatum and therefore should not be vaccinated.

To assist providers in identifying persons that should defer smallpox (vaccinia) vaccination, the ACIP offers the following two screening questions: 1) Have you, or a member of your household ever been diagnosed with eczema or atopic dermatitis—if you answered "yes," you may NOT receive the smallpox (vaccinia) vaccine due to the risk that you or your household contact might develop a severe and potentially life-threatening illness called eczema vaccinatum; and 2) Eczema/atopic dermatitis usually is an itchy red, scaly rash that lasts more than 2 weeks and often comes and goes. If you or a member of your household have **ever** had a rash like this—you should NOT receive the smallpox (vaccinia) vaccine at this time unless you and a healthcare provider are sure that this rash is not atopic dermatitis or eczema. In cases where the dermatological risk factor or diagnosis is uncertain, some organizations, such as the military or CDC, may elect to develop more precise screening tools. These secondary screening tools should weigh the individual's risk of developing an adverse event with the requirement of occupational readiness through safe smallpox vaccination to ensure national security.

5. Screening for Pregnancy as a Contraindication for Vaccination

Fetal vaccinia is a very rare, but serious, complication of smallpox vaccination during pregnancy or shortly before conception. Therefore, vaccinia vaccine should not be administered in a pre-event setting to pregnant women or to women who are trying to become pregnant. Before vaccination, women of child-bearing age should be asked if they are pregnant or intend to become pregnant in the next 4 weeks; women who respond positively should not be vaccinated. In addition, the potential risk to the fetus should be explained and women who are vaccinated counseled not to become pregnant during the 4 weeks after vaccination. Routine pregnancy testing of women of child-bearing age is not recommended.

To further reduce the risk of inadvertently vaccinating a woman who is pregnant, at the time of pre-screening, women of child-bearing age should be educated about fetal vaccinia, and abstinence or contraception to reduce the risk of pregnancy before or within four weeks after vaccination. Any woman who thinks she could be pregnant or who wants additional assurance that she is not pregnant should perform a urine pregnancy test with a “first morning” void urine on the day scheduled for vaccination. Such tests could be made available at the pre-screening and vaccination sites to avoid cost or access barriers to testing.

If a pregnant woman is inadvertently vaccinated or if she becomes pregnant within 4 weeks after vaccinia vaccination, she should be counseled regarding the basis of concern for the fetus. However, vaccination during pregnancy should not ordinarily be a reason to terminate pregnancy. To expand understanding of the risk of fetal vaccinia and to document whether adverse pregnancy outcome may be associated with vaccination, a pregnancy registry should be maintained and any adverse outcomes carefully investigated.

6. Screening for HIV Infection as a Contraindication for Vaccination

Persons with HIV infection or AIDS are at increased risk of progressive vaccinia (vaccinia necrosum) following vaccinia vaccination. Therefore, vaccinia vaccine should not be administered to persons with HIV infection or AIDS. Before vaccination, potential vaccinees should be educated about the risk of severe vaccinial complications among persons with HIV infection or other immunosuppressive conditions; persons who think they may have one of these conditions should not be vaccinated.

The ACIP does not recommend mandatory HIV testing prior to smallpox vaccination, but recommends that HIV testing should be readily available to all persons considering smallpox vaccination. HIV testing is recommended for persons who have any history of a risk factor for HIV infection and who are not sure of their HIV infection status. Because known risk factors cannot be identified for some persons with HIV infection, anyone who is concerned that they could have HIV infection also should be tested. HIV testing should be available in a confidential or, where permitted by law, anonymous setting with results communicated to the potential vaccinee before the planned date of vaccination. Persons with a positive test result should be told not to present to the vaccination site for immunization. Information about local testing options should be provided to all potential vaccinees, including sites where testing is performed at no cost.

7. Simultaneous Administration of Smallpox Vaccine with Other Vaccines

Vaccinia vaccine may be administered simultaneously with any inactivated vaccine, such as influenza vaccine, to encourage appropriate receipt of all indicated vaccines, e.g., in populations such as health care workers. With the exception of varicella vaccine, vaccinia vaccine may be administered simultaneously with other live virus vaccines. To avoid confusion in ascertaining which vaccine may have caused post-vaccination skin lesions or other adverse events, and facilitate managing such events, varicella vaccine and vaccinia vaccine should only be administered $\geq$4 weeks apart.

8. Vaccination of Smallpox Vaccinators

In order to minimize the clinical impact of inadvertent inoculation, should it occur, ACIP recommends that persons who will be handling and administering smallpox vaccine in the proposed pre-event smallpox vaccination program be vaccinated. Vaccination of this group will also contribute to preparedness for smallpox response, should a smallpox release occur, with development of a cadre of vaccinated, experienced vaccinators who could immediately be deployed for outbreak response.

Source: CDC, 2002e.