

Protecting the Frontline in Biodefense Research: The Special Immunizations Program

The U.S. Army's Special Immunizations Program is an important component of an overall biosafety program for laboratory workers at risk of exposure to hazardous pathogens. The program provides immunizations to scientists, laboratory technicians and other support staff who work with certain hazardous pathogens and toxins. Although first established to serve military personnel, the program was expanded through a cost-sharing agreement in 2004 to include other government and civilian workers, reflecting the expansion in biodefense research in recent years. This report examines issues related to the expansion of the Special Immunizations Program, considering the regulatory frameworks under which the vaccines are administered, how additional vaccines might be considered for inclusion in the Program, and the factors that might influence the development and manufacturing of vaccines for the Special Immunizations Program.

The Special Immunizations Program fills an important niche in biosafety: it is the only program in the United States that makes investigational vaccines available to laboratory workers who may be exposed to a range of viruses, bacteria, and toxins. Its mission is to assure the safety and well-being of program participants through regular medical evaluations and the treatment of occupational exposures to hazardous pathogens, and to further medical research on the vaccines through the collection of safety and immunogenicity data.

The program is administered by the United States Army Medical Research and Materiel Command, through its Medical Materiel Development Activity and its Medical Research Institute of Infectious Diseases (USAMRIID) in Fort Detrick, Maryland, and when first launched provided vaccines to military laboratory workers. In the years following the 2001 anthrax mailings the biodefense research field grew rapidly, and in 2004 a cost sharing



Credit: CDC/James Gathany

agreement was reached to expand the Special Immunizations Program to include additional government and civilian biodefense researchers. However, enrollment has not increased to anticipated levels.

The Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human

Services requested that the National Research Council convene a committee of experts to examine issues related to the expansion of the Special Immunizations Program. The committee was asked to consider the role of immunizations

Box 1. The Vaccines of the Special Immunizations Program

Currently, the Special Immunizations Program includes investigational vaccines against botulism, equine encephalitis diseases (eastern, western, and Venezuelan), Rift Valley fever, Q fever, and tularemia. The program also provides Food and Drug Administration-licensed vaccines for anthrax, hepatitis B, Japanese encephalitis, rabies, smallpox, and yellow fever.

for at-risk laboratory workers, the regulatory frameworks under which Special Immunizations Program vaccines are administered, and how additional vaccines currently available in the U.S. or in other countries might be considered for inclusion in the Program. The committee also considered other factors that might influence the development and manufacturing of new vaccines for the Special Immunizations Program.

The Role of Immunizations in Protecting Workers

The committee found that, as biosafety procedures have improved, incidents of laboratory-acquired infections have decreased markedly. However, biosafety procedures such as following best laboratory practices, using personal protective equipment (such as gloves or biohazard suits), and using engineering controls (such as biocontainment cabinets) have not reduced the risk of infection to zero, particularly when combined with human error. Infections continue to occur sporadically, and researchers working with pathogens for which exposure to a very small quantity of the microbe can cause an infection, for example Venezuelan equine encephalitis virus, may be particularly at risk. Therefore, the committee found that although immunization should never be a substitute for careful adherence to biosafety best practices, vaccines remain an important additional

component in ensuring the occupational safety of biodefense researchers.

The Use of Investigational New Drug Status Vaccines

The vaccines offered through the Special Immunizations Program include both Food and Drug Administration-licensed products and vaccines that have not been licensed and remain under Investigational New Drug status.

Licensed products have generally undergone large-scale clinical trials and the safety and efficacy of the vaccines is well known; on the other hand, investigational vaccines are still in clinical trials. From the laboratory worker's perspective, even an unlicensed vaccine with a good safety record and strong history of eliciting an immune response to a hazardous pathogen might be expected to provide additional protection, even though its protective efficacy in humans cannot yet be considered known. Furthermore, using investigational vaccines in the Special Immunizations Program permits the ongoing collection of data on the safety and immunogenicity of vaccines, information that could be of substantial value to other researchers working on medical countermeasures development or if, in a future national biodefense emergency, there were a need to make the vaccine widely available.

The use of investigational vaccines in the Special Immunizations Program is not ideal for several reasons. The investigational vaccines currently used within the Special Immunizations Program were largely developed and manufactured in the 1970s and 1980s, under standards that are different from those in use today. Although the vaccines in the Special Immunizations Program were completely re-tested from 2000-2003 under current standards, the vaccine composition and immune responses of some investigational vaccines is less than optimal. Because they must be administered as part of clinical trials, using them also presents significant cost and regulatory burdens to the program.

However, the committee noted that for many pathogens, newer or superior vaccines do not yet exist. In these cases, immunization with investigational vaccines continues to offer benefits to at-risk personnel. The use of investigational vaccines must be evaluated on a case-by-case basis along with an appropriate risk analyses that consider the types of work being performed by the individual, the individual's medical history, and other factors. Performing this case-by-case evaluation and offering

Box 2. The Supply of Special Immunizations Program Vaccines

The bulk of the investigational vaccines available through the Special Immunizations Program were manufactured under military contracts at the Salk Institute vaccine production plant in Swiftwater, PA in the 1960s-1980s. Since the closure of the Salk Institute Government Services Division in 1998, no new lots of these vaccines have been produced.

Conservative estimates suggest that the supply of these investigational vaccines is sufficient to meet program needs (estimates range from 10–11 years for Rift Valley fever vaccine to 73 years for Venezuelan and eastern equine encephalitis vaccines using the current vaccine lots; additional lots of vaccine would also be available if needed). As vaccines against hazardous agents of interest to the Special Immunizations Program have become licensed (e.g. Japanese encephalitis, hepatitis B, rabies, anthrax, smallpox, and yellow fever vaccines) the program has continued to purchase these vaccines and administer them to eligible personnel.

the investigational immunizations on a voluntary basis, subject to informed consent, will help ensure that immunizations are available for those researchers for whom the benefits of vaccination outweigh the risks. As newer, safer, or improved vaccines become available against pathogens in the Special Immunizations Program, these replacement vaccines should be incorporated into the program to phase out the older or less effective ones.

Extension of the Program to Meet Civilian Needs

The committee found that the Special Immunizations Program has generally functioned well for military researchers. The U.S. Army Medical Research and Materiel Command has the facilities, personnel, operating procedures and infrastructure to successfully administer, monitor, and document immunizations given through the Program.

However, the Program has not met the anticipated need of researchers beyond the military, particularly laboratory workers involved in civilian biodefense countermeasures and public health research. When the program expanded in 2004, it was estimated that 1000 to 5000 workers might be candidates for vaccination, but enrollment in the program has remained relatively constant at about 600 participants per year. This may reflect the cost to participate in the program, which is about \$10,000 to \$15,000 per year, in addition to the cost of travel to Fort Detrick in order to receive the vaccinations and medical monitoring.

Encouraging agency contract and grant awards to cover the costs of immunizing personnel would help reduce the burden of cost borne by institutions working on government supported programs. Furthermore, establishing a limited number of satellite clinic locations could reduce travel costs for program participants.

The static enrollment may also indicate that the Program does not offer vaccines against the agents of most interest to civilian biodefense researchers. The committee noted that vaccines offered through the current program largely reflect the needs and priorities of historical Department of Defense biodefense research programs, which may not match current or future biodefense needs.

Developing a system to enable Special Immunizations Program stakeholders, including the

Box 3. Who Uses the Special Immunizations Program?

Approximately 600 participants per year are enrolled in the Program. About 60% of these participants work at USAMRIID and the other 40% at other agencies within the Department of Defense, other governmental agencies, and external organizations. The types of workers for whom Special Immunizations Program vaccination may be most relevant include not only laboratory workers, but also:

- animal technicians working to develop next generation medical countermeasures for military and civilian use
- personnel working on biodefense vaccines, or human and veterinary vaccines against zoonotic diseases—diseases that can be transmitted between humans and animals
- scientists and laboratory technicians engaged in field studies of the ecology and epidemiology of hazardous pathogens
- scientists in public health diagnostic laboratories

Department of Defense, Department of Health and Human Services, and Department of Agriculture, to regularly review and assess the vaccines included in the program, the pathogens against which these vaccines are directed, and the existence and stage of development of new vaccines, would help ensure that the program reflects evolving civilian and military biodefense priorities. For example, vaccines of potential value to the Special Immunizations Program are either under development in the U.S. or abroad or already licensed for use in other countries. In addition, as research on medical countermeasures to hazardous pathogens continues, new vaccines may become available.

Vaccine Development

Prioritizing a list of pathogens for inclusion in the Special Immunizations Program would help ensure that the program remains relevant. The committee concluded that the list should be based on the characteristics of the agent, such as the infectious dose, transmission potential, and fatality rate; and the characteristics of the threat, such as the presence of the pathogen on government threat lists, if the pathogen is the subject of active research, and the current availability of vaccines.

Pharmaceutical companies usually develop and obtain licenses for new vaccines. However, the vaccines offered in the Special Immunizations Program typically have little or no commercial value, and therefore are of little interest to industry. The committee noted procurement initiatives put forward by the Department of Health and Human Services and the Department of Defense to support industry partnerships in vaccine development, and encouraged the federal agencies, when making major U.S.

investments in this area, to consider the immunization needs of the Special Immunizations Program. There is also a need for the Food and Drug Administration or other relevant regulatory agencies to consider new options for the development and licensure of vaccines (both newly developed in the U.S. or in use or in development outside the U.S.) that might be included in the Special Immunizations Program.

The Role of the Special Immunizations Program

The Special Immunizations Program sits at a critical intersection of military and civilian biodefense research and development. With the expansion of biodefense research and the shifting nature of national security and public health threats, the mandate for producing biodefense countermeasures now extends well beyond the Department of Defense to include significant investments from civilian research and public health agencies.

However, as currently structured and managed, the Program appears to lack a coordinated civilian and military perspective on policy, management, and funding. Revising the governance of the Special Immunizations Program would help develop processes for shared priority-setting and operational oversight by key stakeholders from civilian as well as military agencies. The history and expertise available at the U.S. Army Medical Research Institute of Infectious Diseases and the U.S. Army

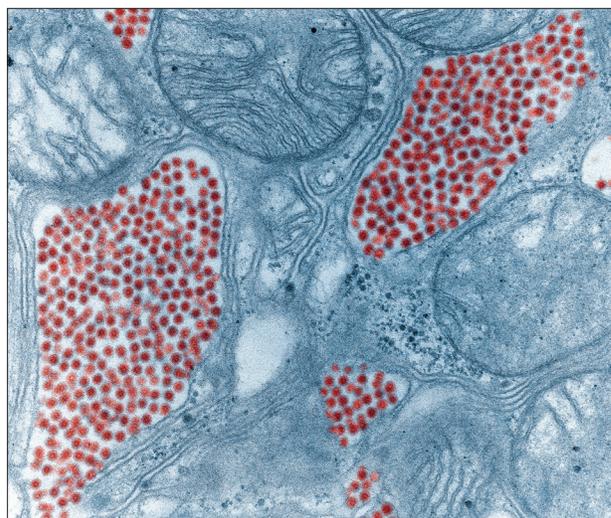


Figure 1. This colorized transmission electron micrograph depicts a salivary gland extracted from a mosquito infected by the Eastern equine encephalitis virus, which has been colorized red.

Credit: CDC/ Fred Murphy; Sylvia Whitfield

Medical Material Development Activity in establishing and operating the Special Immunizations Program remain extremely valuable, and provide a strong foundation on which to base an effective 21st century occupational immunization program to support hazardous pathogen research.

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The National Academies appointed the above committee of experts to address the specific task requested by the Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services. The members volunteered their time for this activity; their report is peer-reviewed and the final product signed off by both the committee members and the National Academies. This report brief was prepared by the National Research Council based on the committee's report.

For more information, contact the Board on Life Sciences at (202) 334-2187 or visit <http://dels.nas.edu/bls>. Copies of *Protecting the Frontline in Biodefense Research: The Special Immunizations Program* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.

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