THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

AUG - 6 2002

HEALTH AFFAIRS

MEMORANDUM FOR SECRETARIES OF THE MILITARY DEPARTMENTS
CHAIRMAN OF THE JOINT CHIEFS OF STAFF
UNDER SECRETARIES OF DEFENSE
ASSISTANT SECRETARIES OF DEFENSE
GENERAL COUNSEL, DEPARTMENT OF DEFENSE
INSPECTOR GENERAL, DEPARTMENT OF DEFENSE
DIRECTORS OF DEFENSE AGENCIES
COMMANDANT OF THE US COAST GUARD

SUBJECT: Policy on Clinical Issues Related to Anthrax Vaccination

This memorandum establishes policy on medical issues involving anthrax vaccination: dosing schedule; education materials; medical screening before immunization; pregnancy screening; injection-site selection; medical exemptions; and adverse events management.

Dosage Schedule

As stated in all previous Anthrax Vaccine Immunization Program (AVIP) policies, full immunization requires six doses administered at proper intervals: 0, 2, and 4 weeks, and 6, 12, and 18 months. Annual boosters are given to sustain immunity. This is the only dosage schedule approved by the Food & Drug Administration (FDA) at this time. Do not administer anthrax vaccine on a compressed or accelerated schedule.

Take reasonable steps to ensure that shots are given on or as soon after recommended dates as possible. Encourage commanders to remind personnel about upcoming shots and recall people who do not appear as scheduled. Accurate documentation in both individual medical records and automated immunization tracking systems is required. Encourage commanders to pay special attention to units with a significant fraction of personnel more than 30 days late for vaccination.

Whenever a vaccine dose is received after a scheduled date, base the date for the next shot on the interval between doses. For anthrax vaccine, the approved dosing intervals are: two weeks between doses 1 and 2; two weeks between doses 2 and 3; five months between doses 3 and 4; six months between doses 4 and 5; and six months between doses 5 and 6. For example, if dose 3 is received three weeks after dose 2 (rather than the normally scheduled two weeks), dose 4 should still be given five months after dose 3. Any dose administered one or more days earlier than the date of the prescribed minimal interval will not be considered valid.

Personnel whose vaccination series was interrupted during the previous AVIP slowdown will not need to repeat any doses already received in the vaccine series or receive extra doses. Rather, they will resume the vaccination schedule from the point of deferment (subject to any applicable medical or administrative exemption). This guidance is consistent with the best practice of medicine, guidance of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) and consultation with the FDA. This DoD policy

supercedes the DoD Policy for Deviation from Anthrax Vaccine Immunization Schedule, dated 11 September 1998.

Educational Materials

Educational materials provided to all personnel before anthrax vaccination shall address the benefits, side effects, and other medical information concerning the vaccine. For personnel for whom the dosing schedule was interrupted, the educational materials shall include information on the interruption and the deferred dosing schedule.

Medical Screening Before Immunization

The national standard of practice for all immunizations, including the anthrax vaccine, shall be adhered to when immunizing personnel. This includes medical screening prior to immunization. Education and screening shall be conducted for medical conditions for which immunization deferral or further medical evaluation before immunization is indicated. A sample screening questionnaire is provided at Example 1.

Pregnancy Screening

DoD policy is to defer routine anthrax vaccinations until after pregnancy. In accordance with FDA and ACIP recommendations, all efforts will be taken to avoid unintended vaccination during pregnancy. All immunization clinics and providers will display in a prominent place written warning against unintentionally vaccinating pregnant women. This warning shall be visible during the screening process. Women of childbearing age are to be questioned/screened for pregnancy prior to receiving immunizations. Women who are uncertain about pregnancy status shall be medically evaluated for pregnancy prior to immunization IAW service policies.

Injection-Site Selection

The Anthrax Vaccine Expert Committee (AVEC), an independent civilian review panel, evaluates all reports submitted to the Vaccine Adverse Event Reporting System (VAERS) involving anthrax vaccine. This committee identified several reports related to ulnar nerve irritation that may be prevented through a choice of site injection. The committee concluded that subcutaneous (SC) injections given over the triceps muscle may result in localized inflammation, that could compress the nearby ulnar nerve and produce temporary paresthesia (i.e., numbness, tingling).

The preferred injection site is the subcutaneous tissue over the deltoid muscle. This minimizes the chance of temporary paresthesias. Most people have sufficient SC tissue over the deltoid for proper SC deposition of the vaccine. Unusually lean people might avoid injection-site reactions by vaccination in the anterolateral thigh. Additionally, providers should rotate injection sites. As always, appropriate clinical judgement is warranted.

Medical Exemptions

The vast majority of individuals will complete the vaccine series though some may experience minor side effects. Some individuals will have either acute or chronic pre-existing

conditions that may warrant medical exemption from anthrax vaccination. Furthermore, a small proportion of individuals will develop a more serious reaction during the vaccination series that may warrant medical exemptions, temporary and permanent, from anthrax vaccination.

Granting medical exemptions is a medical function performed by a privileged health-care provider. The provider will grant individual exemptions when medically warranted, with the overall health and welfare of the patient clearly in mind, balancing potential benefits with the risks while taking into consideration the threat assessment.

The two most common medical exemptions utilized are medical temporary (MT) and medical permanent (MP).

Temporary medical exemptions are warranted when a provider has a concern about the safety of continued immunizations. Examples of situations that warrant a temporary medical exemption are listed below:

1. Immunosuppressive Therapy. Individuals receiving systemic corticosteroid therapy, other immunosuppressive drug therapies, or radiation therapy may be in a state of temporary immunodeficiency. Because they may not respond fully to vaccination, defer these individuals from receiving the anthrax vaccine until immune function returns, as clinically appropriate.

2. Acute Situations. Serious acute diseases, post-surgical situations, or acute injuries potentially may warrant temporary vaccination deferment, if immune response to vaccination might be impaired or adverse events affected. This includes acute febrile illnesses. Vaccinations may resume when clinically appropriate.

3. Pregnancy. Under normal circumstances, defer anthrax vaccine until after pregnancy. Anthrax immunization is largely based on occupational risk, therefore vaccination should resume with full assumption of duties following pregnancy, unless a longer postpartum interval is clinically indicated. Breast-feeding is not a contraindication to any immunization.

4. Other Conditions. In situations where a medical condition is being evaluated or treated, a temporary deferral of anthrax vaccination may be warranted, up to 12 months. This would include significant vaccine-associated adverse events that are being evaluated or while awaiting specialist consultation. The attending physician will determine the deferral interval, based on individual clinical circumstances.

Medical permanent exemptions are generally warranted if the medical condition or adverse reaction is so severe that the risk of continued immunization is not justified. Examples of situations, which warrant a permanent medical exemption, are listed below:

1. Severe reaction after a previous anthrax vaccination, such that additional doses would pose an undue risk to the vaccine recipient.

2. Human immunodeficiency virus (HIV) infection or other chronic immune deficiencies.

3. Evidence of immunity based on serologic antibody tests or documented previous anthrax infection.

If the situation changes, a permanent medical exemption can be removed by a provider experienced in vaccine safety assessment.

If an individual's clinical case is complex or not readily definable, consult an appropriate medical specialist with vaccine safety assessment expertise, before a permanent medical exemption is granted. In addition, the original health care provider may consult with physicians located at the Vaccine Healthcare Center Network, DoD's vaccine centers of excellence. If a permanent medical exemption is indicated, appropriate DoD and Service policies will be pursued for granting such exemptions. Service members who disagree with a given provider or consultant's recommendations regarding an exemption may be referred for a second opinion to a provider experienced in vaccine adverse-event management. Medical records will be accurately and appropriately annotated pertaining to any temporary or permanent medical exemptions. When no longer clinically warranted, medical exemptions will be revoked.

If a patient disagrees with an initial medical decision or diagnosis, he or she may request a second opinion at the next higher medical treatment facility. If the second opinion is one with which the patient again disagrees, he or she may be referred directly to the Vaccine Healthcare Center Network.

Each military treatment facility will assist Service members in obtaining appropriate specialty consultations expeditiously and assist in resolving patient difficulties. Specialists may grant permanent medical exemptions. Return of the patient to his or her primary-care provider is not required if the referring specialist deems a permanent medical exemption is warranted. The following medical exemption codes relate to all vaccines. A Vaccine Adverse Event Reporting System (VAERS) report should be filed for any permanent medical exemption due to a vaccine related adverse event.

Medical Exemption Codes:

Code	Meaning	Explanation or Example	Duration
MI	Medical, Immune	Evidence of immunity (e.g., serologic antibody test); documented previous anthrax infection	Indefinite
MR	Medical, Reactive	Severe adverse reaction after immunization (e.g., anaphylaxis). Code can be reversed if an alternate form of prophylaxis is available. Probably warrants VAERS report	Indefinite
MT	Medical, Temporary	Pregnancy, hospitalization, temporary immune suppression, convalescent leave, any temporary contraindication to immunization	Specified period
MP	Medical, Permanent	HIV infection, pre-existing allergy, permanent immune suppression. Can be reversed if the condition changes.	Indefinite
MD	Medical, Declined	Declination of optional vaccines (not applicable to anthrax vaccine), religious waivers	Indefinite
MS	Medical, Supply	Exempt due to lack of vaccine supply	Indefinite

Adverse Events Management

As with any vaccine, some individuals receiving anthrax vaccine will experience side effects or adverse events. Experience has shown that serious adverse events are no more likely with anthrax vaccine than with other commonly administered vaccines.

The attached clinical guidelines offer advice for managing adverse events that may occur after vaccination with any vaccine. These clinical guidelines are also available on the DoD AVIP web site at www.anthrax.osd.mil.

Adverse reactions from DoD directed immunizations are line of duty conditions.

Immunizations are provided as part of the Department's Total Force Protection program. At the time of immunization, personnel are to be provided documentation that identifies date and location of immunization, general information on expected adverse events, location of the nearest military treatment facilities (MTFs), a toll free 24-hour medical provider assistance line, and the toll free telephone number of the Military Medical Support Office, in the event medical treatment is required from non-military treatment facilities. Emergency essential DoD U.S. civilian employees and contractor personnel carrying out mission essential services are entitled to the same treatment and necessary medical care as given to the Service members. This includes follow-up and/or emergency medical treatment from the MTF or treatment from their personal healthcare providers or non-military treatment facilities for emergency medical care as a result of immunizations required by their DoD employment.

Whenever a Service member presents at an MTF, expressing a belief that the condition for which treatment is sought is related to an immunization received during a period of duty, the member must be examined and provided necessary medical care. Once treatment has been rendered or the individual's emergent condition is stabilized, a Line of Duty and/or Notice of Eligibility will be determined as soon as possible. Reserve Component members, who seek medical attention from their personal healthcare providers, or any non-military treatment facility, must ensure that the Military Medical Support Office is notified as soon as possible.

In the case of Emergency-Essential civilian employees presenting to a military treatment facility or occupational health clinic, the initial assessment and any needed emergency care should be provided consistent with applicable occupational health program procedures. In the case of contractor personnel covered by the anthrax vaccination policy presenting to a military medical treatment facility or occupational health clinic, Secretarial designee authority shall be used, consistent with applicable Military Department policy, to allow an initial assessment and any needed emergency care. This policy will facilitate awareness by our medical professionals of adverse events and provide to the patient medical expertise regarding anthrax vaccine events not necessarily available in the civilian medical community. This use of Secretarial designee authority does not change the overall responsibility of the contractor under workers' compensation program for all work-related illnesses, injuries, or disabilities.

As provided in HA Policy No. 99-031, Policy for Reporting Adverse Events Associated with the Anthrax Vaccine, 15 October 1999, any serious adverse event temporally associated

with receipt of a dose of anthrax vaccine should be immediately evaluated by a privileged health-care provider and any specialists, as indicated.

Vaccine Adverse Event Reporting System (VAERS) reports shall be filed using Service reporting procedures for those events resulting in hospital admission or lost duty time or work of 24 hours or more or from those events suspected to have resulted from contamination of a vaccine vial. Further, health-care providers are encouraged to report other adverse events that in the provider's professional judgment appear to be unexpected in nature or severity. In other situations in which the patient wishes a VAERS report to be submitted, the health-care provider will work with the patient to submit one. VAERS report forms may be obtained by accessing either the AVIP web site or www.vaers.org or by calling the VAERS at 1-800-822-7967.

Adverse-event management should be thoroughly documented in medical records. A copy of the VAERS report will be filed in an individual's medical record after submitting the original form through DoD reporting channels, as discussed above. Providers are encouraged to provide a copy of the VAERS report to the patient.

These policies are effective immediately and should be communicated to appropriate commanders, health-care providers, and others involved in the implementation of the AVIP.

William Winkenwerder, Jr., MD

Attachments:
As stated

cc:
Chief of Staff of the Army
Chief of Naval Operations
Commandant of the Marine Corps
Chief of Staff of the Air Force
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force

CLINICAL GUIDELINES
FOR MANAGING ADVERSE EVENTS AFTER VACCINATION

July 2002 edition

1. **Purpose:** To help medical personnel individually manage and document adverse events after vaccination. Based on clinical experience with adverse-drug-reaction management and with vaccines in general, this document offers treatment and reporting recommendations. Adapt these guidelines to individual clinical cases, according to the judgment and scope-of-practice of the health-care provider.

2. **Adverse Events After Vaccination:** Most people tolerate vaccination without significant side effects. But adverse events may occur after vaccination, sometimes requiring treatment to relieve symptoms. Although many side effects respond to self-medication, people experiencing an adverse event should advise a health-care provider before the next dose of the same vaccine. Several studies indicate that women are more likely than men to experience temporary injection-site reactions and systemic symptoms that typically resolve on their own.

a. *Injection-site reactions, such as redness and swelling.* These reactions are not unusual. Antibiotics are not typically warranted to treat injection-site reactions. Anthrax vaccine, administered subcutaneously (SC), is associated with a high frequency of nodules (also called knots or lumps). Although mild to moderate local reactions can be self-medicated, worsening local reactions should be reported to a health-care provider and documented in the medical record, before the next dose.

b. *Systemic events such as immediate hypersensitivity, fever, or muscle aches.* Systemic events are less common than injection-site reactions, and may or may not be caused by the vaccine. Systemic events may appear later after vaccination than injection-site reactions.

c. *Vaccination and the differential diagnosis.* Some events are caused by vaccination. Others simply coincide in time and may be unrelated to the vaccine. The frequency of the events listed in the attached tables is not uniform. Some are common, while others are rare, if they occur at all. Events may occur that are not listed. Regardless, it is paramount for health-care providers to provide the best care possible for the person in need, regardless of causality. Identify and document clinical problems that follow vaccination before the next dose. Vaccination should be considered in the differential diagnosis, as clinically appropriate. When planning future actions, assess the risk-benefit ratio for continued vaccination versus medical exemption.

d. *Additional evaluations.* While most adverse events after vaccination require no treatment, some people may need further evaluation, therapy, and/or exemption from further doses of the vaccine. Document all adverse events requiring pre-vaccination treatment, post-vaccination treatment, relief from work, hospitalization, or other medical care on the Service's clinical-encounter form. Report as discussed below.

3. Treatment Guidelines: See algorithms depicted in Figures 1, 2, and 3, plus companion tables with text-based details. Based on published literature and clinical experience, these guidelines are divided into two major groups: injection-site reactions and systemic events. Consider relevant footnotes. Patients may present with symptoms corresponding to more than one category.

4. VAERS Reporting:

a. Adverse events after vaccination are reported to the Vaccine Adverse Event Reporting System (VAERS) using the official VAERS form. DoD and the Coast Guard require submission of a VAERS report, *at a minimum*, for adverse events after vaccination that involve hospitalization, a life-threatening event (such as anaphylaxis), loss of duty of 24 hours or longer, or an event related to suspected contamination of a vaccine vial. These are minimum requirements. The Department encourages clinicians to report all other clinically relevant adverse events after administration of any vaccine or medication to VAERS or MedWatch.

b. Clinicians who file a VAERS report are not making a determination that the two events are linked in a cause-and-effect manner. Ideally, initial VAERS forms should be submitted by primary-care providers, with follow-up VAERS forms filed by subspecialists as additional information comes to light. Anyone identifying a qualifying case, and uncertain whether a VAERS report was submitted previously, should submit one.

c. If the patient considers his or her adverse event significant and due to the vaccine, the clinician should file a VAERS report. Vaccine recipients may complete VAERS forms themselves and submit them directly to the Food & Drug Administration (FDA). Reporting by a health-care provider is preferred, to enhance the quality and completeness of the clinical data reported.

d. VAERS forms may be downloaded from the Service surveillance centers, or from www.anthrax.mil/vaers/vaers.htm. Additionally, one may obtain VAERS forms by contacting VAERS at 1-800-822-7967 or www.vaers.org.

e. Attach pertinent information from the vaccine recipient's medical record to the VAERS report. Forward the original VAERS form and attachments to VAERS, P.O. Box 1100, Rockville, MD 20849-1100. At the same time, send a copy of the VAERS report and attachments through the local Preventive Medicine or Preventive Health Officer, as applicable, to the Service surveillance center (Annex A). Reports also should be submitted to the local pharmacy-and-therapeutics (P&T) committee, because institutions have an accreditation requirement to encourage adverse-drug-reaction reporting. Do not delay reporting while awaiting a P&T committee meeting. Pharmacists can assist in filing VAERS reports.

f. The Department of Defense forwards all VAERS reports to the FDA and the Centers for Disease Control & Prevention (CDC) without screening or restriction. VAERS reports on anthrax vaccine are reviewed for causality by the FDA and CDC, as well as an independent civilian committee, known as the Anthrax Vaccine Expert Committee (AVEC), under the auspices of the U.S. Department of Health and Human Services.

5. Medical and Administrative Exemptions

a. Good medical practices for the management of an adverse drug reaction apply to the evaluation of any adverse event after vaccination. Good medical practices also apply to the medical-decision process for granting exemptions or continuing to vaccinate in the face of an adverse event potentially linked to vaccine administration.

b. The primary-care provider may grant indefinite medical exemptions. However, if additional clinical consultation is needed to assess a patient's condition, the primary-care provider should perform the initial clinical work-up appropriate to the presenting symptoms. Under these conditions, primary-care providers may grant a temporary medical exemption pending the results of a referral to a subspecialist appropriate to the individual's clinical condition (e.g., dermatology, neurology, otolaryngology, rheumatology, allergy/immunology). Multidisciplinary consultations may be appropriate in some circumstances.

c. Subspecialists may grant indefinite medical exemptions. Return to primary-care providers is not required if the referring subspecialist deems an indefinite medical exemption is warranted.

d. Granting administrative exemptions is a non-medical function, usually controlled by an individual's unit. Granting medical exemptions is a medical function performed by a credentialed health-care provider. Medical exemptions should be applied only when medically warranted. If the case is complex or not readily definable, a clinical summary should be sent to the regional clinical subject matter expert or group for review. Medical records of Service members who disagree with a given provider or consultant's recommendations regarding the exemption should be referred for a second opinion to a provider or consultant group with experience in vaccine adverse reaction management. Review exemptions periodically to confirm continued applicability.

Use the following exemption codes for electronic tracking of vaccinations. These codes may also be available in Service automated immunization tracking systems.

Medical Exemption Codes:

Code	Meaning	Explanation or Example	Duration
MI	Medical, Immune	Evidence of immunity (e.g., serologic antibody test); documented previous infection (e.g., chickenpox)	Indefinite
MR	Medical, Reactive	Severe adverse reaction after immunization (e.g., anaphylaxis). Code can be reversed if an alternate form of prophylaxis is available. Probably warrants VAERS report	Indefinite
MT	Medical, Temporary	Pregnancy, hospitalization, temporary immune suppression, convalescent leave, any temporary contraindication to immunization	Specified period
MP	Medical, Permanent	HIV infection, pre-existing allergy, permanent immune suppression. Can be reversed if the condition changes.	Indefinite

MD	Medical, Declined	Declination of optional vaccines (not applicable to anthrax vaccine), religious waivers	Indefinite
MS	Medical, Supply	Exempt due to lack of vaccine supply	Indefinite

7. Acknowledgements & Revisions:

a. This revision, the second edition of these guidelines, is issued by the Anthrax Vaccine Immunization Program (AVIP) Agency, within the Office of The Army Surgeon General, Falls Church, Virginia. The guidelines were developed based on published literature and clinical consensus, beginning at the Biological Warfare Defense Immunizations Conference, 25-27 May 1999. The major authors of this document are LTC Phillip Pittman, COL Renata Engler, LTC Bryan Martin, LTC John Grabenstein, along with clinicians from the medical departments of the U.S. Army, Navy, Marine Corps, Air Force, and Coast Guard.

b. This document will be revised periodically, based on clinical experience and epidemiological data. This document provides general guidelines to adapt to individual clinical cases, according to the judgment and scope-of-practice of each health-care provider.

c. Forward suggestions for improvements to this document to: Office of the Assistant Secretary of Defense for Health Affairs, Force Health Protection & Readiness, 1200 Pentagon, Washington DC 20301-1200. Medical command channels will disseminate revisions periodically; they will also be available at the AVIP website, www.anthrax.mil.

8. Selected Bibliography on Anthrax & Other Vaccines:

a. Advisory Committee on Immunization Practices. General recommendations on immunization. *MMWR* 2002;51(RR-2):1-35. ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr5102.pdf

b. Advisory Committee on Immunization Practices. Update: Vaccine side effects, adverse reactions, contraindications, and precautions. *MMWR* 1996;45(RR-12):1-35, errata 227, ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr4512.pdf.

c. Advisory Committee on Immunization Practices. Use of anthrax vaccine in the United States. *MMWR-Morbidity & Mortality Weekly Report* 2000;49(RR-15):1-20. http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf

d. American College of Physicians. *Guide for Adult Immunization*, 3rd ed. Philadelphia: American College of Physicians, 1994.

e. Atkinson W, Wolfe C, Humiston S, Nelson R, ed. *Epidemiology & Prevention of Vaccine-Preventable Diseases*, 6th ed. Atlanta: Centers for Disease Control & Prevention, 2000, http://www.cdc.gov/nip/publications/pink/.

f. Centers for Disease Control & Prevention. Surveillance for adverse events associated with anthrax vaccination - U.S. Department of Defense, 1998-2000. *Morbidity & Mortality Weekly Report (MMWR)* 2000;49(Apr 28):341-5. [reprinted in *JAMA* 2000;283(May 24/31):2648-9] http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/mm4916a1.htm

g. Food & Drug Administration. Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS). *MedWatch* November 1998, http://www.fda.gov/medwatch/articles/vaers/vaersce.pdf.

h. Franz DR, Jahrling PB, Friedlander AM, McClain DJ, Hoover DL, Bryne WR, Pavlin JA, Christopher GW, Eitzen EM Jr. Clinical recognition and management of patients exposed to biological warfare agents. *JAMA* 1997;278(Aug 6):399-411. http://jama.ama-assn.org/issues/v278n5/ffull/jsc71014.html

i. Friedlander AM, Pittman PR, Parker GW. Anthrax vaccine: Evidence for safety and efficacy against inhalational anthrax. *Journal of the American Medical Association* 1999;282:2104-6. http://jama.ama-assn.org/issues/v282n22/pdf/jct90025.pdf

j. Grabenstein JD. *ImmunoFacts: Vaccines & Immunologic Drugs*. St. Louis: Facts & Comparisons, February 2002.

k. Inglesby TV, Henderson DA, Bartlett JG, et al. Anthrax as a biological weapon: Medical and public health management. *JAMA* 1999;281:1735-45, http:// jama.ama-assn.org/issues/v281n22/full/jst90000.html.

l. Pittman PR, Kim-Ahn G, Pifat DY, Coonan K, Gibbs P, Little S, Pace-Templeton JG, Myers R, Parker GW, Friedlander AM. Anthrax vaccine: Safety and immunogenicity of a dose-reduction, route comparison study in humans. *Vaccine* 2002; in press.

m. Pittman PR, Mangiafico JA, Rossi CA, Cannon TL, Gibbs PH, Parker GW, Friedlander AM. Anthrax vaccine: Increasing intervals between the first two doses enhances antibody response in humans. *Vaccine* 2000;18:213-216.

n. Plotkin SA, Orenstein WA, ed. *Vaccines*, 3rd ed. Philadelphia: W.B. Saunders, 1999.

o. White CS III, Adler WH, McGann VG. Repeated immunization: Possible adverse effects: Reevaluation of human subjects at 25 years. *Annals of Internal Medicine* 1974;81:594-600. http://www.anthrax.osd.mil/Site_Files/articles/INDEXclinical/anthraxlibrary/Repeated.pdf.

p. Zimmerman B, Zimmerman RS. Adverse reactions to vaccines. In: Middleton E Jr, Ellis EF, Yunginger JW, Reed CE, Adkinson NF Jr, Busse WW, eds. *Allergy Principles and Practice*, 5th ed. St. Louis: Mosby, 1998:1199-1211.

q. Anthrax vaccine adsorbed, BioThrax, product labeling. Lansing, Michigan: BioPort Corporation, 2002.
http://www.anthrax.mil/Site_Files/articles/INDEXclinical/package_insert.htm

r. Joellenbeck LM, Zwanziger L, Durch JS, Strom BL, ed. *The Anthrax Vaccine: Is it Safe? Does it Work?* Washington, DC: National Academy of Sciences, March 2002. www.nap.edu

Annex A. Service Surveillance Centers

Army Medical Surveillance Activity
Bldg T-20, Rm 213 (Attn: MCHB-EDS)
6825 16th Street, N.W.
Washington, DC 20307-5000
Phone: 202-782-0471 (DSN 662)
Fax: 202-782-0612
http://amsa.army.mil/AMSA/amsa_home.htm

Navy Environmental Health Center
620 John Paul Jones Circle
Suite 110
Portsmouth, VA 23708-2103
Phone: 757-953-0700 (DSN 377), after hours 757-621-1967
Fax: 757- 953-0685
http://www-nehc.med.navy.mil/

Air Force Force Health Protection and Surveillance Branch
Institute for Environment, Safety and Occupational Health (ESOH) Risk Analysis
2513 Kennedy Circle
Brooks AFB, TX 78235-5123
Phone: 210-536-5454 (DSN 240)
Fax: 210-536-6841
http://www.afms.mil/afiera/

Coast Guard Headquarters Directorate of Health and Safety
Commandant (G-WKH)
2100 Second Street SW
Washington, DC 20593
Phone: 202-267-1098
Fax: 202-267-4685

IMMUNIZATION SERVICES: SCREENING QUESTIONNAIRE

Please answer the questions below by checking the appropriate boxes (Yes, No or Don't Know).

Your careful responses will help us determine which vaccines may be safely given in the clinic today. If the question is not clear, please ask a nurse or doctor to explain it.

Item Number	Question or Educational Point of Information	Yes	No	Don't Know
1	Are you sick today?			
2	Do you have a fever today?			
3	**Do you have allergies: Egg?___ Thimersol? ___ Neomycin? ____ Gelatin? ____ Rubber/Latex? ____ Drugs? ____ Preservatives/Other?____**			
4	Do you have a **history of adverse reactions** to ANY vaccines? If yes, please ask for adverse reaction questionnaire from the front desk.			
5	Do you take a **blood thinner** like Coumadin AND/OR do you (does the child/patient) have a **bleeding problem**?			
6	Do you have a chronic illness such as: chronic heart/lung/liver/kidney or skin disease, diabetes, sickle cell, or had your spleen removed, G6PD, frequent infections? Please indicate:			
7	Do you (or anyone living with you or other close contact) have **cancer, leukemia, HIV/AIDS, transplantation, or any other immune system problem or chronic skin disease, rash or eczema, atopoic dermatitis**? Please indicate:			
8	Have you (taken **cortisone, prednisone, other steroids, anticancer drugs, or x-ray treatments in the past 3 months**?			
9	Have you received **a transfusion of blood or plasma, or been given a medicine called immune (gamma) globulin in the past year**?			
10	Could you be **pregnant?** Last menstrual period?			
11	Is there a chance that you could **become pregnant in the next month**?			
12	Have you received any vaccinations in the past 4 weeks?			
13	If yes, indicate (Example: MMR-measles, mumps, ruebella-,varicella/chicken pox, yellow fever, smallpox, anthrax, polio by mouth, other):			
14	Have you had a seizure, brain or psychiatric problem?			
15	Are you here today to receive the next shot in a series?			
16	If so, please indicate which series? **Anthrax ___ Hepatitis A ___ Hepatitis B ___ JEV ___ Rabies ___ Other ___**			
17	Are you traveling abroad?			
18	If yes, indicate departure date and countries			

Patient Signature: _____ **Date:** _____

CLINIC USE: **Reviewing Provider:**_____ **Date**_____

Cleared for Immunization ____

Not cleared for Immunization ____

Other _____

Example 1. Sample Immunization Screening Questionnaire

Thank you for completing the following questionnaire regarding your experience with a prior vaccine. Please check **YES** if you have had the type of reaction described after receiving any prior vaccine. If the reaction occurred after a vaccine administered as a series indicate which dose by entering the dose number at column **D#**__

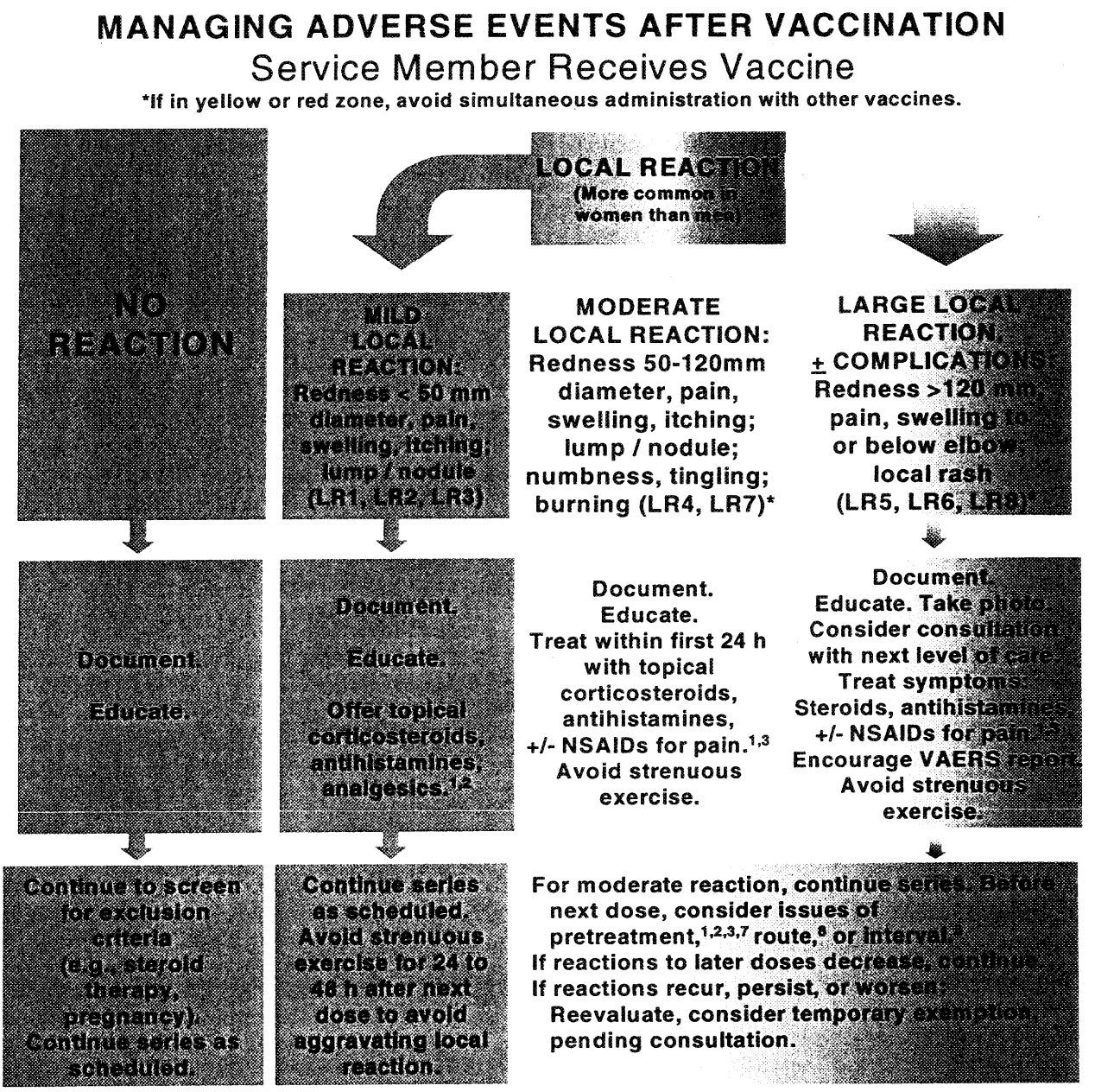
	Information Elements	**YES**	**NO**	**D#**__	**D#**__
1	**Vaccine:** **Date Administered:**				
2	**Indicate in which arm shot was received (R = right or L = left)**				
3	Did you receive educational printed material and/or a verbal briefing about the vaccine prior to the series and/or specific doses?				
4	**Local Reaction at the Site of the Shot**				
	• Pain/reaction limiting motion lasting for _____ hours				
	• Redness less than 5 cm (< 2 inches) lasting for _____ hours				
	• Redness more than 5 cm lasting for _____ hours				
	• Redness more than 12 cm (> 4 inches) lasting for _____ hours				
	• Swelling extending from the upper arm to below the elbow and lasting for _____ hours				
	• Itching at the site of the shot lasting _____ hours				
	• Knot or lump at the site lasting for _____				
	• Any other local reactions: _____				
	• Joint swelling or stiffness lasting more than 12 hours in the shot arm				
5	**Generalized Reaction:** Immediate (within 60 minutes of the shot)				
	• Generalized itching and/or hives				
	• Shortness of breath, asthma, chest tightness				
	• Loss of consciousness, low blood pressure				
	• Acute illness: _____				
	• Did you receive emergency or immediate treatment?				
6	**Generalized Reaction:** Prolonged and Delayed in Onset. If none, **Check NO**				
	• Generally feeling bad for more than a few hours: _____ hours				
	• Chills or Fever: How high? _____				
	• Fatigue lasting more than a few hours: _____ hours				
	• Headaches: _____				
	• Generalized muscle aches lasting _____ hours				
	• Joint aches lasting _____ hours				
	• Dizziness or light-headedness lasting _____ hours				
	• Nausea and/or poor appetite lasting _____ hours				
	• Abdominal cramping and/or diarrhea lasting _____ hours				
	• Ringing in the ears lasting _____ hours				
	• Numbness or tingling or sharp pains lasting _____ hours				
	• Swollen and/or tender lymph glands lasting _____ hours				
	• Generalized rashes and/or hives persisting for _____ hours				
7	**Impact**: None, (able to work, exercise, recreate) check **NO.** If YES, indicate: **Missed work: Yes No Days:** ____ **Missed PT: Yes No Days:** ____				
8	**How severe was your reaction compared to other vaccines you have received? Scale 1-5 with 5 = Most severe reaction**				

Name_____ **Date**_____

Age (at time of reaction to shot) ____ **Sex:** ____

On BACK of SHEET: Indicate if seen by a physician and whether or not symptoms have resolved completely.
PLEASE return this form to the Allergy-Immunology Clinic

Example 1a. Sample Adverse Event to Previous Immunization Questionnaire



Clinical guidelines for managing adverse events after vaccination: *Version February 2001.* This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform: some are quite common and some are rare. See cover sheet for details.

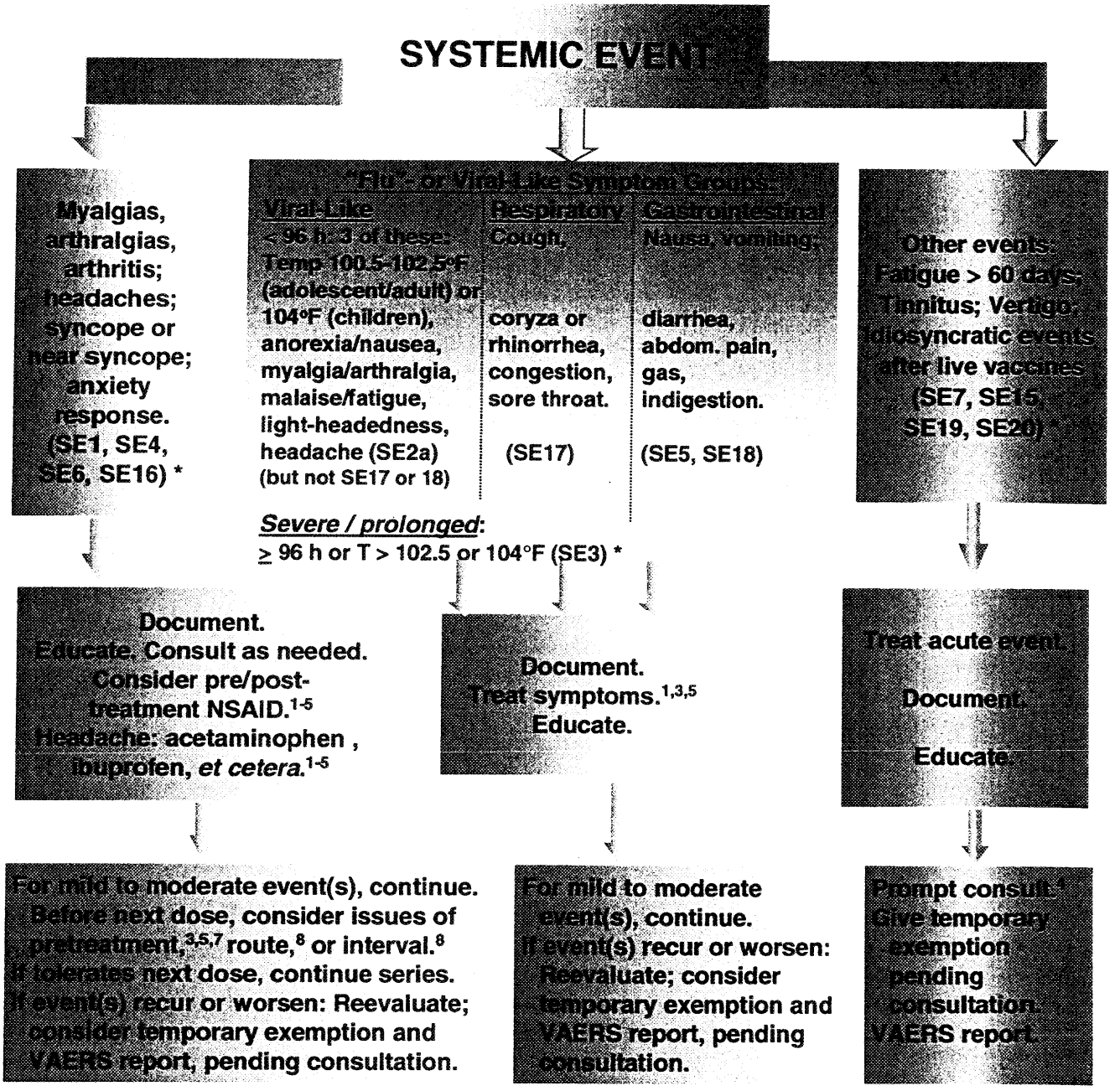
Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Presumption of causation is not required to submit Form VAERS-1. Forms available at www.anthrax.osd.mil/vaers/vaers.htm.

Figure 1. Managing Adverse Events After Vaccination

MANAGING ADVERSE EVENTS AFTER VACCINATION

Service Member Receives Vaccine

*If in yellow or red zone, avoid simultaneous administration with other vaccines.



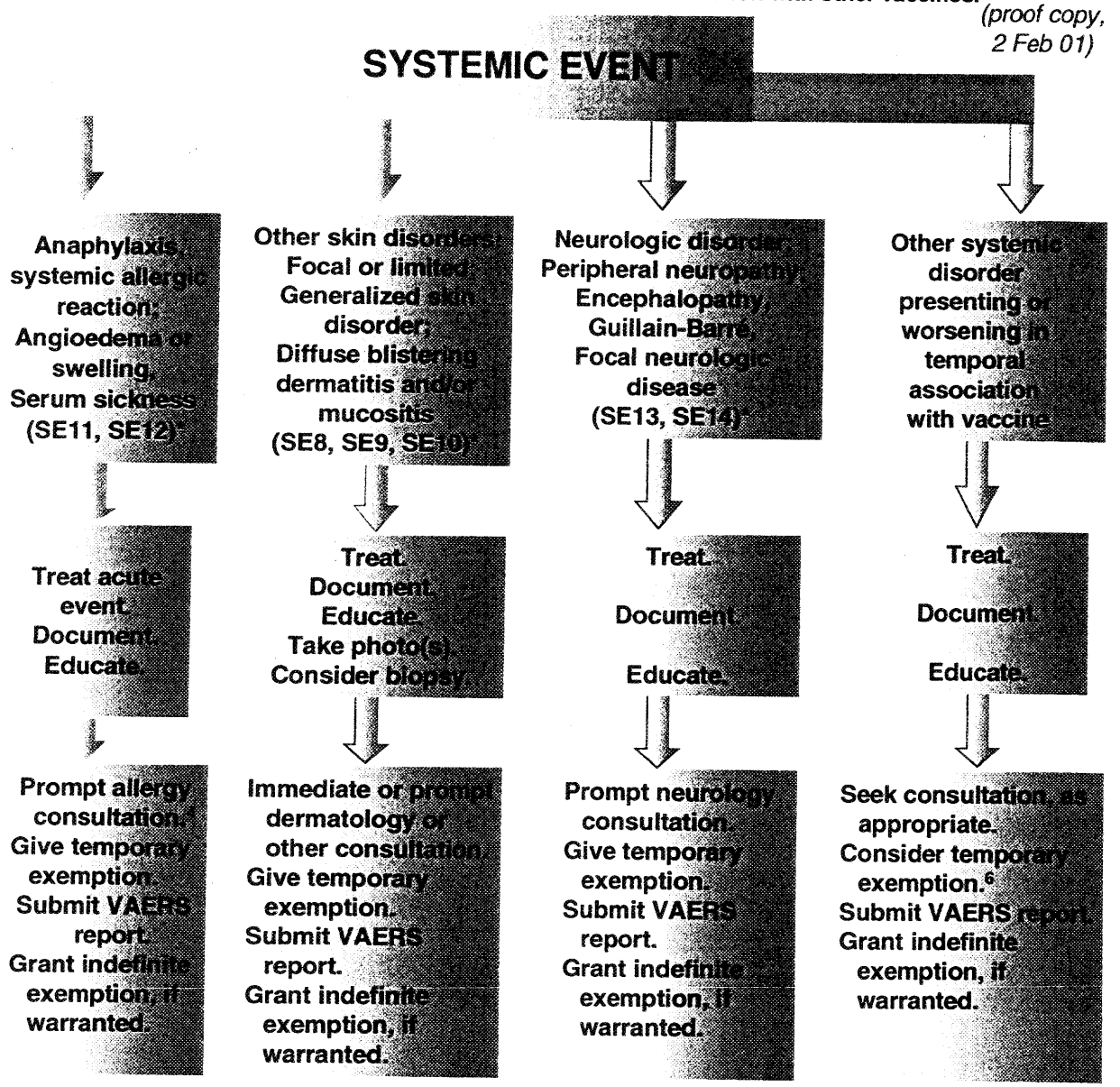
Clinical guidelines for managing adverse events after vaccination: *Version February 2001.* This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform: some are quite common and some are rare. See cover sheet for details.

Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Presumption of causation is not required to submit Form VAERS-1. Forms available at www.anthrax.osd.mil/vaers/vaers.htm.

Figure 2. Managing Adverse Events After Vaccination

*If in yellow or red zone, avoid simultaneous administration with other vaccines.

(proof copy, 2 Feb 01)



Clinical guidelines for managing adverse events after vaccination: *Version February 2001.* This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform: some are quite common and some are rare. See cover sheet for details.

Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Presumption of causation is not required to submit Form VAERS-1. Forms available at www.anthrax.osd.mil/vaers/vaers.htm.

Figure 3. Managing Adverse Events After Vaccination

Table 1A: Localized Reactions (LR) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Local (Injection-Site) Reactions (LR) typically involve changes at the injection site with contiguous spread. Signs of inflammation (e.g., itching, redness, heat, swelling) may be present, with occasional bruising. Record specific observations, along with a photo, if needed to preserve the image. Biopsy may be warranted in some cases (e.g., scaling, crusting).	Remote electronic consultation (e.g., telephonic, e-mail, telemedicine) can be used to request assistance. Reassure vaccine recipient that local reactions typically resolve and do NOT result in long-term disease. Although some of these reactions may mimic cellulitis, antibiotic therapy is not warranted for post-vaccination inflammation.	Unless LR was very large or complicated, Service member usually can proceed with subsequent doses. Credentialed health-care providers may make clinical decisions to alleviate future discomfort for individual Service members who develop large or persistent injection-site reactions.[8]	Most local reactions require no treatment. Topical or oral treatment to control symptoms depends on reaction severity. Complications may warrant consultation with a specialist. May benefit from treatment and/or pretreatment programs.[1,2] VAERS reporting discussed in text.
Subcutaneous Nodules (LR1): • Usually painless with no redness or heat at the site • Usually present within 1-2 days of the injection, may persist for weeks, gradually dissipating	Record size (in mm) of nodule in longest diameter and duration of palpable presence. Usually requires no treatment. Reassure vaccine recipient that these are common and will resolve spontaneously.	Proceed with subsequent doses at different site (e.g., contralateral side, antero-lateral thigh). Anthrax: For unusually large, bothersome or persistent nodules, consider route.	Do not inject into or through nodule. If painful, consider topical corticosteroid cream or ointment applied 2 to 3 times per day for as long as symptoms persist. Dermatology consult if persistent (> 4 to 6 months).
Local Redness or Swelling **(LR2):** • < 30 mm in longest diameter • "Mild"	Usually requires no treatment. Resolves within < 72 hours in most cases. Reassure.	Proceed with subsequent doses.	May benefit from topical steroid therapy or antihistamines, if itching is present.[1]
Local Redness or Swelling 30 to 50 mm (LR3): • 30 to 50 mm in longest diameter • "Mild"	May warrant treatment. Rash management noted in LR8.	Proceed. Consider topical corticosteroids and/or antihistamines just after injection.[1,2]	May benefit from topical corticosteroids and/or antihistamines just after injection.[1,2]

Table 1B: Localized Reactions (LR) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Local Redness or Swelling 50 to 120 mm, but NOT extending below elbow (LR4): • Patient may exhibit concern about progression and risk from next injection • "Moderate"	Treat with topical therapy, analgesics, antihistamines to prevent complications or progression. May benefit from short course of oral prednisone, if symptoms persist or worsen. Consider consultation with next level of care.[7] Rash management noted in LR8.	Consider consultation with next level of care,[7] before proceeding with next dose. Consider pre-treatment options. Anthrax: Consider route.[8]	Consider treatment before or at time of next vaccination.[1,2,3] Avoid simultaneous vaccination.
Local Redness or Swelling > 120 mm without complications (LR5): • "Large – Simple"	Rash management noted in LR8.	Consider consult with next level of care.[7] Temporary exemption may be warranted. Consider pretreatment options.[1,2] Anthrax: Consider route and/or interval.[8]	If repeats or worsens, consider temporary exemption, pending consultation. Consider pretreatment.[1,2,3] Encourage submission of VAERS report. Avoid simultaneous vaccination.
Local Redness or Swelling > 120 mm or extending below elbow (LR6): • "Large – Complicated" • Peri-articular soft-tissue swelling, soreness, stiffness may be present • May occur with systemic symptoms **Note: May see swelling at or below wrist. Consider possibility of gravitational settling of edema.**	Provide treatment by physician. Consider potent topical and/or oral corticosteroids to prevent complications or progression.[1] Seek consultation, as needed. If reaction occurs after ≥ 2 doses, may be immune (i.e., a "hyper-responder," although booster doses may still be needed). Rash management noted in LR8.	Give temporary exemption, pending consultation. Anthrax: Consider route and/or interval.[8] Avoid simultaneous vaccination.	If repetitive or worsening, may merit a temporary exemption from subsequent vaccination, pending consultation. Benefit-risk ratio may merit pretreatment trial.[1,2,3] Encourage submission of VAERS report.

Table 1C: Localized Reactions (LR) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Numbness, Burning, or Tingling At or Distal to Injection Site (LR7_): • 7a. Prolonged lack of sensation (numbness, hypesthesia, anesthesia) near or over injection site • 7b. Burning or painful sensation (dysesthesia) near or over injection site • 7c. Tingling, altered, cold, or other sensation without stimulus (paresthesia) near or over injection site • 7d. Any unusual sensation distal to injection site If physical exam and/or nerve studies establish diagnosis of focal neurologic disease (e.g., ulnar nerve neuropathy, see SE14.	Record detailed description, size of area affected. No specific treatment. Usually resolves in < 1 to 2 weeks. Reassure. May benefit from topical corticosteroids.	Reinforce avoiding injection over triceps. Proceed with subsequent doses at different site, to avoid ulnar nerve. Anthrax: Consider route.[8]	Value of topical anti-inflammatory therapy not established. Encourage submission of VAERS report. Avoid simultaneous vaccination.
Focal Rash At or Near Injection Site (LR8): • May involve vesicles or papules	May treat with topical steroid cream and new-generation antihistamine.[1] May be associated with LR3, LR4, LR5, LR6, or other categories.	After rash resolves, continue doses. Give temporary exemption, pending consultation. Obtain photo and consider biopsy.	If etiology is not clear or rash is slow to resolve, consult with dermatologist. Avoid simultaneous vaccination.
Other Events At or Near Injection Site (LR-xx)	Treat according to clinical condition. Seek consultation, as appropriate.	Base decision on complete medical evaluation and consideration of benefit-risk ratio.	

Table 2A: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Systemic Events (SE): Symptoms and signs of illness after vaccination. Any reaction that does not involve the injection site. Temporal relationship does NOT prove a cause-effect relationship, particularly if multiple vaccines were given and/or other specific diagnoses of illness have occurred.	Health-care provider should provide appropriate diagnostic evaluation. In some cases, give pretreatment to avert symptoms with next vaccination, to avoid morbidity, but allowing for continued vaccination.	If mild and self-limited, may proceed with next dose. Avoid multiple vaccines in one session for this patient, if possible. Credentialled health-care providers may make clinical decisions to alleviate future discomfort for individual Service Members who develop substantial or persistent reactions.[8]	VAERS reporting discussed in text.
Myalgias and/or Arthralgias **(SE1a)** Arthritis **(SE1b)** • Primary • Secondary (exacerbation of existing condition)	Acetaminophen or NSAIDs may be administered. Pretreatment may be necessary.	Subsequent doses can usually be given. Anthrax: For symptoms persisting > 96 h, seek specialty consultation; consider route.[8]	If persistent, start work-up to rule out other etiologies. Consult, if needed. VAERS report encouraged when symptoms persist > 48 hours.

Table 2B: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Mild "Viral"-Like Symptoms (SE2a): At least three of the following, lasting < 96 hours: • Fever (100° to 102.5°F (adolescent/adult) or 104°F (children)) [oral equivalent] • Anorexia • Nausea • Myalgia • Arthralgia • Malaise • Fatigue • Light-headedness (colloquial "dizziness," but not true vertigo. See also SE19b) • Headache (including photophobia or aching eyes) But without (or only one) symptom referable to either the respiratory (SE17) or gastrointestinal tract (SE18). May be associated with moderate or large local reactions. Usually resolves spontaneously with no treatment or with analgesics and rest. ========== **"Flu"-like or "Viral"-like**, not otherwise specified (SE2b)	Options include antihistamines and analgesics to prevent complications or progression.	Proceed with next dose, in most cases..[2,4] For fever > 102.5°F (adolescent / adult) or 104°F (children) [oral equivalent], consider benefit-risk ratio for continuing doses if patient or provider is concerned about risk with future doses.	Consider treatment before or at time of next vaccination, particularly if large local reaction as well.[1,2,4]
Severe and/or Prolonged Nonspecific Symptoms (sometimes called severe or prolonged "viral"-like illness) (SE3) • Includes temperature > 102.5°F (adolescent/adult) or 104°F (children) [oral equivalent] • Includes temperature > 100.5°F and/or systemic symptoms lasting > 96 hours	May benefit from short course of oral prednisone, if not stabilized. May warrant consultation.[5] Evaluate for coincident disease, treat appropriately. High temperatures warrant consultation.	Consult with next level of care. Consider temporary exemption, pending consultation. If unexplained by other causes, may warrant contraindication.	VAERS report encouraged, if no other cause identified. Avoid simultaneous vaccination.

Table 2C: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Headaches (SE4): • Usually bitemporal without migraine features, "tension" type or dominant feature of "flu"-like syndrome • Usually resolve in several days	Acetaminophen 650 to 1000 mg orally every 4 to 6 hours or ibuprofen 600 to 800 mg orally every 8 hours (or other non-steroidal anti-inflammatory drugs, NSAIDs); can start this treatment 1 hour before next dose.[5]	Proceed with next dose, unless worsening pattern. Anthrax: For symptoms persisting > 96 h, consider route.[8]	Pretreatment generally effective. If pattern worsens, give temporary exemption, pending consultation with neurology. If referred, neurologist should submit follow-up VAERS.
Nausea and/or Vomiting (SE5): • No other signs or symptoms of anaphylaxis • Usually resolves without treatment • Can be vasovagal	Usually resolves without treatment, but standard anti-emetics and even (sedating) antihistamines may provide relief.	Proceed with next dose, with precautions for a vasovagal reaction. Anthrax: For symptoms persisting > 96 h, consider route.[8]	Not reproducible from one injection to the next on initial observations, unless part of vasovagal reaction. Typically, no predictive value for more serious reaction.
Syncope or Near-Syncope (Fainting, Light-headedness) Shortly After Vaccination (SE6): • May be accompanied by prolonged malaise • Fainting or near-fainting with signs of vasovagal reaction (diaphoresis, nausea, vomiting, usually bradycardia, widening pulse pressure and/or frank hypotension) • May result in a fall with secondary injury • Asking people before vaccination about this predisposition may avoid injury	Position in sitting or supine position with legs elevated, head down. • Rarely requires atropine to reverse profound bradycardia • Encourage hydration as soon as stabilized and before future injections • Advise that future injections be given in supine position	Proceed, but with precautions as outlined under treatment. Anthrax: If syncope or near-syncope was related to pain or burning at injection site after injection, consider route.[8]	Occurs in about 1% of healthy, fit adults. Procedures when giving injections of any kind should anticipate this reaction, to avoid traumatic injury.

Table 2D: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Tinnitus **(SE7):** • New onset ringing in the ears developing within less than 1 to 2 weeks after an injection • Other cause unlikely (e.g., neurogenic hearing loss from noise injury)	Therapy for nasal congestion may help in some cases. If symptoms persist > 1 to 2 weeks, consult with ear-nose-throat (ENT) specialist.	Consider temporary exemption, pending routine consultation with specialist.	No well-defined association with any vaccine recognized at this time. If event recurs with later dose, give temporary exemption, pending consultation.
Focal or Limited Skin Reaction, not near most recent injection site **(SE8):** Take photo while acute (or have local dermatologist and/or allergist evaluate)	Treat as indicated. Consult with dermatology, if symptoms persist.	Subsequent doses can usually be given.	May be a rash, erythema, bruising, swelling, etc., at a distance from most recent injection site, such as at previous injection site. May be unrelated to vaccination.
Generalized Skin Reaction (pruritic or non-pruritic), not suggestive of anaphylaxis **(SE9):** • Maculopapular or target lesions • Must involve skin sites remote from injection site, not just on the injection arm • Take photo while acute (or have local dermatologist and/or allergist evaluate)	Antihistamine.^1,2. Consider high-dose prednisone (50 to 60 mg daily for 5 to 7 days with rapid taper) if severe.[1,2] If rash is early erythema multiforme, Stevens-Johnson, or toxic epidermal necrolysis, see section SE10. Longer therapy may be needed. Note: accurate diagnosis may call for skin biopsy.	Consider temporary exemption, pending routine consultation with specialist.	In rare circumstances, additional vaccine doses may result in a more serious generalized skin reaction. Additional doses should be given with caution after expert evaluation and consideration of benefit/risk ratio. Encourage submission of VAERS report.

Table 2E: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Diffuse Blistering Dermatitis and/or Mucositis **(SE10):** • Erythema multiforme • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Others (fixed drug eruptions, etc.)	Treat acutely, record visually with photo; immediate dermatology and allergy consultation for full treatment program and follow-up. Accurate diagnosis may call for skin biopsy.	Give temporary exemption, pending consultation.	Submit VAERS report. There are no safety data for challenge dosing and/or desensitization of these types of potentially life-threatening skin reactions.
Anaphylaxis, Generalized Allergic Reaction: onset typically within the first few hours after vaccination (SE11): • **Anaphylaxis:** Watery eyes, nasal congestion, general itching, hives, coughing, throat tightness, wheezing, short of breath, light-headed, rapid heart rate, hypotension, anxiety reaction ("sense of doom"), nausea, vomiting, diarrhea, loss of bladder or bowel control with loss of consciousness • **Generalized rash, itching and shortness of breath:** Treat as anaphylaxis, unless immediate evidence of other cause.	Potentially life-threatening allergic reaction, treat immediately with epinephrine. Oral corticosteroid therapy prevents delayed-phase anaphylaxis, which can also become life threatening. Admit to hospital if laryngeal edema or other life-threatening condition is present. Physician or physician assistant evaluation required.	Give temporary exemption, pending consultation with allergist.	Submit VAERS report. Seek allergy consult.[4] Review benefit-risk ratio carefully with patient. Consult patient regarding treatment options and further vaccination under controlled desensitization conditions. Avoid simultaneous vaccination.

Angioedema/Swelling – Diffuse or distant from injection site, with or without pruritus within 2 weeks of vaccination (SE12): • If onset immediate (within ~ 2 hours after injection) may be early cutaneous presentation of serious anaphylactic reaction (see SE11) • If delayed onset (typically within 2 to 3 weeks), consider serum sickness	If initial manifestation is consistent with anaphylaxis, treat as in SE11. If onset > 4 hours, consider treating with corticosteroids and anti-histamines for 5 to 7 days. Note risk of relapse of serum sickness, if steroids are tapered too quickly. Evaluate with CBC, ESR, CRP, LFTs, and UA. Store serum sample before steroid therapy.	Give temporary exemption, pending consultation with allergist.	Submit VAERS report. Seek allergy consult.[4] Review benefit-risk ratio carefully with patient. Consult patient regarding treatment options and further vaccination under controlled desensitization conditions.

Table 2F: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Neurologic Disease, Severe **(SE13):** Possible diagnoses include: • Peripheral neuropathy, nonfocal • Encephalopathy • Guillain-Barré syndrome • Progressive focal neurologic disease (see also SE14) Assumes no other etiologic factor	Consult with neurology for diagnosis and treatment. Some cases may benefit from rapid treatment with high-dose intravenous immunoglobulin.	Give temporary exemption, pending consultation with neurology.	Submit VAERS report. Consider risk for recurrent reaction before administering additional doses.
Focal Neurologic Disease **(SE14):** • Cranial nerve palsy • Neuropathy/neuritis • Radiculopathy • Paresthesias / blepharospasms • Optic neuritis • Ulnar nerve neuropathy (if diagnosis based on physical exam and/or nerve studies. If by symptoms only, give precedence to LR7 group)	Consider compression or trauma to ulnar nerve due to act of injection. Perform clinical work-up. Consult with neurology.	Give temporary exemption, pending consultation with neurology. Emphasize injection in deltoid rather than triceps area.	Submit VAERS report. If persistent, specific treatment may be necessary after neurology consultation.
Prolonged Fatigue (> 60 days)[6] (SE15): < 50% functionality (work, recreation, school), compared to before vaccination • Loss of exercise tolerance • Non-restful sleep a frequent feature • Reduced concentration, decreased memory, as seen in many other chronic illnesses and/or depression	Treat and consult appropriately before 60-day threshold. Consult with specialty center with expertise in chronic fatigue and related syndromes.	Give temporary exemption, pending consultation.	Currently no recognized association with any vaccine. Cases are often eventually linked with other diagnoses. Close follow-up and sequential evaluations may be warranted. Submit VAERS report.

Table 2G: Systemic Events (SE) After Vaccination: July 2002

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Acute Anxiety Response (SE16):	Educate. Reassure. Treat according to clinical condition.	Anthrax: If response related to burning at injection site or related events, consider route.[8]	Some personnel may benefit from psychiatry consultation to assist with diagnosis and management.
Respiratory Illness: symptoms such as cough, coryza, congestion, sore throat and rhinorrhea with or without accompanying systemic symptoms (SE17a—one symptom, SE17b—two or more symptoms)	Treat symptomatically. If symptoms persist ≥ 2 weeks, consider other etiologies.	Proceed with next dose, in most cases.[2,4]	Contrast with SE2a. Some patients may jointly experience SE17 and SE2a.
Gastrointestinal Illness: symptoms such as vomiting and/or diarrhea, with or without accompanying systemic symptoms (e.g., loose stool, abdominal pain, gas, indigestion). Note that category SE5 includes uncomplicated nausea and/or vomiting. (SE18a—one symptom, SE18b—two or more symptoms)	Treat symptomatically. Treat symptomatically. If symptoms persist ≥ 2 weeks, consider other etiologies.	Proceed with next dose, in most cases.[2,4]	Contrast with SE2a. Some patients may jointly experience SE18 and SE2a.
Dizziness (SE19a) Note alternate categories of SE2a and SE6. **"True" Vertigo** (SE19b) • Dysequilibrium characterized by spinning or impulsion, often with nystagmus	An agent such as meclizine or scopolamine may help symptoms of vertigo.	As clinically appropriate.	
Idiosyncratic Response(s) to Live Vaccine(s) (SE20), for example: • Rash after measles, rubella, varicella vaccines • Fever after yellow-fever vaccine • Abdominal cramps, diarrhea after oral typhoid vaccine	As clinically appropriate.	As clinically appropriate.	
Other Systemic Events (SE-xx)	Treat according to clinical condition. Seek consults, as appropriate.	Base decision on complete medical evaluation and	

		consideration of benefit-risk ratio.	

Notes

July 2002

1 - Treatment program for moderate to large local reactions:

- Apply topical corticosteroid cream or ointment at least 2 to 3 times per day until reaction has resolved. Rarely requires oral corticosteroids (e.g., prednisone at 1 mg/kg or 50 to 60 mg per day for 3 to 4 days, tapering off by 10 to 20 mg per day over the next 2 to 4 days). Avoid unprotected sun exposure at the treated sites and use sunscreen aggressively.
- If itching is present, use second-generation antihistamines such as fexofenadine (*Allegra*®) 180 daily . If not available, use first-generation antihistamines (e.g. hydroxyzine, cyproheptadine), recognizing sedating side effects.
- If swelling extends below elbow, a sling may be useful. Some vaccine recipients may benefit from an ice pack within first 24 hours.

2 - Pretreatment program to prevent future large local reactions:

- If localized itching was a dominant feature, pretreat with a second-generation antihistamine such as fexofenadine (*Allegra*®) 180 daily (at least 12 hours before next immunization) , continuing for 48 to 72 hours after the injection (longer if local reaction persists or reflares). If not available, use first-generation antihistamines(e.g. hydroxyzine, cyproheptadine), recognizing their sedating side effects.
- Avoid unprotected sun exposure at the treated site for at least 1 to 2 weeks and use sunscreen aggressively. For at least 3 to 4 days, avoid strenuous exercise using the arm that has received the vaccination.

3 - Comment: Some vaccine recipients will tolerate these types of reactions less well than others, and may be apprehensive about the health risk from the next injection. Careful education and/or willingness to consult with specialists may prevent unnecessary polarization or potential refusal of subsequent vaccinations. Because most of these vaccine recipients can receive additional doses safely, it is important to avoid unnecessary indefinite exemptions, considering the threat and mortality risk of weaponized anthrax.

4 - Prototype Allergy-Immunology Evaluation: Anthrax vaccine skin testing (full-strength prick test, 1:1,000 then 1:100 volume/volume dilution intradermal) with both prick and intradermal histamine (histamine base: prick test 1 mg/ml, intradermal 0.1 mg/ml) and diluent controls (sodium chloride 0.9%). If patient understands risks and benefits of further vaccination and seeks desensitization, provide progressive dose challenge without pretreatment initially, treat any reactions appropriately, and pretreat subsequent doses as needed. Save serum from before and 3 to 4 weeks after procedure, to evaluate immune response later. Serum can be sent to central repository or local medical treatment facility (MTF) serum bank. Use generic consent form for serum collection for patient care, but specifying permission for subsequent use of sera for anonymous retrospective research.

5 - Treatment program for mild to moderate systemic events: Symptomatic treatment to prevent recurrence of adverse events has been very effective for many vaccines, including anthrax vaccine.

6 - Prolonged fatigue linked to vaccination is extremely rare, and has not been characterized as a well-defined vaccine-related adverse event. However, if the patient so desires, VAERS report may be filed. In many cases, other diagnoses are made when more extensive evaluation and follow-up occurs.

7 - Next level of care indicates review by provider with more specialized scope of practice.

8 – **Route and Interval:** DoD and USCG policy is to administer anthrax vaccine using the subcutaneous route, as described in the manufacturer's product labeling ("package insert"). This policy, however, does not preclude a physician or other credentialled health-care provider from making clinical decisions to alleviate future discomfort for an individual Service Member who developed a large or persistent injection-site reaction or experienced a significant systemic event after an earlier dose of anthrax vaccine. Information to be given to these Service Members appears on the following page.

According to the guidelines of the Advisory Committee on Immunization Practices (ACIP. Use of anthrax vaccine in the United States. *MMWR* 2000;49(RR-15)(Dec 15):1-20, http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf or http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4915a1.htm): "At this time, ACIP cannot recommend changes in vaccine administration because of the preliminary nature of this information. However, the data in this report do support some flexibility in the route and timing of anthrax vaccination under special circumstances. As with other licensed vaccines, no data indicate that increasing the interval between doses adversely affects immunogenicity or safety. Therefore, interruption of the vaccination schedule does not require restarting the entire series of anthrax vaccine or the addition of extra doses."

Regarding immunogenicity considerations in individualizing medical treatment: "Because of the complexity of a six-dose primary vaccination schedule and frequency of local injection-site reactions (see Vaccine Safety), studies are under way to assess the immunogenicity of schedules with a reduced number of doses and with intramuscular (IM) administration rather than subcutaneous administration. Immunogenicity data were collected from military personnel who had a prolonged interval between the first and second doses of anthrax vaccine in the U.S. military anthrax vaccination program. Antibody to PA was measured by enzyme-linked immunosorbent assay (ELISA) at 7 weeks after the first dose. Geometric mean titers increased from 450 μg/mL among those who received the second vaccine dose 2 weeks after the first (the recommended schedule, n = 22), to 1,225 for those vaccinated at a 3-week interval (n = 19), and 1,860 for those vaccinated at a 4-week interval (n = 12). Differences in titer between the routine and prolonged intervals were statistically significant ($p < 0.01$)."

Regarding immunogenicity and safety considerations in individualizing medical treatment: "...a small randomized study was conducted among military personnel to compare the licensed regimen (subcutaneous injections at 0, 2, and 4 weeks, n = 28) and alternate regimens (subcutaneous [n = 23] or intramuscular [n=22] injections at 0 and 4 weeks). Immunogenicity outcomes measured at 8 weeks after the first dose included geometric mean IgG concentrations and the proportion of subjects seroconverting (defined by an anti-PA IgG concentration of $\geq$ 25 μg/mL). In addition, the occurrence of local and systemic adverse events was determined. IgG concentrations were similar between the routine and alternate schedule groups (routine: 478 μg/mL; subcutaneous at 0 and 4 weeks: 625 μg/mL; intramuscular at 0 and 4 weeks: 482 μg/mL). All study participants seroconverted except for one of 21 in the intramuscular (injections at 0 and 4 weeks) group. Systemic adverse events were uncommon and similar for the intramuscular and subcutaneous groups. All local reactions (i.e., tenderness, erythema, warmth, induration, and subcutaneous nodules) were significantly more common following subcutaneous vaccination. Comparison of the three vaccination series indicated no significant differences between the proportion of subjects experiencing local reactions for the two subcutaneous regimens but significantly fewer subcutaneous nodules ($p < 0.001$) and significantly less erythema ($p = 0.001$) in the group vaccinated intramuscularly (P. Pittman, personal communication, USAMRIID, Ft. Detrick, MD)." [now published as Pittman PR, et al. Anthrax vaccine: Safety and immunogenicity of a dose-reduction, route comparison study in humans. *Vaccine* 2002; in press.]