

APPENDIX I: INFORMED CONSENT

Protocol #4167

BB IND 11184

**INFORMED CONSENT
FOR
USE OF DIPHTHERIA ANTITOXIN (DAT) FOR SUSPECTED DIPHTHERIA CASES
Investigational New Drug (IND) BB 11184
IRB # 4167**

Flesch-Kincaid: 7.8

INFORMED CONSENT

Your doctor suspects that you/your child have diphtheria. Your doctor has decided that you need diphtheria antitoxin (DAT) and to give it to you/your child. The Food and Drug Administration (FDA) has not approved DAT for diphtheria treatment in this country. The Centers for Disease Control and Prevention (CDC) and your State Health Department can provide DAT for emergency treatment of diphtheria. So, we are offering you/your child treatment with investigational DAT. Diphtheria antitoxin is obtained from horse serum. The company that makes DAT has tested the product to make sure that it is potent for the specified and FDA-approved shelf life.

BACKGROUND

Diphtheria is a serious illness caused by a toxin (poison). This toxin is produced by a bacterium called *Corynebacterium diphtheriae*. The toxin causes life-threatening illness in many people infected with the bacteria. This is because the toxin kills many types of human cells, mainly those in a person's throat, windpipe, heart, and nerves. Harm to these cells can lead to blockage of the windpipe, heart damage, and paralysis of many nerves. This can lead to death in up to 50% of untreated patients. It can also disable those who survive. Airway blockage can occur within the first week of illness. But, the signs of heart and nerve damage most often show in the second or third week.

Use of DAT is vital to treat diphtheria. DAT can greatly lower the risk of lasting health problems or very severe outcomes. DAT works better if given as soon as the doctor suspects diphtheria. Signs of diphtheria usually show slowly from 1 to 5 days after infection. These signs include fever, sore throat, problems swallowing, widespread weakness, and, at times, problems breathing. Often, but not always, the doctor can see a gray, white, or yellow patch (membrane) in the throat or tonsils.

Until January 1997, there was a FDA-approved DAT in the U.S., but the supply of this product has been used up. Since there are so few cases of diphtheria in the U.S. each year, the company decided to stop making it. There is DAT available from a foreign country. FDA considers it "investigational" because it is not licensed in this country. This DAT has been used for years to successfully treat diphtheria patients in other countries. It is like the product that was made in the U.S. previously except that it is made by a different company. We are offering this product to you/your child. In the judgment of your doctor, it is the best treatment you/your child can get.

WHAT IS THE PURPOSE OF THIS TREATMENT?

You/your child may have been exposed to diphtheria. We are offering DAT to you/your child because your doctor suspects you/your child have diphtheria. Without DAT, diphtheria can get worse and life-threatening complications can result. Because DAT is made from horse serum, you/your child may have an allergic reaction after receiving it. Your doctor will give you/your child a skin test. This is to see if you/your child could have an allergy to DAT. For this test the doctor will inject a small amount (less than a drop) of DAT into the skin with a needle. The doctor will check after 20 minutes to see if your/your child's skin gets red or swells. If the skin test is positive for redness and swelling, the doctor may give you/your child DAT in very small doses to lower the risk of an allergic reaction. The doctor may also give you/your child other medicines to lower the risk.

Your/your child's doctor will give you/your child DAT with a needle directly into a vein or muscle. The doctor will take samples (using a swab that looks like a Q-tip) from your/your child's throat and nose before treatment. Also, if there is a patch on your/your child's throat, the doctor may need to scrape off a small piece of this patch and sent to the lab. These tests allow us to confirm that you/your child have diphtheria. You/your child's doctor will send the samples and any scraping to the CDC so we can culture the bacteria and find the toxin.

ARE THERE ANY BENEFITS?

DAT can reduce the bad effects of diphtheria toxin. It does not reverse any problems that have already happened. DAT will prevent later problems if it is given early in the illness. Without DAT, severe problems due to diphtheria can happen. About 3 out of 10 persons with diphtheria do not survive without DAT.

ARE THERE ANY RISKS?

Treatment with DAT is not without risk. As with all treatment, there is a slight chance that there are some risks that we do not know about.

The risks of getting any medicine by vein include brief pain, bleeding, and bruising of the skin around the site where the needle went in. Other risks are soreness and swelling at that site and possible infection.

You/your child may react to DAT in a number of ways. These include fever and chills, usually within the first 24 hours. These will go away by taking aspirin or Tylenol (aspirin should not be used in children due to risk of Reye syndrome).

A few people (<1%) may have a more serious allergic reaction called *anaphylaxis*. It can happen in people who are allergic to horse products. Most of them do not know they are allergic. This reaction can be mild, with only hives and a hoarse voice. Or, at rare times, it can be more severe, with a quick and serious drop in blood pressure and problems breathing. Severe anaphylaxis can be fatal. Anaphylaxis requires emergency medical treatment, medications, and, at times, a machine to help in breathing. Skin testing just before giving DAT can show if a person is allergic, and things can be done to lower the risk.

Also, a small number of people (<5%) getting horse serum may get pains in their joints and back, fever, and a rash a few weeks after treatment. These problems can last a couple of weeks. This is called serum sickness. Rarely, persons with serum sickness can have a more severe illness with kidney, nerve, or heart inflammation. Doctors can treat serum sickness with standard medicines.

ARE THERE RISKS RELATED TO PREGNANCY?

There are no known extra risks from DAT for a pregnant woman or her unborn baby (fetus). Because about a third of all patients who have diphtheria do not survive without DAT, treating diphtheria is of much greater benefit to the mother or the fetus than the possible risk of DAT treatment. Facts we learn from this test will be used only to help us learn if this product has any harmful effects on the mother or fetus.

WHAT ABOUT PRIVACY?

The medical records with this protocol are subject to the terms of the Privacy Act of 1974, 5 U.S.C. Section 552a. People who work for the local health department, the CDC, and FDA may read your/your child's medical records. They may obtain personally identifying information from these records. All data we gather about you/your child will be kept private to the extent allowed by law. You/your child will not be named when we present the results.

IS THIS PROTOCOL VOLUNTARY?

It is your/your child's choice to receive DAT. You/your child may refuse or stop treatment at any time. If so, you/your child will not lose the right to other health care or services that you/your child might be due apart from this. You/your child are not giving up any of your legal rights by signing this form. We will give you a copy of this form.

WHAT ARE THE COSTS?

CDC is providing DAT to you/your child at no cost. CDC does not pay for skin tests or lab tests. Thus, you (or your health insurer, Medicare, or Medicaid) will have to pay for any care that is needed

WHAT OTHER CHOICES DO YOU/YOUR CHILD HAVE BESIDES THIS PROTOCOL?

No other treatment for diphtheria infection exists.

WHAT HAPPENS IF I OR MY CHILD ARE HARMED?

If you are or your child is harmed because of receiving DAT, treatment will not be provided by CDC. CDC does not normally pay for harm done to you/your child because of receiving DAT treatment. Thus, you (or your insurer, Medicare, or Medicaid) will have to pay for any care that is needed. However, by signing this consent form and agreeing to receive DAT treatment, you are not giving up any of your or your child's rights.

WHO DO YOU CALL WITH PROBLEMS OR QUESTIONS?

You can ask your treating physician any question you have about this treatment. If you/your child have concerns or questions about the DAT treatment, please call your treating physician at _____ or the Meningitis and Vaccine Preventable Diseases Branch, National Center for Immunization and Respiratory Diseases, CDC at (404) 639-3158. If you think you or your child have been injured or have questions about your or your child's rights as a participant in this protocol, please call **CDC's Human Research Protection Office** at 1-800/584-8814. Please leave a message including your/your child's name and phone number, including your area code. Say that you are calling about CDC Protocol # 4167. Someone will call you back as soon as possible.

CONSENT STATEMENT

- I have read and understood the above information or had it read to me/my child.
- I have had my questions answered.
- I agree to take investigational DAT to treat diphtheria or for my child to take DAT to treat diphtheria.
- I agree to let the local/state health department, CDC, and the FDA see my/my child's medical records.
- I **DO NOT** agree to take investigational DAT to treat diphtheria or for my child to take DAT to treat diphtheria.

Signature of patient or guardian _____

Date _____

Type/Print name of patient _____

IF PATIENT IS INCAPABLE OF PROVIDING INFORMED CONSENT

If the patient is too ill to give informed consent; and if next of kin cannot be found after an effort is made to locate them; and if the illness is life threatening, a physician has made the decision to begin this treatment:

Signature of physician: _____

Date: _____

Time of day: _____ AM/PM (circle one)

Type/print name of physician: _____

Efforts to reach the next of kin have included the following (describe):

This document can be found on the CDC website at:

<http://www.cdc.gov/vaccines/vpd-vac/diphtheria/dat/downloads/consent.pdf>