APPENDIX 1: INFORMED CONSENT/PARENT PERMISSION FORM FOR USE OF DAT FOR SUSPECTED DIPHTHERIA CASES
Protocol #4167
BB IND 11184

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

Flesch-Kincaid: 7.8

INFORMED CONSENT

The doctor thinks you/your child have diphtheria. Diphtheria is a serious disease caused by a toxin (poison) made by bacteria. The toxin can make people infected with the bacteria get very sick and even die.

Your doctor has decided that diphtheria antitoxin (DAT) may help prevent you/your child from a more serious illness from diphtheria. The Centers for Disease Control and Prevention (CDC) and your State Health Department can provide DAT for emergency treatment of diphtheria.

The Food and Drug Administration (FDA) has not approved DAT for diphtheria treatment in this country. However, FDA allows CDC to offer it to you/your child through a special program. This program is important for two reasons. First, there are no FDA-approved treatments for diphtheria. Second, diphtheria is a very serious disease.
So, we are offering you/your child treatment with investigational DAT. Diphtheria antitoxin is obtained from horse serum. The DAT product has been tested to make sure it meets the standards for potency.

After administering DAT, your doctor will also give you/your child appropriate antibiotics**.**

BACKGROUND

Diphtheria is a serious disease caused by a toxin (poison) made by bacteria called *Corynebacterium diphtheriae*. The toxin can make people infected with the bacteria get very sick and even die.

Symptoms of diphtheria usually start slowly from 2 to 5 days after infection. They can include

- Fever
- Sore throat
- Problems swallowing
- A gray, white, or yellow patch (membrane) in the throat
- Problems breathing
- Widespread weakness

The toxin often kills cells in the throat, windpipe, heart, and nerves. During the first week of illness, damage to the throat and windpipe can block air from getting to the lungs. Signs of heart and nerve damage most often show in the second or third week.

Up to one in three patients who do not get treated for diphtheria will die. Patients who survive may have long-term health problems.

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?

Taking DAT may greatly lower the risk of bad effects from diphtheria toxin. We are offering DAT to you/your child because the doctor thinks you/your child have diphtheria. Without treatment, diphtheria can get worse, and cause deadly or long-term problems.

WHAT WILL HAPPEN IF I ACCEPT THIS TREATMENT?

Because DAT is made from horse serum, you/your child may have an allergic reaction after receiving it. DAT is currently the only treatment available for diphtheria in the US.

Before treatment, the doctor will

1. Give you/your child a skin test. This is to see if you/your child could have an allergy to DAT.
    a. For this test the doctor will inject a small amount (less than a drop) of DAT into the skin with a needle.
    b. The doctor will check after 20 minutes to see if your/your child's skin gets red or swells.
        i. 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.
        ii. The doctor may also give you/your child other medicines to lower the risk.
2. Rub swabs that look like Q-tips against your/your child's throat and nose.
3. Try to scrape off a small piece of the patch (if there is one) in your/your child's throat.
4. Send the swabs and sample to labs for testing.

These lab tests will make sure it is diphtheria that is making you/your child sick. A lab at CDC may do some of these tests. Since these lab tests take time, the doctor will not wait for results before starting treatment.

During treatment, the doctor will

1. Give you/your child DAT to stop the toxin from causing more damage. The doctor will use a needle to give the medicine directly into a vein.
2. Give you/your child an antibiotic to kill the bacteria that are making the toxin.

ARE THERE ANY BENEFITS?

Yes. DAT can lessen or stop the bad effects of diphtheria toxin. It works better if given early in the illness. It does not reverse any problems that have already happened. 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?

Yes.

All medicines given through a needle have risks

The risks of getting any medicine by vein include issues at or around the site where the needle went in:

- Pain that doesn't last a long time or soreness
- Bleeding
- Bruising of the skin
- Swelling
- Possible infection

General side effects are most common

You/your child may get a fever or chills, usually within the first 24 hours. These will go away by taking aspirin (for adults only) or Tylenol (for children and adults).

Allergic reactions are rarely serious

Mild allergic reactions can occur, usually soon after starting or receiving treatment. Examples of mild allergic reactions include hives and a hoarse voice.

Serious allergic reactions, called *anaphylaxis,* to medicines like DAT are rare and usually happen soon after starting or receiving treatment. Examples of anaphylaxis include a quick drop in blood pressure and problems breathing. Severe anaphylaxis can be deadly. Anaphylaxis requires emergency medical treatment, medicines, 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

Some allergic reactions can occur later

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. This is called serum sickness. Serum sickness is one type of allergic reaction that can start a few weeks after treatment and can last a couple of weeks. Rarely, serum sickness can cause serious kidney, nerve, or heart problems. Doctors have medicines to treat serum sickness.

Unknown risks

There is a small chance that there are risks that we do not know about.

ARE THERE RISKS RELATED TO PREGNANCY?

There are no known extra risks from DAT for a pregnant person or their 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 pregnant person or the fetus than the possible risk of DAT treatment.

WHAT ABOUT PRIVACY?

Medical records related to you/your child's DAT treatment are also protected under something called Certificate of Confidentiality from the Centers for Disease Control and Prevention (CDC). Unless you say it is okay, anyone involved in providing DAT cannot release information that may identify you/your child for a legal action or lawsuit or as evidence. This protection applies

to requests from federal, state, or local civil, criminal, administrative, legislative, or other proceedings. For example, the Certificate would protect your/your child's information from a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop

- Reporting required by a federal, state, or local law.
  - o For example, some laws require reporting of abuse, communicable diseases, and threats of harm to yourself or others.
- Federal or state government agency from checking records or evaluating programs.
- Reporting required by the FDA.
- Your DAT treatment information from being used to learn more about the drug , if allowed by federal regulations.

Information related to you/your child's DAT treatment may also be released whenever you say it is okay. The Certificate of Confidentiality does not stop you from releasing or getting copies of your own or your child's information.

Forms sent to CDC will be encrypted or password protected and transmitted directly to the CDC Meningitis and Vaccine Preventable Diseases Branch by fax (678-669-2771) or e-mail to: lzn6@cdc.gov. The data will be stored in a password protected, limited access database that is housed on CDC's secure server.

IS THIS PROTOCOL VOLUNTARY?

It is your/your child's choice to receive DAT. You/your child may choose for you/your child not to receive it. You can also choose you/your child to receive it and then stop treatment at any time.

No matter which choice you make, 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 your physician and to you/your child at no cost. CDC does not pay for skin tests or lab tests. *CDC does not pay for medical care.*
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/your child can ask your treating physician any question you have about this treatment. If you have concerns or questions about the DAT treatment or feel that you or your child have been harmed as a result of participating in the DAT program, please call Dr. Erin Tromble at (404) 498-5020 (in the Meningitis and Vaccine Preventable Diseases Branch, National Center for Immunization and Respiratory Diseases, CDC. If you have questions about your rights as a participant in this program, please call **CDC's Human Research Protection Office** at 1-800-584-8814 and say that you are calling about CDC protocol # 4167. Leave a brief message with your name, area code, and phone number. Someone will call you back as soon as possible.

CONSENT STATEMENT
I have read the form or it has been read to me. I have been given a chance to ask questions, My questions have been answered. I agree to receive (or have my child receive) DAT to treat diphtheria. I agree to allow the local/state health department, CDC, and the FDA see my/my child's medical records.

Print Patient's Name:_____

Patient's/Parent's Signature: _____ Date:_____

Note: If patient is unable to sign, a legally authorized representative may sign.

Legally Authorized Representative Signature: _____

Print Name: _____ Date: _____

IF OBTAINING INFORMED CONSENT IS NOT FEASIBLE
In the event that obtaining informed consent is not feasible because the patient is unable to respond and make wishes known about DAT treatment *and* no legal guardian or next-of-kin is present, the following provides for the treating physician to make a clinical determination to treat with DAT provided that an independent physician also certifies to the following within 3 working days of treating the patient with DAT:

1. Patient is confronted by a life-threatening situation necessitating the use of DAT.
2. Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally-effective consent from, the patient.
3. Time is not sufficient to obtain consent from the patient's legal representative.
4. There is no alternative method of approved or generally recognized therapy available that provides an equal or greater likelihood of saving the life of the patient.

☐ Documented as such in the patient's medical record and will ensure the patient or patient's legally

authorized representative will be made aware that investigational DAT was administered.

☐ Name and signature of treating physician who made the determination to administer DAT to the patient when informed consent could not be obtained:

_____	_____	_____
Name	Signature	Date

☐ Name of second physician, who is not otherwise participating in this treating protocol, who reviewed and evaluated the decision to administer DAT to the patient:

_____	_____	_____
Name	Signature	Date

☐ Return an encrypted or password protected copy of this signed page to the CDC Meningitis and Vaccine Preventable Diseases Branch via fax (678-669-2771) or e-mail to lzn6@cdc.gov within 5 working days.