CAROLINAS HEALTHCARE SYSTEM

SUBJECT INFORMATION AND CONSENT FORM

Name of Research Study: Multicenter, Double-blind, Randomized, Parallel-group, Monotherapy, Active-control Study to Determine the Efficacy and Safety of Daclizumab High Yield Process (DAC HYP) versus Avonex® (Interferon β-1a) in Patients with Relapsing-Remitting Multiple Sclerosis

Protocol #: 205MS301

Sponsor: Biogen Idec

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PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

This Subject Information and Consent Form may contain words you do not understand. Please ask the study doctor or the study staff to explain any words or procedures that you do not clearly understand.

The purpose of this form is to give you information about the research study and, if signed, will give your permission to take part in the study. The form describes the purpose, procedures, benefits, risks, discomforts and precautions of the research study. You should take part in the study only if you want to do so. You may refuse to take part or withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. Please read this Subject Information and Consent Form and ask as many questions as needed. You should not sign this form if you have any questions that have not been answered to your satisfaction.

PURPOSE AND DESCRIPTION OF THE RESEARCH STUDY

Dr. Jill Conway is asking you to participate in this research study of the experimental drug DAC-HYP at the Neuroscience & Spine Institute (NSSI) and Carolinas HealthCare System (CHS). "Experimental" means that it has not been approved by the Food and Drug Administration (FDA) for sale in the United States. You are being asked to take part because you have Relapsing-Remitting Multiple Sclerosis (RRMS). The study will involve about 1,500 subjects at about 250 different centers. You will be one of about 10 subjects at the NSSI. The study is scheduled to take place for 96 to 144 weeks and will include approximately 38 visits to the study doctor.

The purpose of this study is to test the superiority of DAC HYP, a type of antibody made in the laboratory, compared to the drug Avonex® in preventing MS relapse in patients with RRMS. (Avonex® is approved by the FDA for treatment of relapsing-remitting MS). The hypothesis for using DAC HYP to treat MS is that it selectively inhibits the activity of white blood cells – specifically those known as T cells that attack the brain and spinal cord. This study will also allow researchers to learn more about the safety of long-term treatment with DAC HYP in people with MS.

Avonex® is approved by the FDA for treating RRMS.

The Sponsor also wants to see if DAC HYP affects the MS lesions (abnormal spots) in your brain by checking whether certain types of MS lesions change in number and/or size during DAC HYP treatment. This will require that you have up to 4 MRI (Magnetic Resonance Image) scans during this study, which will be explained later in this Subject Information and Consent Form. The Sponsor also wants to learn if receiving DAC HYP treatment for a long time causes your body to develop antibodies against DAC HYP. Antibodies are made naturally by your body in response to an unfamiliar substance (for example, to fight germs that cause diseases). Sometimes antibodies can interfere with effects of a medicine. This study will also measure the levels of DAC HYP in your blood at different times.

Finally, this study will test blood samples for biomarkers, which are naturally-occurring substances in the body. Examples of biomarkers include insulin and blood sugar, which are changed in diabetes. The presence or amount of biomarkers can be detected by testing samples (such a blood or tissue). This study will try to learn more about biomarkers in MS and how they might be used to predict a patient's response to treatment with DAC HYP. Additional information about sample collection and testing for biomarkers is provided later in this Informed Consent Form.

EXCLUSION CRITERIA

Subjects will be excluded from study entry if any of the following exclusion criteria exist at randomization or at the time point specified in the individual criteria listed below:

Medical History

1. Diagnosis of primary progressive, secondary progressive, or progressive relapsing MS (as defined by Lublin and Reingold, 2001). These conditions require the presence of continuous clinical disease worsening over a period of at least 3 months. Patients with these conditions may also have superimposed relapses, but are distinguished from relapsing remitting patients by the lack of clinically stable periods or clinical improvement.
2. Known intolerance, contraindication to, or history of non-compliance with Avonex 30 mcg.

(Note: Current or prior use of an approved Inteferon beta – also written as IFN β – preparations, including Avonex, is allowed, as long as the subject is currently appropriate for Avonex® treatment according to local prescribing information. Avonex and other IFN β preparations are proteins made and released by white blood cells called "lymphocytes" in response to the presence of viruses, bacteria, parasites and other infectious agents that invade the body.

3. History of malignancy; however, subjects with a history of excised (removed) or treated basal cell carcinoma (cancer) or fewer than 3 squamous cell carcinomas are eligible to participate in this study.
4. History of severe allergic or anaphylactic reactions, in which the body severely reacts to a foreign or external protein or drug.
5. Known hypersensitivity (extreme sensitivity) to study drug or their excipients (the inactive substances used as a carrier for the active ingredients of a medication).
6. History of abnormal laboratory results that, in the opinion of the investigator, are indicative of any significant cardiac (heart), endocrine (hormone), hematological (blood), hepatic (liver), immunologic (immune), metabolic, urologic (urinary), pulmonary (lung), gastrointestinal (digestive), dermatologic (skin), psychiatric (mental), renal (kidney), neurological (brain) (other than MS), and/or other major disease that would preclude administration of DAC HYP.
7. History of human immunodeficiency virus (HIV) or other immunodeficient conditions.
8. History of drug or alcohol abuse (as defined by the Investigator) within the 2 years prior to randomization.
9. History of seizure disorder or unexplained blackouts OR history of a seizure within 6 months prior to Baseline.
10. History of suicidal ideation or an episode of clinically severe depression (as determined by the Investigator) within 6 months prior to Day 1.
    (Note: Subjects receiving ongoing antidepressant therapy will not be excluded from the study unless the medication has been increased within the 6 months prior to Baseline.)
11. An MS relapse that has occurred within the 50 days prior to randomization AND/OR the subject has not stabilized from a previous relapse prior to randomization.

12. Known history of, or positive screening test result for hepatitis C virus (HCV) or hepatitis B virus.
13. Varicella or herpes zoster virus infection or any severe viral infection within 6 weeks before screening.
14. Exposure to varicella zoster virus within 21 days before screening.
15. Any of the following abnormal blood tests at screening:

    - Hemoglobin ≤9.0 g/dL
    - Platelets ≤100 x 109/L
    - Lymphocytes ≤1.0 x 109/L
    - Neutrophils ≤1.5 x 109/L
    - Alanine aminotransferase/serum glutamate pyruvate transaminase (ALT/SGPT), aspartate aminotransferase/serum glutamic oxaloacetic transaminase (AST/SGOT), or gamma-glutamyltransferase ≥2 times the upper limit of normal (ULN)
    - Serum creatinine ≥ULN.

Treatment History

16. Any previous treatment with daclizumab or other anti-CD25 monoclonal antibody
17. Any of the following types of live virus vaccine from 4 weeks before randomization:

    - measles/mumps/rubella vaccine, varicella zoster virus vaccine, oral polio vaccine, and nasal influenza vaccine.

18. Infection (viral, fungal, bacterial) requiring hospitalization or intravenous (IV) antibiotics within 8 weeks before randomization.
19. Elective surgery performed from 2 weeks prior to randomization or scheduled through the end of the study.
20. Treatment with another investigational drug or approved therapy for investigational use within the 6 months prior to randomization.
21. Prior treatment with the any of the following:

    - Total lymphoid irradiation
    - Cladribine
    - Mitoxantrone
    - T-cell or T-cell receptor vaccination
    - Any therapeutic monoclonal antibody, except natalizumab (Tysabri)

22. Prior treatment with cyclophosphamide or natalizumab within 1 year prior to randomization.
23. Prior treatment with any of the following medications or procedures within the 6 months prior to randomization:

- Cyclosporine
- Azathioprine
- Methotrexate
- Mycophenolate mofetil
- Intravenous immunoglobulin (IVIg)
- Plasmapheresis or cytapheresis.

24. Treatment with any of the following medications within the 30 days prior to randomization:

    - IV corticosteroid treatment
    - Oral corticosteroid treatment
    - 4-aminopyridine or related products
    - Glatiramer acetate

(Note: Subjects who are currently receiving an approved IFN β preparation are not required to washout from IFN β prior to randomization.)

Miscellaneous

25. Female subjects considering becoming pregnant while in the study.
26. Female subjects who are currently pregnant or breastfeeding.
27. Previous participation in this study.
28. Subjects for whom MRI is contraindicated – e.g., have pacemakers or other contraindicated implanted metal devices, are allergic to gadolinium, or have claustrophobia that cannot be medically managed.
29. Unwillingness or inability to comply with the requirements of the protocol, including the presence of any condition (physical, mental, or social) that is likely to affect the subject's ability to comply with the protocol.
30. Other unspecified reasons that, in the opinion of the Investigator and/or Biogen Idec, make the subject unsuitable for enrollment.

HOW THE STUDY WORKS

If you agree to take part in this study, you will first sign this Subject Information and Consent Form before any study-related procedures are performed, including discontinuation of any disallowed medications.

Study Drug Administration Groups

If you agree to be in the study, you will be randomized to one of two study drug administration groups. Being randomized means that you are put in a group by a chance process, like flipping a coin. You have 50% chance of being in either group. You will not know what group you are in, (and neither will your doctor). We are using this method because it is not clear at the present time which drug is better.

To prevent you from knowing what group you are in, you will receive injections of a placebo of which ever study drug you are not assigned to. A placebo is a substance that *looks* like the study drug, but does not contain the active ingredient. All subjects in the study will receive active study drug in addition to placebo.

The study drug administration groups for this study are:

- Group 1: DAC HYP at a dose of 150 mg given as a subcutaneous (SC) injection (an injection just under the skin) every 4 weeks, and placebo given as an intramuscular (IM) injection (injected into the muscle) every week.
- Group 2: Avonex® at a dose of 30 mcg (which is the dose approved to treat MS) given as an IM injection every week, and placebo given as an SC injection every 4 weeks.

Your participation in this study is expected to last for up to 144 weeks (about 36 months). During that time, you will receive study drug (either DAC HYP or Avonex). You, the study doctor, and the study staff will not know whether you are receiving DAC HYP and placebo, or Avonex and placebo. Although you and your doctor will not know which study drug you are receiving, this information can be determined in the event of an emergency.

Throughout the study, all your subcutaneous (SC) injections (given every 4 weeks) will be performed in the clinic under supervision. Your first IM (intramuscular) injection will also be performed in the clinic. After that, you will give yourself the weekly IM injections at home, or you may have a friend or relative give your IM injections. The study staff will teach you, or your friend or relative, how to give IM injections.

Clinic Visits

For the study, you will come to the clinic for about 38 visits over about 36 months. The first visit will be a "screening visit" to see if you are eligible to be in the study. If you qualify for the study, you will return to the clinic for a "baseline visit" within 4 weeks, at which time you will have additional tests, your study drug administration group will be assigned, and you will receive your first injections of study drug. For the rest of the study, you will have a clinic visit about every 4 weeks. Extra visits may be needed if you have symptoms of an MS relapse or if you have other significant changes in your health that may be related to the use of the study drug. You may also be asked to have follow-up visits at 16 weeks and 24 weeks after your last dose of study drug.

"Study drug" refers to both your active study drug and the placebo study drug in the rest of this form.

During the study, we will do the following tests at some or all of the visits:

- Medical history
- Physical examination (including weight)
- Vital signs (heart rate, blood pressure, and temperature)
- ECG (an electrocardiogram to determine heart function)
- Routine and special blood tests (some of the blood samples will also be used to gather information about how DAC HYP works in the body and how the body affects DAC HYP; some of the blood tests will check for antibodies to DAC HYP. As part of this testing, ribonucleic acid (RNA), which tells the cells in your body which proteins to produce, may be separated out from your blood samples and tested to see how your body responds to treatment. These samples will only be used for research in MS and will not be used for genetic studies [DNA will not be taken from these samples]. (You will be asked to sign a separate consent section at the end of this main consent form for these biomarker samples.)
- Blood tests for hepatitis B and hepatitis C. The study doctor or study staff may report a positive test result to the local health department. The hepatitis tests are confidential, and the study doctor or study staff will not share your results outside this study unless state law requires it. The results of these tests must be negative in order for you to be in the study.
- Urine tests
- Blood and urine pregnancy tests in women able to have children
- Neurological evaluations including dexterity, walking, and visual tests
- Patient questionnaires including questions about physical functioning, bodily pain, general health, social functioning, emotions, and mental health
- Brain MRIs [see below for more information]
- Study drug injection site examination
- You will be asked about any new MS symptoms or worsening of symptoms you may be experiencing
- Any side effects you may have will be recorded
- Skin biopsies and/or photographs of areas of your body may be taken if you get a rash or other skin condition. These photographs may be reviewed by study personnel during the safety reviews that are conducted for this study. These photographs may also be shared with regulatory agencies, if appropriate. (You will be asked to sign a separate consent at the end of this main consent form for photographs.)
- You will be asked about medications you are taking, including over-the-counter medications, vitamins and other supplements.

We will collect about 920 mL (about 62 tablespoons) of blood during this study. The most blood collected at any one visit will be about 65 mL (about 5 tablespoons). We may also do more tests, if needed for your safety.

MRIs

MRIs (Magnetic Resonance Images) can detect the changes in your brain that occur as a result of MS. For the MRI scans, you will need to lie down in the scanner and keep still for approximately 45 minutes. At one point in the procedure, you will be injected with an imaging agent (dye) called gadolinium so that the scanner can detect particular changes in the brain. This imaging agent is not experimental and is routinely used in MRIs.

Before your MRI, the technician will discuss the MRI procedures with you. Prior to each scan, you may be asked to complete an MRI Safety Checklist to ensure there are no reasons why you should not have the MRI scan. MRIs should not be performed when you are pregnant. You should not be in the study if you are pregnant. If you think that you are pregnant or think that there is a chance that you are pregnant, you must inform the study staff before the procedure. MRI is a procedure that uses a magnetic field and radio waves to make a special picture of the brain. The MRI technician will discuss the requirements or restrictions with you. Some of the risks associated with MRI scans are described later in this Subject Information and Consent Form.

You will be asked to remove the following before entering the scanning room:

- watches
- hairclips
- earrings and non-gold jewelry
- braces and corsets
- keys and coins
- hearing aids
- credit and cashpoint/debit cards
- dentures
- travel cards
- any other metal objects in your pockets (e.g., cigarette lighters, scissors)

You should **NOT** undergo this MRI test scan if you:

- have claustrophobia (a fear of confined spaces) that cannot be medically managed
- have a severe kidney disorder
- have any metallic implants such as:
    - pacemakers
    - bladder implants
    - pain-relief implants
    - timed-release drug dispenser implants
    - skull plates
    - artificial heart valves

  - aneurysm clips
  - ear implants
  - artificial joints, bone screws, pins or plates for broken bones

- have ever had metal enter your body through industrial injury or military service (e.g., bullets)
- have ever worked on drilling or milling machines where metal may have entered your eyes
- have any tattoos or permanent eyeliner
- have ever consulted an eye doctor to have something removed from your eye
- have ever had heart trouble
- are female and could be, or are trying to become pregnant. If you are a woman able to have children, you may be required to have a pregnancy test before you have the MRI scan

Treatment of Flu-Like Symptoms

To help reduce the severity of any flu-like symptoms you may experience from the study drug, you will take acetaminophen (paracetamol), ibuprofen, naproxen, or aspirin (your doctor can choose which one is best for you) before each IM injection and after each IM injection (following the schedule the study doctor gives you). You will continue treatment for flu-like symptoms for at least the first 24 weeks of the study or until your study doctor tells you to stop.

Your Responsibilities

- Come to the study site for all study visits, and other visits requested by the study staff.
- Follow all instructions about the study drug. If you are injecting at home, you will be given a study diary to record dosing information (bring the diary with you to your visits).
- Tell the study staff immediately if you get any new or worsening symptoms or any unwanted effects.
- If you have any symptoms of an MS relapse, develop a rash, think you might have an infection, or notice unusual pain, redness, or swelling around your injection site, you must telephone your study doctor within 48 hours and you may be required to visit the clinic within 72 hours of the start of the symptoms. At this visit, neurological tests, physical examination, and other blood tests may be done. You are allowed to have intravenous steroids (IVMP) for treatment of a MS relapse. Your study doctor will discuss this treatment with you if a relapse occurs.
- The study doctor may ask you to see a dermatologist if you have any skin reactions.
- The study doctor may tell you to miss some doses of study drug if you develop certain medical conditions, such as a significant fever or infection, or abnormal blood tests. Do not restart study drug treatment until your study doctor gives permission.

- Males and females of childbearing potential must use effective contraception during the study and for 4 months after the last dose of study drug. Your study doctor will discuss this with you in more detail. Some females may not have to use contraception if they are post-menopausal for at least 1 year or are surgically sterile (no uterus or no ovaries).
- DAC HYP stays in a person for approximately 4 months after the last dose, so do not donate blood or get any live vaccines – oral polio vaccine (the Sabin vaccine), the nasal spray version of the H1N1 flu vaccine or vaccines for rubella, measles, mumps or chicken pox vaccines – during the study or for 4 months following your last dose of study drug. Your study doctor will discuss these restrictions with you in more detail.
- Tell the study staff about any other medicines you have taken (including vitamins, herbal or alternative remedies or medicines you buy over the counter).
- Do not start taking any new medications (including non-prescribed drugs, vitamins or herbal preparations,) unless you have permission from your study doctor.
- During the study you will not be allowed to use the following (your study doctor will discuss this in more detail):
    - any alternative drug treatments for the treatment of MS such as chronic immunosuppressant therapy or other immunomodulatory treatments (including, but not limited to: interferon-beta, interferon-alpha, glatiramer acetate, natalizumab, cyclophosphamide, methotrexate, azathioprine, 4-aminopyridine or related products, except for Fampridine SR, if you were already taking this before you entered the study).
    - any investigational product, including investigational therapies for MS symptoms and investigational therapies for non-MS uses.
    - total lymphoid irradiation, cladribine, T-cell or T-cell receptor vaccination, any therapeutic monoclonal antibody, mitoxantrone, cyclosporine, intravenous (IV) immunoglobulin, plasmapheresis or cytapheresis.
    - any systemic steroid therapy including, but not limited to, oral corticosteroids (for example, prednisone) or periodic treatment with IVMP, except for the protocol-defined treatment of MS relapses, or short-term use to treat a general medical condition.

- During the study you will be allowed to use the following (your study doctor will discuss this):
    - steroids that are applied topically or inhaled.
    - treatments for MS symptoms such as muscle spasms, depression, or fatigue, but you should try to continue with the same dose throughout the study.
    - IV methylprednisolone for treatment of an acute MS event (under the conditions of the protocol).

RISKS

The study has several risks. First, it is possible that you will get the new drug (DAC HYP)but do less well than you have been doing. Because DAC HYP is new, we may not yet know all the side effects: something unexpected could happen.

Daclizumab Risks

Overall, DAC HYP has been given to more than 320 subjects including 71 healthy volunteers who received DAC HYP in 3 completed clinical studies and more than 250 subjects with Multiple Sclerosis (MS) have received DAC HYP in ongoing MS studies.

Side Effects Reported in Healthy Volunteer Studies

In the healthy volunteer studies, DAC HYP appeared to be well tolerated. The most common side effects seen across the studies were common cold, headache, throat pain, injection site pain or injection site reaction, skin rashes, fatigue or tiredness, and dizziness. An increased number of infections and skin rashes were reported in subjects treated with DAC HYP compared to placebo (a placebo looks like the study drug but does not contain any active ingredients). The majority of these were mild, but some serious events were reported.

Serious adverse events reported in the healthy volunteer studies included a serious bacterial infection in the blood, viral pneumonia (inflammation of the lungs), inflammation of the lymph nodes, and appendicitis.

Other Important Side Effects

You should not take DAC HYP if you are allergic to DAC HYP, other forms of daclizumab, or any of its ingredients.

DAC HYP works by acting on your immune system, so it is possible that you may be more likely to get an infection during the study. An increase in infections, some serious, have been seen during studies with DAC HYP. If you have any signs of an infection during treatment with DAC HYP, you should tell your doctor immediately.

Treatment with DAC HYP may increase your risk of having a skin reaction or rash during the study. An increase in skin reactions, some serious, have been seen during studies with DAC HYP. If any new skin rashes or conditions appear, you should tell your doctor as soon as possible. Subjects who experience a significant skin reaction, like a serious rash, or skin inflammation, will be evaluated by a dermatologist. The dermatologist is to take photographs, and if appropriate, obtain a biopsy prior to prescribing treatment.

About 25% of subjects treated with DAC HYP developed antibodies against the drug (antibodies are made naturally by your body in response to an unfamiliar substance). It is not known if these antibodies will affect the way DAC HYP works or whether they will cause adverse events. It is unknown if antibodies to DAC HYP will have any long-term effects.

The safety and effectiveness of vaccines (such as tetanus, measles, or flu shots) during treatment with DAC HYP is not known. You should not receive a live or live-attenuated (which means a live but weakened organism) vaccine during treatment with DAC HYP.

Side Effects Seen with Another Form of Daclizumab

Daclizumab (Roche Penzberg) is a different form of DAC HYP. In an MS study, 153 MS patients were treated with daclizumab in combination with interferon-beta. Daclizumab appeared to be well tolerated. The most common side effects in the daclizumab group were multiple sclerosis relapse, fatigue, headache, urinary tract infection, common colds, injection site irritation or pain, inflammation of the sinuses, decrease in sensation, nausea, and rash. There were more serious infections reported in the patients treated with daclizumab than patients treated with placebo. Serious infections included pneumonia, other infections in the lung or airways, kidney infection, serious bacterial infection in the blood, appendicitis, and meningitis (infection or inflammation of the membranes of the brain). Patients treated with daclizumab had more skin-related events such as rashes, eczema, and psoriasis, including some serious events.

Studies in Animals

Changes in the skin (redness, dryness, broken skin), including a serious rash, were seen in animals treated with DAC HYP. When animals were given high doses of DAC HYP, clusters of a particular type of cell were seen in their brains and a few of their spinal cords. These cell clusters were not seen in animals given lower doses of DAC HYP (doses about 5 times greater than what you would be given). These cells are normally in the brain, but are not usually found in these clusters. At doses about 100 times greater than what you would be given, clusters were occasionally accompanied by microscopic areas of blood and/or inflammation. The clusters of cells did not appear to have any harmful effects on the brain or spinal cord and went away in most animals after they stopped being given DAC HYP. It is not known if these clusters of cells could also occur in people treated with DAC HYP. Some animals made antibodies against DAC HYP. The antibodies made the levels of DAC HYP in the blood go down, which might prevent the drug from working.

Animal studies do not always predict what happens in people. Please talk with your study doctor if you have any questions.

Cancer Risk

At present, we do not know the risk of developing cancer from taking DAC HYP. Studies to find out if DAC HYP increases the risk of cancer have not been done.

Unknown Risk

As with any new drug, there is a risk of rare or previously unknown side effects, and/or a chance that DAC HYP might interact with other drugs. The study staff will tell you if new information about DAC HYP becomes available that may affect your willingness to be in the study.

Avonex® Risks

Avonex® (interferon beta-1a) is made by Biogen Idec Inc. and is a form of a protein that occurs naturally in the body, which helps regulate your body's immune system. Avonex® is currently approved to treat relapsing forms of multiple sclerosis (MS). Avonex® will not cure MS, but it has been shown to decrease the number of flare-ups and slow the progression of physical disability that may occur in people with MS.

Some people treated with interferons, including Avonex®, have become depressed (feeling sad, feeling low, or feeling bad about oneself). Some people have had thoughts about killing themselves and a few have committed suicide. Depression is common in people with MS. If you are noticeably sadder or feeling more hopeless, you should tell a family member or friend right away and call your doctor as soon as possible. You should tell the doctor if you have ever had any mental illness, including depression, and if you take any medicines or herbal remedies for depression.

People who may be allergic to any component of the final drug product should inform their doctor before beginning treatment with Avonex®. Some people taking AVONEX® have had severe allergic reactions leading to difficulty breathing, and/or decreases in blood pressure that required emergency treatment. Allergic reactions can happen after your first dose or may not happen until after you have taken Avonex® many times. Less severe allergic reactions such as rash, itching, skin bumps or swelling of the mouth and tongue can also happen. If you think you are having an allergic reaction, stop using study drug immediately and call your doctor.

Some people taking AVONEX® develop changes in the function of their thyroid gland. Symptoms of these changes include feeling cold or hot all the time, a change in your weight (gain or loss) without a change in your diet or amount of exercise you get, or feeling emotional.

Abnormal blood test results of liver function, which are a sign of liver injury or disease (such as hepatitis), have been reported in post-marketing surveillance of Avonex® (monitoring of possible side effects in patients who are taking Avonex®). In some cases, these events have occurred in the presence of other drugs that may cause liver injury. The potential added effects of taking drugs or other agents that can damage the liver (such as alcohol) while taking Avonex® have not been determined. Please talk to your doctor before starting any new medications or if you choose to drink alcohol. Additionally, very rare cases of liver failure have been reported in post-marketing surveillance of Avonex®. Symptoms of changes in your liver function include yellowing of the skin and whites of the eyes and easy bruising.

In post-marketing surveillance of Avonex®, severe decreases in platelets (a type of blood cell important for blood clotting) that required treatment have been reported. Also, rare cases of pancytopenia (severe decreases in all blood cell types including white blood cells, which are important for fighting infection, red blood cells which carry oxygen to the cells in your body, and platelets) have been reported. Any decreases in red blood cells, white blood cells, or platelets require evaluation by your doctor.

Some patients have had seizures (convulsions) while taking Avonex®, including some patients who have never had seizures before. It is not known whether the seizures were related to the effects of their MS, to Avonex®, or to a combination of both. If you have a seizure while taking study drug, you should stop taking study drug and call your doctor.

While Avonex® is not known to have direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems such as cardiomyopathy (disorder of the heart muscle) or congestive heart failure (failure of the heart, resulting in fluid build-up in the lungs and other body tissues) after taking Avonex®. Some of the symptoms of heart problems are swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, and not being able to lay flat in bed. If you develop these symptoms or any heart problems while taking study drug, you should call your doctor right away.

The most common side effects associated with Avonex® are "flu-like symptoms," headache and dizziness. "Flu-like symptoms," such as fever, chills, sweating, muscle aches, and tiredness may be relieved with over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time.

Other events that have been seen in subjects participating in Avonex® studies include loss of appetite, problems sleeping, vomiting, nausea, increased sweating, muscle aches, joint aches, pain in arms and legs; injection site pain, redness, and bruising; pain, tiredness, general discomfort and loss of energy, depression, muscle tightness (spasticity), runny nose, body stiffness, and night sweats.

Additional events that have been seen in the general Avonex® patient population include irregular heartbeat, heart disease, diarrhea, chest pain, hepatitis, very rare cases of possible autoimmune hepatitis (a condition in which an individual's immune system starts reacting against his or her own liver), very rare cases of injection site abscess or cellulitis (deep skin infection) that may require surgical intervention, arthritis (swelling of joints), temporary increased muscle tightness and/or severe muscle weakness, tingling sensations, fainting, anxiety/nervousness, confusion, mood changes, changes in behavior, psychosis (severe mental disorder), shortness of breath, menstrual changes (bleeding between periods and/or heavier or longer periods), hair loss, itching, rash (including a blister-like rash, known as a vesicular rash), hives, and flushing.

As with any drug, there is always a risk that a rare or previously unknown side effect will occur. Tell your doctor if you experience any of the effects listed above or notice anything else unusual while you are receiving treatment with study drug.

As part of the body's disease-fighting system, the body makes substances called antibodies. Some people treated with Avonex® have made antibodies directed against interferon beta. Such antibodies are not currently known to cause any harmful effects. However, whether these antibodies will prevent or affect future therapy with interferon beta is unknown at this time.

If you become pregnant while taking study drug, you should stop using study drug immediately and contact the study doctor.

MRI Risks

There are no known risks to the types of magnetic fields and radio waves that are used in these studies, but there is always a possible unknown risk to this or any test. Rarely (one in thousands of exams), a sunburn-like skin burn may occur over a small area of the body. We take special precautions for this not to occur. In addition, you must lie still in a small space and may experience claustrophobia (a fear of being in closed or narrow spaces). If you develop claustrophobia, you may need a mild sedative medication to allow you to comfortably complete the study.

MRI scanners can be noisy at times. This is normal and not harmful. You will be given earplugs and/or a headset to wear. Lying on the MRI table without moving for the duration of the MRI Test Scan may be uncomfortable. The MRI personnel will explain these risks to you in more detail.

A severe allergic reaction can rarely occur with use of the imaging agent (gadolinium). The imaging agent may also cause you to experience headache, dizziness or faintness, a decrease in your blood pressure, nausea, vomiting, sweating, changes in how you taste things, and injection site symptoms. If you have experienced any of these symptoms previously with an imaging agent, please inform the study doctor. In addition, a rare, but serious and sometimes fatal condition (Nephrogenic Systemic Fibrosis) has been associated with some gadolinium contrast agents in patients with severely impaired kidney function. Study personnel will discuss these risks with you prior to your MRI scan.

Women who are pregnant should not have an MRI scan.

Other Risks

If you think you are having an allergic reaction to the study drug (you develop hives, shortness of breath, swelling of the face, dizziness, or other symptoms as explained by study personnel) contact your study doctor or seek medical attention immediately. Although rare, allergic reactions can be life-threatening.

The examinations and drug administration may cause discomfort. During the collection of blood samples, there may be pain, bruising, or localized bleeding at the site where the needle is inserted. Local infections or fainting occur rarely during blood collection. Although one attempt at drawing blood is usually all that is needed, additional tries may be necessary if the first try is not successful.

Skin biopsies require the removal of small amounts of tissue by incision, and may cause bruising, localized bleeding, infection, scarring, and a small amount of pain.

Some people have discomfort or pain when the SC or IM injections are given. There are people who feel faint or pass out when given an injection. There is a risk of infection, bleeding, bruising, and pain, swelling, and/or itching at the injection site.

REPRODUCTION RISKS

Daclizumab

In animal studies, one female animal given a high dose of DAC HYP stopped having periods (menstruating) and had a change in ovary function (the ovary is the female egg-producing reproductive organ). The animals' ovaries were increased in size and had many cysts. In a study with pregnant female animals, there was a slight increase in miscarriages (the animals lost their babies before full term) at a dose more than 45 times higher than what humans will be given. In studies with male animals, no changes in male reproductive organs or their function were seen.

Women

We do not know the effects of DAC HYP on the unborn baby, so you can only enter this study if you are past menopause, surgically sterile, or using reliable birth control methods. During the study, we will carry out pregnancy tests on women who are able to become pregnant. It is important that you do not become pregnant during the study and for approximately 4 months after your last dose of study drug. Acceptable methods of birth control are: surgical sterilization (no uterus and/or ovaries), intrauterine contraception/device, hormonal contraception, or any 2 barrier methods (a combination of male or female condom with spermicide; diaphragm, sponge, cervical cap). Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not considered acceptable methods of contraception. If you practice complete abstinence from sexual activity you should discuss with the study doctor whether this is an acceptable method of birth control. Females are considered post-menopausal if they have experienced 12 months of natural (spontaneous) amenorrhea or are 6 weeks post-surgical bilateral oophorectomy or Post-hysterectomy.

You must tell your study doctor immediately if you think you are pregnant. You must stop taking the study drug immediately.

The study doctor will follow your pregnancy to its outcome.

If you are breastfeeding you cannot participate in this study because DAC HYP may enter breast milk. The effects of DAC HYP on newborn children are unknown.

Men

The effects of DAC HYP on male reproductive organs are unknown. Therefore, you must use effective birth control during study participation and for 4 months after the last dose of study drug. If you practice complete abstinence from sexual activity you should discuss with the study doctor whether this is an acceptable method of birth control. Effective male contraception includes a vasectomy with negative semen analysis at follow-up, or the use of condoms with spermicide.

If your partner becomes pregnant while you are taking the study drug, you should notify the study doctor immediately. With your partner's permission, the study doctor may ask for information regarding the outcome of the pregnancy.

Avonex®

Avonex® may cause you to lose your baby (miscarry) or may cause harm to your unborn child. Do not take Avonex® if you are pregnant or are trying to become pregnant. Women should not breastfeed while taking Avonex®.

NEW FINDINGS

During the course of the study, you will be informed of any important new findings (either good or bad) such as changes in the risks or benefits resulting from participation in the research study or new alternatives to participation in this study that might change your decision to be in the study. You may contact the study doctor at any time after your participation ends to find out if any new information about this study has become available.

BENEFITS

Your MS may or may not improve while participating in this study. Your participation in the study will contribute to information about the study drug and may benefit other patients in the future.

PAYMENT FOR PARTICIPATION

You will not receive any payment for taking part in this research study. You will be reimbursed for any reasonable travel costs that result from your participation in this study.

ALTERNATIVE TREATMENT OPTIONS

You do not have to take part in this study to receive treatment for your MS. Other treatments for MS are available, including Avonex. These treatments have been shown to be effective in reducing the number of relapses suffered by patients, in some cases prolonging the time before a worsening in disability occurs. Discuss these options with your study doctor to determine if they

are appropriate for you. At the end of the study, you and your study doctor will discuss your future care, including any additional care you may need that is beyond what you would normally receive for your MS.

DAC HYP is an experimental drug that can only be given to you in research studies approved by regulatory authorities. If you complete this study according to the rules of the protocol and meet certain eligibility requirements, you may be able to enroll in another study where all subjects would receive extended treatment with DAC HYP.

ADDITIONAL COST

You do not have to pay for study drug, study visits and tests that have to be done for the study.

The described physical examinations, and laboratory and diagnostic procedures involved in this study are considered standard of care in the treatment and monitoring of your disease. Your insurance company or national health scheme should cover the cost of any treatment for your disease that you would receive whether you were in the clinical trial or not. However, if any of the standard of care items are not covered by your insurance company or a third party payer., Biogen Idec will pay for them.

COMPENSATION FOR RESEARCH-RELATED INJURY

You can obtain medical treatment for an injury related to treatment with DAC HYP at the Neuroscience & Spine Institute. For further details, or if you believe you have been injured as a result of your receiving DAC HYP, please contact **Jill Conway, MD, at 704 446-1902**.

If you have any injury that is related to DAC HYP, Biogen Idec will pay for the reasonable cost of emergency and/or acute medical care to the extent the cost is not paid by your medical insurance or another party.

You may not be compensated for uninsured emergency and/or acute medical care if you do not follow instructions about the study, administer the study drug incorrectly, or if the law limits Biogen Idec's legal responsibility. If you have an injury related to DAC HYP, your doctor will decide what medical care you will need. Biogen Idec will not pay for the normal progress of your disease, or any injury or complication due to the medical condition you already have. Biogen Idec will not provide any other kind of compensation such as lost wages, disability or discomfort.

This paragraph on compensation for injury is not applicable to patients treated with commercially approved Avonex.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. You do not waive any legal rights by signing this Subject Information and Consent Form.

VOLUNTARY PARTICIPATION

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not be in the study, that will not in any way harm your relations with your doctors or with Carolinas HealthCare System. You are free to stop being in the study if you change your mind after entering it. You may choose to stop taking study drug or leave the study at any time. Before you do, for your safety, you should discuss your decision with the study doctor. This would not harm your relations with your doctors or Carolinas HealthCare System.

If you stop taking study drug but decide to remain in the study, you will have a reduced schedule of study visits.

WITHDRAWAL

Your doctor, the sponsor company, or the FDA has the right to stop your participation in the study at any time, with or without your consent.

Study drug administration will be stopped if:

- you become pregnant
- you have symptoms of an allergic reaction to the study drug
- you have a medical reason that makes it necessary to stop taking study drug
- you do not follow the rules of the study
- your study doctor decides that it is not in your best interest to continue or that it is necessary for medical reasons
- the study is cancelled by the FDA or the sponsor company.

The sponsor may decide to stop the study and your access to the study drug under certain circumstances even if the study drug appears to be safe and effective.

CONFIDENTIALITY

The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify you. Your record for this study may, however, be reviewed and/or photocopied by the drug/device manufacturer, by Carolinas HealthCare System, by Copernicus Group Independent Review Board (IRB), or by representatives of the Food and Drug Administration or other government agencies. To that extent, absolute confidentiality cannot be guaranteed.

Your name will not be used in any study reports, and these reports will be used for research purposes only. Biogen Idec, its designee(s), Copernicus Group Independent Review Board (IRB), and various government health agencies may inspect and/or copy your records of this study. In addition, copies of these data will be sent to and reviewed by an independent company for the purposes of assessing your response to the study drug. Information about your disease status may be requested and reviewed on a regular basis after you have completed all visits in this study.

Every effort will be made to keep your personal medical information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed, if required by law. In addition, results from this study may be published. In such a case, your identity will still be confidential, but the results of the study will be more widely distributed.

STUDY FUNDING

Biogen Idec will pay the clinic or institution where the study is conducted for the costs of running the study.

Biogen Idec will supply the study drug (DAC HYP or Avonex®) while you participate in this study.

STUDY SAMPLES

All specimens and samples obtained from you during this study will be used and kept for the purposes described in this Subject Information and Consent Form, and that all data and materials created during this study will be the property of Biogen Idec. Biogen Idec has no plans to pay you or to share with you any potential profits that Biogen Idec may receive from such specimens, samples, data or materials.

FINANCIAL INTEREST OF INVESTIGATOR

Investigator **Dr. Jill Conway** does receive money from the sponsoring company for work that is not part of the study. These activities may include consulting, service on advisory boards, giving speeches or writing reports. You may ask the doctor any questions necessary to assure yourself that these benefits have not overly influenced the doctor's request for you to take part in this study. The decision whether to enroll in the study is yours alone. You should have all the information you need to be comfortable with your decision.

QUESTIONS

If you have any questions about your participation in this research study, or if you feel that you have experienced a research-related injury or reaction to the study drug, contact:

Principal Investigator: **Jill Conway MD**

Daytime telephone number(s): 704-446-1902, 704-304-5061or 704-376-9849

24-hour contact number(s): 704-355-4088 ID#7380

If you have questions about your rights as a research subject, you may contact the Copernicus Group IRB at 1-888-303-2224 (toll free). An Independent Review Board is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed

and approved the research study described in this Subject Information and Consent Form. If you have study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you want to talk to someone other than the study investigator or have difficulty reaching the study investigator. For further information regarding the clinical trials process and your role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

HIPAA AUTHORIZATION

If you wish to take part in this research study, you will be asked to sign this consent and authorization form. It allows the study sponsor and the study investigator to collect, process and pass on to the sponsor organizations any relevant personal health information collected from you during the study. These are activities routinely carried out during all clinical studies.

You have been told that personal information about you (including sensitive personal health information, such as your medical history and your racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- the clinical study investigator, **Dr. Conway**, and research staff
- the study sponsor and/or its associated companies
- regulatory or other governmental authorities of the United States and other countries
- other persons authorized by the study sponsor
- Carolinas HealthCare System employees
- Copernicus Group IRB
- other persons or agencies as required by law or allowed by federal regulations

You have been told that your personal data are being collected and processed to:

- check your suitability to take part in the study
- monitor your treatment with the study medication
- compare and pool treatment results with those of other subjects in clinical studies
- support the development of the study medication
- support the licensing application for regulatory approval of the study medication or device in the world
- support the marketing, distribution, sale and use of the study medication or device anywhere in the world

You have been told that your personal information may be processed within the U.S. or elsewhere in the world or transferred to or from the U.S. for review, processing and/or storage by an associated company or a carefully selected third-party organization. By signing this document, you explicitly consent to the transfer of your personal information, including sensitive personal information, collected during this clinical study, for review, processing and/or storage. Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health confidential.

You may refuse this authorization to transfer your personal information. If you choose not to agree to this authorization, you might be ineligible to participate in the study. If you decide not to sign this authorization, that will not harm your relations with your doctors or with Carolinas HealthCare System.

You have the right to inspect your medical record at any time. Your research record may be unavailable until the conclusion of the study. At that point, it will be available. Please speak with the study doctor if you desire to access your record.

You have been told that whenever your personal information is processed, it will be kept confidential and secure to the best of our ability. It will be used only for the purpose for which it was collected.

You have been told that if you withdraw from the study and withdraw your Authorization, no new information will be collected for study purposes unless the information concerns an adverse event (a bad effect) related to the study. If an adverse event occurs, your entire medical record may be reviewed. All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

This Authorization does not have an expiration date. You have been told that according to the guidelines for good clinical practice, the study investigator and sponsor will keep your personal information for at least 6 years. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. If you wish to revoke authorization to use your personal information, you will notify the study doctor, **Jill Conway MD, Neuroscience & Spine Institute, 1010 Edgehill Road, N, Charlotte, NC 28207**, in writing. Some of the data obtained from your record prior to your revocation may still be used if considered necessary for the study.

SUBJECT'S STATEMENT OF CONSENT

Multicenter, Double-blind, Randomized, Parallel-group, Monotherapy, Active-control Study to Determine the Efficacy and Safety of Daclizumab High Yield Process (DAC HYP) versus Avonex® (Interferon β-1a) in Patients with Relapsing-Remitting Multiple Sclerosis

- This is a research study of the investigational drug, DAC HYP.
- I have been given sufficient opportunity to consider whether to participate in this study.
- My taking part in this research study is voluntary. I may decide not to take part or to withdraw from the research study at any time without penalty or loss of benefits or treatment to which I am entitled.
- If I meet the criteria, I would like to take part in this research study, and my doctor may enroll me in the research study.
- The research study may be stopped at any time without my consent either by the study doctor or by the company sponsoring the research.
- My study doctor will be receiving payment from the sponsor to conduct the research.
- I have had an opportunity to ask my study doctor questions about this research study. My questions so far have been answered to my satisfaction.
- I have been told how long I may be in the research study.
- I have been informed of the procedures and tests that may be performed during the research study.
- I have been told what the possible risks and benefits are from taking part in this research study. I may not benefit or my condition may worsen if I take part in this research study.
- I authorize the use of my personal health information.
- I do not give up my legal rights by signing this form.
- I have been told that prior to any study related procedures being performed, I will be asked to voluntarily sign this Subject Information and Consent Form.
- I will receive a signed and dated copy of this Subject Information and Consent Form.

_____	_____	_____
Subject Print Name	**Date**	**Time**
_____	_____	_____
Subject Signature	**Date**	**Time**

I certify that the information provided was given in language that was understandable to the subject.

Print Name of Person Obtaining Consent	**Date**	**Time**
Signature of Person Obtaining Consent	**Date**	**Time**
Investigator Print Name	**Date**	**Time**
Investigator Signature	**Date**	**Time**

PERMISSION TO USE BLOOD SAMPLES FOR FUTURE NON-GENETIC BIOMARKER TESTING

The study doctor who is conducting the research study described in the first part of this consent document, the "Main Study," is collecting your blood samples to also allow Biogen Idec to conduct additional research in the future. You are being asked to give Biogen Idec permission to use your samples for this additional research because you have been diagnosed with MS and you have been asked to participate in the Main Study.

Prior research has shown that certain diseases can affect naturally-occurring substances in the body. These substances are called biomarkers, and the presence or amount of these biomarkers can be detected by testing samples. Biomarker testing can help to diagnose a particular disease, determine the severity of the disease, or evaluate how well and safely a drug may work in treating the disease.

Some biomarkers for MS have already been identified, but new discoveries are being made and new biomarkers may be identified in the future. Some of the blood samples being collected in the study are to allow Biogen Idec to conduct additional research in the future. You are being asked to give Biogen Idec permission to use your blood samples for future biomarker testing purposes because you have been diagnosed with MS. Biogen Idec will save your samples and then potentially use them in the future to study biomarkers that may be involved in MS. Either Biogen Idec or a laboratory working for or on behalf of Biogen Idec, not the study doctor, will be conducting the biomarker research.

Permission to use your samples for future biomarker testing is a requirement for participation in the study. If you chose not to give your permission for Biogen Idec to use your samples for future biomarker testing, you cannot participate in the study. In such case, it will not change your present medical care in any way.

Collection Procedures and Storage of Samples

If you agree to give Biogen Idec permission to use your samples for future biomarker research, you will not have to undergo any extra procedures or blood sample collections. Some of the blood samples collected during the study will be sent to Biogen Idec by the study doctor or the study's central laboratory, where they will be stored until the future testing is performed. Biogen Idec may also use any leftover samples for future biomarker research.

In addition to the samples collected from you, the study doctor and/or laboratory will also provide Biogen Idec with your health information. Before providing this information to Biogen Idec, the study doctor will replace information that could be used to identify you, such as your name, phone number, or address, with a code number. Biogen Idec will not be able to link the code number with your identity.

Please refer to the main part of this Subject Information and Consent Form for additional details regarding the confidentiality of your samples.

You understand that your samples may be exported for testing purposes to different countries including the United States where the data protection laws may not be as strict as your country.

Samples collected for future biomarker research will be kept until they are used for research or destroyed by Biogen Idec.

Risks

Please refer to the main part of this Subject Information and Consent Form for a description of the risks associated with blood sample collection.

Benefits

There will be no direct benefit to you from participating in this additional research. Information from biomarker testing may help people with a similar condition in the future.

Costs and Payment

There is no cost to you for permitting Biogen Idec to conduct future biomarker research on your samples. You will not be paid for permitting the use of your samples in this additional research. Biogen Idec does not intend to provide any compensation to participants who give permission to use their samples for this additional research if the future biomarker testing is used to develop new or improved drugs or products in the future.

Withdrawal of Consent

If you permit Biogen Idec to use your samples for future biomarker testing, you may withdraw your consent at any time. If your samples have already been provided to Biogen Idec for storage and biomarker testing, Biogen Idec will destroy the samples in accordance with this consent. If biomarker testing has already been conducted on the samples, Biogen Idec will keep the results of that testing or research.

You should notify the Study Doctor or Biogen Idec (call 1-800-456-2255 and ask to speak with the Director of Genetics and Genomics) if you withdraw consent.

If you permit Biogen Idec to use your samples for potential future biomarker testing, you will not be notified when the future research takes place and you will not be provided with the results of the future research.

If you have any question about this permission to use your samples for future biomarker research, you should ask the study doctor.

SUBJECT'S STATEMENT OF CONSENT

Multicenter, Double-blind, Randomized, Parallel-group, Monotherapy, Active-control Study to Determine the Efficacy and Safety of Daclizumab High Yield Process (DAC HYP) versus Avonex® (Interferon β-1a) in Patients with Relapsing-Remitting Multiple Sclerosis

- I have read this portion of the Subject Information and Consent Form or someone has read this informed consent to me. It is written in a language that I understand.
- I have been told what I will be asked to do during this study, and I have had time to think about what the study involves for me.
- I have discussed it with the doctor/study staff, and they have answered my questions satisfactorily.
- I have told the person obtaining this consent if I am involved in other medical research studies.
- I have been told that it is up to me to decide whether to take part in the study, and that I can change my mind later.
- I have been told that whatever I decide, my medical care and legal rights will not be affected.
- I have been told that I will be able to keep a copy of this Subject Information and Consent Form.
- I give my permission for Biogen Idec, its designees, the Copernicus Group IRB, and government health agencies to look at my medical notes and information collected in the study.
- I agree to give permission to Biogen Idec to use my blood samples at any time in the future to evaluate biomarkers that may be related to MS or therapeutic response to DAC HYP or Avonex®.
- I voluntarily agree to take part in this research study.

Please sign your initials and date below.

Initials: _____ Date: _____

PERMISSION TO USE PHOTOGRAPHS FOR EDUCATIONAL PURPOSES

Earlier in this consent document, you were asked for permission to use your samples for future biomarker research. One part of this study includes, among other evaluations, taking photographs of areas of your body if you get a rash or other skin condition. Study personnel may use photographs of you during the safety reviews that are conducted for this study.

Biogen Idec Inc. (Biogen Idec) may determine that the photographs taken of you during the study have educational value, for example in presentations at medical conferences or in articles published in medical journals. This part of the Consent Form provides information about the use of your photographs for this purpose and is supplemental to the Subject Information and Consent form for the main study. Please read this Supplemental Subject Information and ask the study doctor to explain anything that you do not understand. Take time to think about it, and discuss it with other people. Your permission to allow Biogen Idec to use your photographs for educational purposes is voluntary. You are free to decide whether or not to allow Biogen Idec to use your photographs as explained above. If you do not give your permission for Biogen Idec to use your photographs for educational purposes, you can still be in Study 205MS301.

Please indicate whether or not you give Biogen Idec permission to use your photographs for educational purposes by initialing and dating beside either "Yes" or "No" at the end of this document.

Please refer to the Subject Information and Consent Form for the main study for additional information regarding the protection of your confidentiality and personal data.

This document has been approved by the Copernicus Group IRB.

Procedures

If the study doctor decides it is necessary, you may have photographs taken of parts of your body during the study, you will be asked to remove all jewelry and wrist watches for the photographs. Depending on the location of the skin condition, you may be asked to remove clothing, although you may always choose not to do so.

Your identity will not be disclosed. Any photographs taken of you during this study will be modified, if necessary, to protect your identity.

Benefits and Risks

You will not benefit directly from the use of your photographs, but allowing your photographs to be used for educational purposes might help people with a similar condition in the future.

Having the photographs taken will not pose any risk to your health.

Right to Withdraw

You may choose to withdraw permission to use your photographs for educational purposes at any time. You do not need to give a reason. Your medical care will not be affected. Biogen Idec will use your photographs and the resulting evaluation up to the date you withdrew your permission. You may withdraw the photographs from further use and still participate in the study named above.

SUBJECT'S STATEMENT OF CONSENT

Multicenter, Double-blind, Randomized, Parallel-group, Monotherapy, Active-control Study to Determine the Efficacy and Safety of Daclizumab High Yield Process (DAC HYP) versus Avonex® (Interferon β-1a) in Patients with Relapsing-Remitting Multiple Sclerosis

I have been told that the photographs obtained from me during this study will be used and kept for the purposes described in this Supplemental Subject Information and Consent Form, and that all data and materials created from these photographs during this study will be the property of Biogen Idec. I have been told that Biogen Idec has no plans to pay me or to share with me any potential profits that Biogen Idec may receive from such photographs, data or materials.

- I have read this Supplemental Subject Information and Consent Form for Permission to Use Photographs for Educational Purposes or someone has read this informed consent to me. It is written in a language that I understand.
- I have been told what I will be asked to do during this study, and I have had time to think about what the study involves for me.
- I have discussed it with the doctor/study staff, and they have answered my questions satisfactorily.
- I have been told that it is up to me to decide whether to give permission to use photographs taken, and that I can change my mind later.
- I have been told that whatever I decide, my medical care and legal rights will not be affected.
- I have been told that I will be able to keep a copy of this Supplemental Subject Information and Consent Form for Permission to Use Photographs for Educational Purposes.

Please initial and date beside your choice below.

Initials: _____ Date: _____ Yes, I agree to the use of my photographs for the purposes stated in this consent.

Initials:_____ Date:_____ No, I do not agree to the use of my photographs for the purposes stated in this consent.