

INFORMED CONSENT

All To Target Trial-Lantus® (insulin glargine) with stepwise addition of **Apidra® (insulin glulisine) or Lantus® with one injection of Apidra®** vs. a twice-daily premixed insulin regimen (Novolog® Mix 70/30™) in adult subjects with type 2 diabetes failing dual or triple therapy with oral agents: a 64-week, multi-center, randomized, parallel, open-label clinical study.

SPONSOR: sanofi-aventis
PROTOCOL NO: HMR1964A/3515
INVESTIGATOR: **Anuj Bhargava, M.D.**
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Before agreeing to participate in this research study, it is important that you read and understand the following explanation of the proposed procedures. This statement describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

If you are signing this consent form again, it is because new safety information has been added regarding the use of Avandia® -rosiglitazone (**Study Procedures and Possible Risks and Discomforts sections**), and ACCORD study news release (Possible Risk and Discomfort section). This new information is highlighted.

BACKGROUND AND PURPOSE OF THE STUDY

Type 2 diabetes mellitus is a chronic illness (an illness that continues for a long time). The bodies of people who have type 2 diabetes mellitus have problems making and/or using insulin properly. This results in higher than normal blood glucose (sugar) levels. To decrease or delay late complications of diabetes (such as frequent infections, slow healing of wounds or sores, blurred vision, kidney disease, and nerve disorders), it is important that blood glucose levels stay close to or within the normal range. Many people with diabetes inject some form of insulin to help manage their blood glucose levels.

The purpose of this study is to evaluate blood sugar control by using one of three different treatment regimens. You will have an equal chance to be selected for one of the three regimens. The three possible treatments are:

1. Lantus® once a day + Apidra® once a day
2. Lantus® once a day + Apidra® up to 3 times a day
3. Novolog® Mix 70/30™ twice a day

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The two Lantus®/Apidra® regimens are being compared to the Novolog® Mix 70/30™ regimen to see if one works better or the same as another.

Lantus® is a long-acting insulin that provides 24-hour background insulin coverage with a once daily injection. Apidra® is a rapid-acting insulin that begins to work soon after injection and lasts for 3-5 hours. Novolog® Mix 70/30™ is a premixed insulin that also provides daily insulin coverage but needs to be injected twice a day.

All three insulins are approved by the US Food and Drug Administrations for the treatment of diabetes.

You will also need to continue to take certain of your oral medications for diabetes during the study. In order to make all patients as similar as possible when starting study treatment, some of your oral diabetic medications that you are now taking may be replaced by another approved medicine during the 4-week run in phase. At the time you are placed in one of the three treatment regimens, certain of these oral medications may be discontinued. Your study doctor will instruct you on what medicines you can take and when you can take them whether they are taken by mouth or are injected.

NUMBER OF SUBJECTS/LENGTH OF PARTICIPATION

About 576 people, male and female, age 30 to 80 will be in this study. This study will use competitive enrollment. This means that when a target number of subjects have entered the treatment phase of the study, all further enrollment will be closed. Therefore, it is possible that you could be in the screening or run-in phase, ready to enter the treatment phase, and be discontinued without your consent if the target number of subjects has already entered the treatment phase of the study.

Your participation will last up to 64 weeks and require that you come to the study center about 11 or 12 times. This study has 3 parts: Screening Period, Run-In Period, and Treatment Period. The Screening Period will last approximately one week, the Run-in Period will last approximately 28 days, and the treatment Period will last approximately 60 weeks.

The study doctor or study center is being paid by the sponsor, sanofi-aventis, to conduct this study.

STUDY PROCEDURES

Screening Period

Visit 1 (Day -30)

During the screening period, you will not receive any Lantus®, Apidra®, Novolog® Mix 70/30™ or other study medications but will continue with your previously prescribed treatment for type 2 diabetes mellitus. In order to determine if you qualify for this study, the following will be performed over 2 or more days:

- The study will be discussed with you. You will be asked to sign this consent form.

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- You will be asked to read and sign an authorization to use and disclose health information for the privacy rule issued to protect the privacy and rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA)
- Review of your medical history and use of medications
- Physical examination (including height) will be performed. You should ask your study doctor about what will be done during this exam.
- Measurement of vital signs (blood pressure and heart rate) and weight.
- An electrocardiogram (ECG) will be done. The ECG measures the electrical activity of your heart beat and heart rhythm.
- Collection of blood samples for laboratory testing. You must be fasting when these blood samples are drawn, meaning no food or drink (other than water) for eight hours before the sample is taken.
- If you are a woman who could become pregnant, a blood pregnancy test will be done. You will be told if the test results are positive. The results of this test must be negative to participate in the study.

During the Screening Period you will continue to follow your previously prescribed treatment for type 2 diabetes.

Run-In Period

If, based on the above tests and procedures, you continue to qualify to participate in this study; you will begin the run-in period of the study. The run-in period will last approximately 4 weeks and you will be seen at the beginning (Visit 2) and at the end of this period (Visit 3). During this phase you will continue to follow your current oral therapy except that any sulfonylurea (such as glyburide or glipizide) or repaglinide (if applicable) will be replaced with an equal dose of glimepiride (Amaryl®). Your doctor will let you know which medication you should be taking during this period. Glimepiride (Amaryl®) is an FDA approved medication for the treatment of diabetes. This period of the study will be used to make sure you are stable on your new treatment and to assess your compliance with completing your diary entries.

Visit 2 (Day -28)

You will return for Visit 2 approximately 1 week after Visit 1.

The following tests and procedures will be performed:

- You will receive detailed training on how to use and complete required information in the diary. You will be required to collect and record certain information (daily fasting blood glucose values and additional before-meal, after-meal, and bedtime blood glucose values at certain time points during this period) and return the diary when you are enrolled into the study (Visit 4). You will be expected to access the diary over the phone or internet every day and enter your information.
- You will receive a (Accu-Chek Advantage®) blood glucose meter (with test strips) and training on how to use the meter to self-monitor your blood glucose. You will use this blood glucose meter throughout the study, and you will keep it after the study.

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- You will be instructed to measure and record in the diary your daily fasting blood glucose values and your self-monitored blood glucose measurements 4 times a day (before breakfast- fasting, before lunch, before dinner, and at bedtime) for 3 days every week during this period.
- You will receive dietary and lifestyle recommendations from a healthcare professional as well as a food diary and instructions to record your food intake 2 times a week (on 2 consecutive days) for a period of 2 weeks during this time. This diary will be reviewed at your next visit.
- If you are currently taking rosiglitazone (Avandia®) or pioglitazone (Actos®) and are taking the maximum recommended dose (8mg for rosiglitazone or 45mg for pioglitazone) you will be told to decrease the dose (to 4mg for rosiglitazone or 30mg or 15mg for pioglitazone).

You will be asked to record any symptoms of hypoglycemia (low blood glucose) you experience between visits (see the section below called “Possible Risks and Discomforts” for a description of these symptoms). You will be asked to confirm the hypoglycemia by performing a blood glucose measurement at the time the symptoms occur. You will record these measurements in your diary. All blood glucose measurements less than 70 mg/dl and any symptoms of hypoglycemia should be recorded in the diary.

Visit 3 (Day -2)

You will return for Visit 3 at the end of the run-in period. During this visit the following procedures will be done:

- Collection of blood sample for laboratory testing
- Your food diary will be collected and reviewed
- You will be instructed to measure and record in the diary an 8-point blood glucose profile (8 different blood glucose measurements) on 1 day in the week prior to your next visit. This profile will consist of:
 - 3 measurements collected before each of 3 meals (breakfast, lunch, and dinner)
 - 3 measurements collected 2 hours after each of 3 meals (breakfast, lunch, and dinner)
 - A single measurement at bedtime
 - A single measurement at 3:00 a.m. (in the morning)

Visit 4 (Week 0) Baseline Visit

You will come to the study doctor's office in the morning after an overnight fast (nothing to eat or drink other than water for at least 8 hours). The following procedures will be done:

- Measurement of vital signs (blood pressure and heart rate) and weight will be performed.
- Blood sample will be collected for laboratory testing.

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- If you are a woman who could become pregnant, a blood pregnancy test will be done. You will be told if the test results are positive. The results of this test must be negative to participate in the study.
- The study doctor or study staff will review what you have recorded in your diary (and you will be reminded to enter your diary information - on a daily basis.)
- You will receive training by study staff on how to self-inject and titrate your assigned insulin.
- You will be reminded to continue to follow a healthy diet and exercise program.
- You will complete a questionnaire about your diabetes.
- You will return the bottle of glimepiride (Amaryl®) (if taking) and any remaining tablets to the study doctor.

If you have met all the entry requirements and agree to continue in the study, you will be assigned randomly to one of the following 3 study drug groups by an equal chance. This is an open-label study, which means that both you and the study staff will know to which study group you have been assigned:

- PREMIXED REGIMEN ARM: Participants assigned to this group will receive subcutaneous (under the skin) premixed insulin (Novolog® Mix 70/30™) injections 2 times a day, 0-15 minutes before breakfast and dinner each day. Participants will also discontinue glimepiride (Amaryl®) (if taking) and continue their oral medication as instructed by the study doctor.
- LANTUS/APIDRA-1 REGIMEN ARM: Participants assigned to this group will receive subcutaneous (under the skin) Lantus® injections every day, and if required, one injection of Apidra® each day. The Lantus® dose will be adjusted every week based on the middle value of the last 3 fasting blood glucose values collected. Apidra® will be injected 0-15 minutes prior to the largest meal of the day and adjusted periodically throughout the study. Participants will also discontinue glimepiride (Amaryl®) (if taking) and continue their oral medication as instructed by the study doctor.
- LANTUS/APIDRA-3 REGIMEN ARM: Participants assigned to this group will receive subcutaneous (under the skin) Lantus® injections every day, and if required, up to 3 injections of Apidra® each day. The Lantus® dose will be adjusted every week based on the middle value of the last 3 fasting blood glucose values collected. Apidra® will be added, if needed, at specific time points throughout the study and injected 0-15 minutes prior to the start of a meal, with a maximum of 3 Apidra® injections each day. Participants will also discontinue glimepiride (Amaryl®) (if taking) and continue their oral medication as instructed by the study doctor.

You will be given the choice to self-inject Lantus® and/or Apidra® using a cartridge with a pen called OptiClik or a syringe with a vial. You will also be given the choice to self-inject Novolog® Mix 70/30™ using a pen called FlexPen® or a syringe with a vial. Once you make a choice of syringe or pen, you may not switch to the other for the duration of the study. Before you choose either pen or vial, you will receive instructions so that you may decide which method is best for you.

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Throughout the study, the study staff will call you every week to ask about your blood glucose levels and give you instructions about changing your doses of study medications to best control your blood glucose levels.

Starting at Visit 4 and during the rest of the study you will be given appropriate study medication for your treatment arm:

Study medications:

- Lantus® insulin
- Apidra®
- Novolog® Mix 70/30™

You will be given enough study medication to last until your next visit with the study doctor. You will also need to bring in all of the used and unused study medication at each visit with your study doctor.

Only the person taking part in this study must use the study drugs. They must be kept out of reach of children and others who might not be able to read or understand.

You will also be given:

- Alcohol wipes
- A sharps container for used needles
- Syringes and needles or pens, depending on which method of injection you choose with instructions
- Glucose meter (Accu- Chek Advantage®)
- Test strips

You will be required to perform self-monitored blood glucose measurements every day throughout the treatment period as follows:

- **Treatment Period:** You must collect and record your fasting blood glucose values every day, and depending upon the study arm you are assigned to, you will be required to collect and record additional blood glucose values. On at least 3 separate days you must collect and record up to 4 blood glucose measurements (before every meal and at bedtime) each day. Additionally, you will be instructed to measure and record in the diary an 8-point blood glucose profile (8 different blood glucose measurements) on 1 day in the week prior to your next scheduled study visit (visits 4, 7, 8, 9,10, and 11). This profile will consist of:
 - 3 measurements collected before each of 3 meals (breakfast, lunch, and dinner)
 - 3 measurements collected 2 hours after each of 3 meals (breakfast, lunch, and dinner)
 - A single measurement at bedtime
 - A single measurement at 3:00 a.m. (in the morning)

You will be asked to record any hypoglycemia (low blood glucose) you experience between this visit and the next visit (see the section below called “Possible Risks and Discomforts” for a

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description of these symptoms). If at all possible, you will be asked to confirm the hypoglycemia by performing a blood glucose measurement at the time the symptoms occur and record these measurements in your diary each day. All blood glucose measurements less than 70 mg/dl and any symptoms of hypoglycemia should be recorded in the diary.

Visit 5 (Week 2)

You will come to the study doctor's office. The following procedures will be done:

- Review of the information you have recorded in your diary and reminder of the information you should be recording on a daily basis.
- You will return all study drug vials or cartridges, used or unused, to the study doctor.
- You will be provided with appropriate insulin for your treatment arm: Novolog® Mix 70/30™ or Lantus® to cover the period until your next visit. At each visit, your Novolog® Mix 70/30™, Lantus®, Apidra® insulin doses and times of dosing will be reviewed, and the study doctor will advise you about any changes needed in your dosages.
- You will be reminded to continue to follow a healthy diet and exercise program.

Visit 6 (Week 6)

You will come to the study doctor's office in the morning after an overnight fast (nothing to eat or drink other than water for at least 8 hours). The following procedures will be done:

- Blood sample will be collected for laboratory testing.
- Review of the information you have recorded in your diary and reminder of the information you should be recording on a daily basis.
- You will receive dietary and lifestyle recommendations from a healthcare professional as well as a food diary and instructions to record your food intake 2 times a week (on 2 consecutive days) for a period of 2 weeks during this time. This diary will be reviewed at your next visit.
- You will return all study drug vials or cartridges, used or unused, to the study doctor.
- You will be provided with Novolog® Mix 70/30™, Lantus®, Apidra® insulin to cover the period until your next visit. At each visit, your Novolog® Mix 70/30™, Lantus®, Apidra® insulin doses and times of dosing will be reviewed, and the study doctor will advise you about any changes needed in your dosages.
- You will be reminded to continue to follow a healthy diet and exercise program.
- You will also be asked to complete questionnaires about your diabetes.

Visit 7 (Week 12)

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You will come to the study doctor's office in the morning after an overnight fast (nothing to eat or drink other than water for at least 8 hours). The following procedures will be done:

- Measurement of vital signs (blood pressure and heart rate) and weight will be performed.
- Blood sample will be collected for laboratory testing.
- Review of the information you have recorded in your diary and reminder of the information you should be recording on a daily basis.
- Your food diary will be collected and reviewed.
- You will return all study drug vials or cartridges, used or unused, to the study doctor.
- You will be provided with Novolog® Mix 70/30™, Lantus®, Apidra® insulin, to cover the period until your next visit. At each visit, your Novolog® Mix 70/30™, Lantus®, Apidra® insulin doses and times of dosing will be reviewed, and the study doctor will advise you about any changes needed in your dosages.
- You will be reminded to continue to follow a healthy diet and exercise program.
- You will be reminded to complete an 8 point blood glucose profile one time in the week before your next visit.
- You will also be asked to complete questionnaires about your diabetes.

If you are taking Lantus®, based on your laboratory testing results, your doctor may tell you to begin using Apidra® before your largest meal. This could mean you will have to return to the study doctor's office a few days after your visit for training on using Apidra® and to get Apidra® insulin and additional supplies.

Visits 8 (Week 24), Visit 9 (Week 36), Visit 10 (Week 48)

You will come to the study doctor's office in the morning after an overnight fast (nothing to eat or drink other than water for at least 8 hours). The following procedures will be done:

- Measurement of vital signs (blood pressure and heart rate) and weight will be performed.
- Blood sample will be collected for laboratory testing (Visit 8/Week 24 only).
- Review of the information you have recorded in your diary and reminder of the information you should be recording on a daily basis.
- You will return all study drug vials or cartridges, used or unused, to the study doctor.
- You will be provided with Novolog® Mix 70/30™, Lantus® insulin, Apidra®, to cover the period until your next visit. At each visit, your Novolog® Mix 70/30™, Lantus®, Apidra® insulin doses and times of dosing will be reviewed, and the study doctor will advise you about any changes needed in your dosages.
- You will be reminded to continue to follow a healthy diet and exercise program.
- You will also be given a subject food diary (visit 10 only) to record your food intake 2 times a week (on 2 consecutive days) for a period of 2 weeks during this time.
- You will be reminded to complete an 8 point blood glucose profile one time in the week before your next visit.
- You will also be asked to complete questionnaires about your diabetes.

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If you are taking Lantus®, based on your laboratory testing results, your doctor may tell you to begin using Apidra® before one or more meals. This could mean you will have to return to the doctor's office a few days after your visit for training on using Apidra® and to get Apidra® insulin and additional supplies if you have not used Apidra® before.

Visit 11 (Week 60) End of study or if you withdraw from the study early

You will come to the study doctor's office in the morning after an overnight fast (nothing to eat or drink other than water for at least 8 hours). The following procedures will be done:

- Measurement of vital signs (blood pressure and heart rate) and weight will be performed
- Review of the information you have recorded in your diary.
- Your food diary will be collected and reviewed.

- Physical examination (including height) will be performed. You should ask your study doctor about what will be done during this exam.

- An electrocardiogram (ECG) will be done. The ECG measures the electrical activity of your heart beat and heart rhythm.
- Blood sample will be collected for laboratory testing, including a blood pregnancy test.
- You will return all study drug vials or cartridges, used or unused, to the study doctor. You will not have to return your AccuCheck Advantage® blood glucose meter.

- You will also be asked to complete questionnaires about your diabetes.

The study doctor or study staff will follow-up with you by calling you 24 hours after this visit to check on your condition.

Transition Visit of Avandia® to Actos® or Treatment Discontinuation Visit of Avandia®

If you are currently enrolled in this clinical study and on Avandia® (rosiglitazone), and you and your study doctor decide to switch from Avandia® to Actos® (pioglitazone) at a corresponding dose or discontinue your treatment with Avandia®, your doctor will schedule a visit so that the following procedures can be performed before you either start your Actos® (pioglitazone) treatment or discontinue Avandia®

You will arrive in the morning at the study doctor's office after an overnight fast (nothing to eat or drink other than water for at least 8 hours) for the following procedures:

- You will have your blood pressure, heart rate, and weight measured and recorded.
- You will have an ECG done.
- The study doctor or study staff will perform a physical exam. You should ask about what will be done during this exam.
- You will provide a blood and urine sample for laboratory testing.
- If you are a woman who could become pregnant, your blood will be tested to see if you are pregnant. You will be told if the test results are positive.

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- You will be asked about any adverse events or illness that have occurred since your last visit. Adverse events include hypoglycemic events, or any hospitalizations. Adverse events are not limited to hypoglycemic events and hospitalizations.

Standard Care

Some of the study procedures might be done as part of your standard care even if you do not take part in this research study. The study doctor or a member of the study staff can answer any questions you may have about the procedures that are not part of your standard care.

Participant Responsibilities

You will be asked to complete your study diary between visits. This will be entered over the phone or via the internet every day.

If you decide to take part in this research study, following instructions and completing study visits are important to make sure that the study results are accurate. If you wish to stop participating in the study or if you find you have not followed instructions listed above, it is important that you notify the study doctor or study staff.

A number of drug substances may affect glucose metabolism, so it is very important that during the entire study, you notify the study doctor of any other medical treatments, including medications that you may be receiving.

Possible Risks and Discomforts

Apidra[®], Lantus[®], Novolog Mix[®] 70/30[™]

Common Side Effects of Insulins such as Apidra[®], Lantus[®], and Novolog[®] Mix 70/30[™] Used in This Study are:

- symptoms caused by hypoglycemia (low blood glucose)
- symptoms caused by hyperglycemia (high blood glucose)
- allergic reaction at the injection site (such as redness, swelling or itching.)
- generalized allergic reaction to insulin (such as rash, shortness of breath, wheezing, reduced blood pressure, rapid pulse, or sweating.)
- injection site pain
- weight gain

Some of the common symptoms of **hypoglycemia** are:

- sweating
- tremors (shaking)
- increased appetite
- dizziness
- nervousness
- palpitations (fast heartbeat)
- headache
- nausea
- confusion

Severe cases of hypoglycemia could cause unconsciousness and, in extreme cases, death.

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Some of the common symptoms of **hyperglycemia** are:

- increased thirst
- increased urination
- dehydration
- fruity smelling breath or urine
- fatigue
- difficulty thinking

Occasionally, people have allergic reactions to drugs. A severe allergic reaction could be life-threatening. Examples of an allergic reaction include:

- a rash
- shortness of breath
- wheezing
- sudden drop in blood pressure
- swelling around the mouth, throat, or eyes
- fast pulse
- sweating

Amaryl®

Side effects that may occur during this study based on the experience of other people who have taken Amaryl® (glimepiride) may be:

- Dizziness
- Sweating
- Tiredness
- Palpitations
- Nervousness
- Or other symptoms of low blood sugar.

Other less common effects may include:

- Stomach/intestinal effects (nausea, vomiting, diarrhea, heartburn, loss of appetite, feeling of fullness, constipation)
- Headache
- Skin reactions.
- There is a risk of hyperglycemia (high blood sugar) if glimepiride is not effective. Symptoms of high blood sugar might include all or some of the following:
 - Thirst
 - Hunger
 - Weight loss
 - Tiredness
 - Confusion
 - Nausea or vomiting.

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Insufficient doses of glimepiride may result in hyperglycemia (high blood sugar). Severe high blood sugar may lead to diabetic ketoacidosis, a potentially life-threatening condition.

Thiazolidinediones (TZDs)

The most common side effects of TZD include:

- Anemia
- increase in total cholesterol
- increase in level of fats in the blood
- increase in triglycerides
- weight gain
- increased appetite
- flatulence (gas)
- visual disturbance
- hypoesthesia (decreased sensation)
- paresthesia (numbness and tingling)
- insomnia
- glycosuria (sugar in the urine)
- upper respiratory infection
- sinusitis

In May 2007, the FDA issued new safety information regarding Avandia, recommending that “Patients who are taking Avandia, especially those who are known to have underlying heart disease or who are at high risk of heart attack should talk to their doctor about this new information as they evaluate the available treatment options for their type 2 diabetes”.

The package insert for AVANDIA was revised in November 2007. The new package insert included the following risks and warnings about TZDs and AVANDIA:

- Thiazolidinediones (TZDs), including rosiglitazone (Avandia), cause or exacerbate congestive heart failure in some patients and that you should carefully watch for signs and symptoms of heart failure (including excessive, rapid weight gain, dyspnea, and/or edema).
- AVANDIA is not recommended in patients with symptomatic heart failure. The use of AVANDIA in patients with heart failure is contraindicated (not indicated).
- AVANDIA has been shown to be associated with an increased risk of myocardial ischemic events, such as angina (chest pain) or myocardial infarctions (heart attacks).
- Co-administration of AVANDIA and insulin is not recommended.

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PLEASE NOTE: The information listed in this document does not include all risks associated with AVANDIA.

Please review the new package insert and discuss any concerns regarding your treatment with Avandia with your primary care doctor and the study doctor prior to your continued participation in the study.

If are currently enrolled in this clinical study, you must communicate any changes in your medical treatment to the study doctor. You will have the option to continue in this study if your doctor decides to continue the use of AVANDIA, discontinue the use of AVANDIA, or switch your treatment to Actos.

ACCORD Study News Release

On February 6, 2008, the National Institutes of Health stopped the intensive treatment arm within the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study, a large, ongoing North American clinical trial of diabetes and cardiovascular disease. The intensive arm of the ACCORD study enrolled patients with diabetes and vascular disease, or multiple cardiovascular risk factors, to an intensive treatment program targeting normal blood glucose values and an A1C less than 6%. In this arm, the researchers observed a higher death rate. The intensively treated participants in ACCORD are now being switched to the standard treatment program (targeting A1c 7-7.9%).

While the ACCORD researchers have not determined a specific cause for the increase deaths, you should discuss the findings with your study doctor and your primary care doctor, prior to your continued participation in the study.

If the study drug appears to be causing problems that you and/or the study doctor find unacceptable, it will be stopped.

The study drugs may have risks that are not known at this time. If new information is discovered that might change your decision to stay in this study, you will be told about it in a timely manner.

Please notify the study doctor or study staff immediately (for name and telephone number see page one) if you experience any of these or any other side effects during the study. You will be monitored throughout the study in order to minimize risks.

Drug Interactions

It is not known how the drug(s) in this study may interact with other medications including, but not limited to, over the counter medications, herbs, dietary supplements or supplement mixtures and compounds. You **must** discuss with the study investigator any medications you are currently taking or may take in the future including over the counter medications, herbs, dietary supplements and supplement mixtures and compounds.

Pregnancy Risks

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The risks to an unborn baby or a nursing child from the study drug are not known. Therefore, if you are pregnant, planning to become pregnant, or are breast-feeding you cannot participate in this study.

Women who could become pregnant must use methods of avoiding pregnancy approved by the study doctor throughout the study. The study doctor will discuss these appropriate methods and options of avoiding pregnancy with you.

Some drugs may interact with particular methods of avoiding pregnancy so that they may not be as effective.

You will be required to have three pregnancy tests during the study. A pregnancy test does not stop you from becoming pregnant.

If you suspect that you have become pregnant at any time during the study, or if you do not use one of the methods of avoiding pregnancy recommended by the study doctor, you must immediately notify the study doctor. If, during this study, you become pregnant the study drug will be stopped and the study doctor will withdraw you from the study. The study doctor will follow the progress of your pregnancy and birth of your child and report this information to the sponsor and the Institutional Review Committee (IRC). The IRC 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 safety and welfare in mind. Payments for all aspects of obstetrical care, child- or related care would be your responsibility.

Blood Samples

The risks from drawing blood are pain, bruising, infection or inflammation at the site of the blood draw, and feeling faint. The total amount of blood that will be taken during the entire study is approximately 17 tablespoons over a 64 week period which is equal to approximately 1.5 tablespoons per visit. The fingerstick blood sampling may cause some soreness and bruising at the site of the puncture (fingerstick) and rarely infection.

Alternatives to Participation

Participation in this study should not take the place of your usual ongoing medical care. You do not have to participate in this study to receive treatment for your condition or to receive the study medications. There are other ways to treat your condition. Some of these treatments are:

- prescription medications
- other FDA approved insulins
- exercise and diet changes

The study doctor will explain these other treatments to you. The study doctor will tell you more about the risks and benefits of participating in this study as compared to the risks and benefits of alternative treatments.

Benefits of this Study

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The study drug may help your type 2 diabetes mellitus, but there is no guarantee that participating in this study will help you. Your condition might not improve or might get worse while you are in this study. You will receive study-related visits, procedures, tests, study drug, and blood glucose meter and supplies at no cost only during the period that you are participating in the study. Information gained from this study may help develop new treatments for patients in the future.

Costs of Participation

There is no cost to you (and/or your health care payer) for participating in this study. While you are participating in this study, you will receive the study medications (Novolog® Mix 70/30™, Apidra®, Lantus® Insulin, and glimepiride (Amaryl®), blood glucose meter and supplies, and study-related tests and examinations at no cost.

You will still be responsible for the cost of your usual ongoing medical care, including procedures and/or non-study drugs that are not required by this study. If you have any questions, please ask the study doctor, a member of the study staff, and/or your health care payer.

Compensation for Being Part of This Study

If you qualify and agree to participate in this study, you will receive \$300 if you complete the whole study. If you do not finish the whole study, you will receive \$25 for each scheduled visit you complete and \$50 for visit # 11. You may also receive some study and diabetes-related items from the sponsor during the study. The study doctor or study staff can tell you more about when and how you will receive compensation.

Voluntary Participation in and Withdrawal from the Study

Participation in this study is entirely voluntary. You do not have to take part in this study, and if you do decide to take part, you are free to withdraw at any time. Your routine medical care at this study center and the attitude of your study doctor toward you will not be affected if you decide not to take part in this study or if you decide to withdraw later. If you refuse to participate, it will not affect any benefits to which you are otherwise entitled that are unrelated to the research study, such as your health plan benefits or your rights as a patient.

If you want to leave the study early, please notify the study doctor or a member of the study staff. You may be asked questions about your experience while you were in the study. You may be asked to have follow-up evaluations such as laboratory tests or a physical examination to help your withdrawal from the study happen safely. The study doctor may feel that you need additional medication to treat your condition when you leave the study, and he/she will discuss this with you at that time. For your own safety, it is advisable to tell the study doctor if you intend to leave the study early.

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You may be withdrawn from the study even if you want to continue. This could happen if you have serious side effects unknown at this time, if you do not follow instructions about the study, if there is a change in your medical condition, or if the sponsor stops the study for any reason.

Treatment and Compensation for Illness or Injury Resulting From This study

Reimbursement will be made for any reasonable and necessary medical expenses incurred by you as a direct result of adverse reactions from Apidra®, Lantus®, Amaryl® or Novolog Mix® 70/30™, medical procedures required by the study or the administration of Apidra®, Lantus®, Novolog Mix® 70/30™ or Amaryl®, during the study. Financial compensation for such things as lost wages, disability or discomfort due to a study related injury is not routinely available. You will not give up any legal rights by signing this form.

Contact Information

The study doctor, **Dr. Anuj Bhargava**, or study staff will answer any questions you have about this research study or your participation in the study. You can ask questions at any time during the study and ask for more information. If you have any questions about the study, or if you experience an injury, illness, or side effect, you are to contact the study doctor or a member of the study staff at the telephone number listed on page one of this informed consent.

If you have any questions about your rights as a research subject, or complaints regarding this research study, you should call **Dr. Prasad Palakurthy, M.D., Chair of Mercy Medical Center's Institutional Review Committee**, 1111 6th Ave. Des Moines, IA 50314, Phone 515-247-3985. Office hours are Monday through Friday generally 8am to 4pm. The Mercy Medical Center Institutional Review Committee is an independent committee established to help protect the rights of research subjects.

If you have any questions about the privacy or confidentiality of your medical information you should contact: Privacy Officer of Mercy Medical Center at 515-643-4557.

Confidentiality

During your participation in this research study, your study doctor will collect your demographic data and data on your health and ethnic origin. Your collected data will be reported to sanofi-aventis, the sponsor of this study. Sanofi-Aventis will store and process your data with electronic data processing systems and will keep the data as long as the study drug is marketed or under investigation. Your personal identity, that is your name, address, and other identifiers, will remain confidential. In the sponsor's database, you will only be referred to by a code number, initials, and date of birth. Only your study doctor will be able to link the code number to your name and will keep this information for 15 years.

Sanofi-Aventis will analyze the data statistically in order to determine the efficacy and safety of Apidra®, Lantus®, and Novolog Mix® as well as for general health research. Your data may be submitted to domestic and foreign drug regulatory agencies in marketing authorization for Apidra® or Lantus® and may be used in scientific publications. If the results of the study are published, your identity will remain confidential. Your data may also be forwarded immediately

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to domestic and foreign drug regulatory agencies in case you should suffer an adverse reaction to the study drug.

Representatives of sanofi-aventis, the Institutional Review Committee, or domestic or foreign regulatory authorities may directly access your medical records at the study center in order to determine the accuracy of the reported data. These representatives will keep your identity confidential to the extent permitted by law.

You have the right to access your study data at your study doctor's office and to request corrections of any data that are wrong as long as this information is in the study doctor's possession. However, to ensure the scientific integrity of the study, you agree that you may not be able to review some of your records related to the study until after the study has been completed.

REGULAR DOCTOR OR SPECIALIST NOTIFICATION OPTION

With your permission, your regular doctor will be notified of your participation in the study.

Please indicate below whether you want us to notify your regular doctor or your specialist of your participation in this study.

_____ Yes, I want the study doctor to inform my regular doctor/specialist of my participation in this study:

Name of Doctor _____ Phone _____

_____ No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The study doctor is my primary care physician/specialist.

CONSENT STATEMENT

You will be given a signed copy of this informed consent document.

Subject number: _____

1. I have read the informed consent document for this study. I have received an explanation of the nature, purpose, duration, and foreseeable effects and risks of the study and what I will be expected to do. My questions have been answered.

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2. I agree to take part in this study. I agree to cooperate fully with the study doctor and will contact him/her immediately if I suffer any unexpected or unusual symptoms during the study. For the duration of the study, I will notify the study doctor of any other medical treatments that may be necessary for me to undergo.
3. I have informed the study doctor of all my previous or present illnesses and medication and of any consultation that I have had with my regular doctor in the last 12 months.
4. I have further informed the study doctor of any participation by me in other research studies in the past year.
5. I am aware that if I do not cooperate fully with the study doctor's requests and directions, I may harm myself by participating in the study.
6. I have been told that my participation in the study is voluntary and that I may refuse to participate or may withdraw from the study at any time, without penalty or loss of benefits to which I am otherwise entitled. I have been told that any information that becomes available during the course of the study that may affect my willingness to take part will be disclosed to me as soon as practicable.
7. Representatives of the sponsor, Institutional Review Committee, or local or foreign regulatory authorities may wish to examine my medical records to verify the information collected. By signing this document, I give permission for this review of my records.
8. I will also be asked to sign separate forms authorizing the use and disclosure of my Protected Health Information in connection with research.

Printed Name of Participant

Signature of Participant

Date

I certify that under state law I am the legally authorized representative of the Participant named above and that I am authorized to sign this consent to his/her participation in the medical research study described above. I am also authorized to sign this authorization to release medical records and health information as described above.

Printed Name of Legally Authorized Representative

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Signature of Legal Representative

Date

Printed Name of Person Explaining Consent

Signature of Person Explaining Consent

Date

I attest that my representative or I discussed this study with the above named participant or legal representative. This person had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participate in this study.

Signature of Principal Investigator
or Sub-Investigator

Date

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