

## Appendix E. Intravenous Glucose Tolerance Test (IVGTT)

**Definition:** An IVGTT to evaluate First Phase Insulin Response (FPIR) will be completed at the Oral Insulin Trial Initial Visit. The results of this procedure will not affect randomization or entry in the study, but will be used to determine the particular study stratum the participant will be placed in for data analysis.

### Exclusion Criteria for Performing an IVGTT

DO NOT perform the IVGTT if:

1. The fasting blood glucose  $\geq 160$  mg/dl (if reading is by meter then a stat glucose should be performed in local lab if able). **Do not proceed with performing an IVGTT if the subject manifests unequivocal elevation of fasting plasma glucose ( $\geq 160$  mg/dL) in the local laboratory.** In this case, draw all the fasting samples to send to the core laboratories.
2. Subject has used systemic corticosteroids.
3. Subject has used corticosteroids (intra-articular, inhaled, or topical) in the past 1 month.
4. Subject has used diuretics,  $\beta$ -blockers, or niacin in the past 1 month.
5. Subject has an acute sickness or stress (e.g. surgery, injury or infectious disease in the past 2 weeks). The test should be postponed for at least two weeks after resolution of any intercurrent infectious illness or other stress.
6. Subject is pregnant or suspects she might be pregnant.

### Subject Preparation for an IVGTT

Because a large number of factors may affect the IVGTT, care must be taken to properly prepare patients for the test.

### Dietary Guidelines

1. The subject should follow a diet containing at least 150 grams (g) of carbohydrates for at least 3 days prior to the test. If the subject has not consumed sufficient dietary carbohydrates before the test, the insulin secretory response to the glucose may not be as great as it should be and the test results may be unreliable. Dietary sheets providing guidelines for the high carbohydrate diet should be given to each participant in time to prepare for the test.
2. 10 hour fasting, except for water.
3. 10 hour abstinence from cigarettes, alcohol, caffeine-containing drinks and vigorous exercise
4. Water consumption is encouraged, especially for young children.

The test must be started between 6 AM and 10 AM after an adequate night's sleep. Appointments should not be scheduled for mornings on which a subject has had to work during the preceding night.

### IVGTT Administration Eligibility Checklist

<input type="checkbox"/>	Subject fasted (did not eat) after 10:00 PM the night before the test up until the start of the test. <i>Subject avoided all food and drink, with the exception of water.</i>
<input type="checkbox"/>	Subject abstained from consuming <i>coffee, tea, sodas, caffeine containing drinks, cigarettes, alcohol, or chewing gum</i> during the fasting period (10 hours before the test).
<input type="checkbox"/>	Subject refrained from vigorous exercise during the fasting period (10 hours before the test).
<input type="checkbox"/>	Subject refrained from working during the night preceding the test.
<input type="checkbox"/>	Subject ate a high carbohydrate diet (at least 150 grams) ( <i>See Sample Menu in Appendix B for details</i> ) for 3 days prior to testing.
<input type="checkbox"/>	PI reviewed medication list, including over the counter meds, to determine whether ok to proceed with test. Note, PI may contact TN07 CRA or Study Chair if he/she is uncertain about whether IVGTT should be performed.
<input type="checkbox"/>	If subject has had an illness, surgery, or infection, the PI has evaluated the subject and determined whether the test should be done. Note, the PI may contact the TN07 CRA or Study Chair if he/she is uncertain about whether the IVGTT should be performed
<input type="checkbox"/>	Subject is not pregnant, does not have any chronic illness such as cancer, nephritic syndrome, active hepatitis, or some other life threatening illness.
<input type="checkbox"/>	At start of IVGTT, the subject's blood glucose was less than 160 mg/dL.

## Clinic Preparation for an IVGTT

### Supplies

Please refer to the TN07 Laboratory Manual of Operations for IVGTT supplies.

### IVGTT Testing Procedures

#### Procedure:

- Step 1. Ensure the participant is fasting.
- Step 2. Prepping participant for IVGTT:
  - a. The IVGTT must begin between 6:00 - 10:00 a.m. for proper interpretation.
  - b. Obtain the weight of the subject and calculate the glucose load to be administered. The glucose load should be rounded to the nearest tenth (0.1) mL and recorded on source documentation. Prepare glucose solution. Glucose dose will be 0.5 g/kg body weight up to a maximum of 35 g (See box below.)

#### **Glucose Dose Calculation for Administration:**

Subjects weight in pounds \_\_\_\_\_ multiply by 0.454 = \_\_\_\_\_ kg

Subjects weight in kg \_\_\_\_\_ multiply by 0.5g = \_\_\_\_\_ glucose load in grams.

Glucose load in grams \_\_\_\_\_ multiply by 4 = \_\_\_\_\_ volume in ml of 25% glucose solution \* to be administered for the test (maximum dose 140ml)

Glucose (dextrose) is generally supplied as a 50% solution in a 50 mL vial. **To prepare 25% glucose solution**, using a 60 mL syringe, mix 50% Dextrose INJ, USP with an equal volume of normal saline. Invert the syringe several times to mix the glucose with the saline.

**Note: Maximum dose (35 g) represents 140 mL** (requires three 50-60 mL syringes or bag and peristaltic pump)

- c. Set up the glucose delivery system and tubing to be used.
- d. The subject should remain lying in bed throughout the test.
- e. Place an I.V. line into an antecubital vein, using an intracatheter (usually 20 or 22 gauge depending upon the size of the subject). Maintain IV patency per your institution's guidelines. If blood sampling is more than 3 minutes apart, you may flush with 1-3 ml of normal saline.

The IVGTT procedure can be done using either one or two I.V. lines. The standard setup consists of two three-way/four-way stopcocks attached to one line; however, two lines are equally acceptable and may be advantageous for individuals who are less experienced and may feel more comfortable having a second line available- one for injection of glucose and the other for blood withdrawal (or in case one line stops working). If you use 2 lines, you may use a butterfly needle for the blood withdrawal side if necessary.

When using one line, be careful to flush out the line or stopcock after the injection of glucose. Failure to do so may result in falsely elevated glucose values, which would also dilute the 1 and 3-minute insulin values.

Failure to inject the glucose properly will also result in inaccurate glucose values. The following criteria have been adopted by TrialNet:

**•IVGTT samples will be considered unusable and the test must be repeated if the 1-minute blood glucose level is  $\leq 180$  mg/dL or  $\geq 800$  mg/dL.**

Step 3. Suggested Sampling Method for 1 Line

- a. Extreme care must be taken so that samples are not contaminated with saline or with each other. To avoid dilution of the blood sample, place two adjacent disposable 3-way/4-way stopcocks in the saline/specimen collection line; for convenience we will refer to these as the “proximal” stopcock (nearest the subject) and the “distal” stopcock. Please use the proximal stopcock for specimen collection and the distal stopcock for waste. You will attach the appropriate S-Monovette collection tubes to the proximal stopcock. You may connect a S-Monovette collection tube or syringe to the distal stopcock for waste. If your institution requires that you return waste, you will need to use a syringe.
- b. Squeeze air from syringes before attaching. The distal syringe may remain in place throughout the test. The blood from the “proximal” syringe can be divided into tubes for glucose and insulin.
- c. About 15 seconds before the assigned sampling time, close off the distal stopcock and draw a volume of blood equal to 2 times the “dead” volume of the tubing (between stopcock and the proximal tip of the indwelling catheter) up into the syringe (not more than 3 mL). Turn the proximal stopcock to close off the distal stopcock, and draw a blood sample of sufficient total volume for all the determinations into the sampling syringe.
- d. Turn both stopcocks again so that the blood drawn in the distal syringe can be returned to the participant, according to institutional policy. Resume the saline drip.
- e. Refer to the Media Center and review the TN07-IVGTT training video for additional training on the procedures.

Step 4. Obtain baseline samples:

- a. The first sample should be taken at least 10 minutes after establishing the line(s) and when subject is calm and relaxed. This is the “-10 minute” sample.
- b. Throughout the procedure, record the **actual time (24 hour clock)** of each time point in source documentation. Reference key below for 24 hour time clock:

<b>12-Hour Clock</b>	<b>24-Hour Clock</b>	<b>12-Hour Clock</b>	<b>24-Hour Clock</b>
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1:00 am	01:00
2:00 am	02:00
3:00 am	03:00
4:00 am	04:00
5:00 am	05:00
6:00 am	06:00
7:00 am	07:00
8:00 am	08:00
9:00 am	09:00
10:00 am	10:00
11:00 am	11:00
12:00 pm (noon)	12:00

1:00 pm	13:00
2:00 pm	14:00
3:00 pm	15:00
4:00 pm	16:00
5:00 pm	17:00
6:00 pm	18:00
7:00 pm	19:00
8:00 pm	20:00
9:00 pm	21:00
10:00 pm	22:00
11:00 pm	23:00
12:00 am (midnight)	00:00* (next day)

- c. The second sample should be taken exactly 6 minutes after the first one. This is the “- 4 minute” sample.
- d. In order to minimize hemolysis, which may alter insulin concentration, avoid mechanical shear (e.g., small gauge needle transfers, shaking).

Step 5. Glucose infusion:

- a. Injection of concentrated glucose may cause the subject to feel flush and/or hot; some describe it as a “rush”. Before injecting the glucose, describe these symptoms to the subject and mention that this is a normal reaction that will only last about a minute.
- b. Infusion should be both preceded and followed by a vigorous saline flush (~ 5 -10 mL each time) to avoid clogged lines, phlebitis and delayed distribution of glucose.
- c. Withdraw blood into line before injecting glucose to be sure the I.V. has not infiltrated. The duration of the infusion may be measured on a separate device (e.g., wall clock or second timer). **NOTE:** Do not proceed to infuse the glucose if the line is not patent or if blood flow is impaired. It is extremely painful if the glucose infiltrates into the tissues.
- d. Start infusion exactly one minute after taking the second baseline sample, i.e. at -3 minutes.
- e. Allow 3 min ± 15 seconds for infusion (so that infusion time lasts from - 3 minutes until 0 minutes). Record any deviations from the sampling protocol in your source documentation.
- f. Attempt to infuse the glucose solution smoothly throughout the three-minute period (HINT: divide the total volume by 3 for the amount to be infused each minute. Then divide this number by 4 to determine the amount to infuse every 15 seconds.)
- g. Record the 0 minute time in source documentation (at the end of the infusion).

Step 6. Obtain post-glucose blood samples

- a. Before the procedure, fill several 3 mL syringes with luer lock tips with 1 mL normal saline solution to flush the adapter after each blood draw. This is only necessary if the blood sampling is more than 3 minutes apart.
- b. Draw appropriate samples at 1, 3, 5, 7, and 10 min after time 0' (see Sampling Protocol) and record the actual time of each draw in source documentation.
- c. If the withdrawal of the blood sample cannot be completed in 20 seconds, record the time the blood withdrawal ended in source documentation.

Step 7. Termination of an IVGTT

- a. After drawing the final sample at 10 min, the IV line(s) may be terminated. Apply pressure to the site and then apply a sterile strip bandage. The subject should then be given a snack, such as peanut butter or cheese crackers, milk or ginger ale.

Clogged lines, missed samples and other procedural issues should be noted in source documentation. If samples are missed, please select “not collected” in the online specimen collection form. **If the 1 and/or 3 minute samples are not collected, immediately notify the TNCC TN07 protocol CRA to determine if the IVGTT should be repeated.**

**Sampling Protocol:**

Time (min)	Glucose Sample Taken 1.2 mL gray top tube	Insulin Sample Taken 1.2 mL green top Li Heparin Tube
-10		X
-4	X	X
Glucose Infusion		
1	X	X
3		X
5		X
7		X
10		X

**IVGTT Sample Processing, Storage, and Shipping**

Please refer to the TN07 Laboratory Manual of Operations for IVGTT sample processing, storage, and shipping instructions