Manual of Procedures
Section 19. Frequently Asked Questions

Table of Contents

Please note that sections are numbered to correspond to the relevant MOP section. The answers to these questions will eventually be incorporated in the MOP. Some of these questions may result in changes in the inclusion/exclusion criteria, but there likely will be no change until the next DSMB meeting in January of 2014.

19.4 Visit Scheduling

Q1: If a participant ate the morning of the visit, should I complete the visit (e.g. vital signs, other questions) and have participant return for the blood tests the next day?

A: **No**, the entire visit should be rescheduled. All data entered in EDC for a specific visit must be collected the same date, otherwise, there will be confusion with the visit and blood collection dates and laboratory results will not be uploaded correctly.

Q2: Can a participant be scheduled for a visit that requires fasting in the afternoon?

A: In most cases the answer is **No**, visits should be scheduled for the morning after an 8-hour overnight fast. The exception is if the participant regularly works an evening or a night shift and typically sleeps into the late morning or early afternoon, it may be appropriate to schedule the participant's visit for the early afternoon.

Q3: Does a participant's follow-up visit need to be postponed if he donated platelets?

A: No, the visit does not need to be postponed. Unlike donating whole blood, the donation of platelets will not alter the hemoglobin A1c results.

19.6 Screening & Inclusion – Exclusion Criteria

Q1: At the screening visit, can I use the glucose and/or HbA1c results from a finger-stick in lieu of a glucose and/or HbA1c done by the local laboratory?

A: **No**. Sites may use a glucose and/or HbA1c result from a finger-stick as a pre-screening approach to see if the participant should complete the screening visit. However, before qualifying for the baseline visit, fasting plasma glucose (from a sodium fluoride tube) and HbA1c (from an EDTA tube) must be done by the local laboratory

---

Q2: Many participants who qualify otherwise do not want to stop their high dose vitamin D or calcium supplements to meet the study's criteria. How should I handle this?

A: The maximum vitamin D (no more than 1000 IU/day) and calcium (no more than 600 mg/day) intake from supplements allowed for all D2d participants is based on the most objective evidence available. There is no limit in how much vitamin D or calcium participants can take from food or beverage sources (e.g. dairy products). Sites should discuss with participants the rationale behind what the D2d study allows and refer participants to the D2d website for more information. Staff should use the information on the D2d website (d2dstudy.org/about/vitamin-d) as a guide to educate

participants and clinicians. The CC has also developed a more extensive "Talking points about vitamin D and calcium," which is found in the appendix of MOP 6.

Q3: I have a person who is interested in participating in the study but is taking 1200 IU/day of vitamin D supplement. The protocol states she should not be taking more than 1000 IU/day within 12 weeks of the baseline visit. However, since she is only taking a little over the 1000 IU/day limit can the wait period be shorter, e.g., 4 weeks?

A: **No**. The exclusion criteria do not allow for modifications to the wait period dependent upon how much above the 1000 IU/day maximum the person is taking. During prescreening, the potential participant should be asked about all of his/her supplement intake and be asked to read the dosage off of each bottle (individual supplements and multivitamins). If the person is taking more than 1000 IU/day and is willing to reduce the daily dosage to no more than 1000 IU for the duration of the study, the Screening and baseline visit should be scheduled such that *at the baseline visit the person has been taking ≤1000 IU/day for at least 12 weeks.*

Q5: At the screening visit, a participant missed the glycemia criterion by a small margin (e.g. 1 mg/dL). Can I bring the participant back for re-screening? Can I repeat only the FPG or do I have to repeat the entire visit?

A: If a participant misses the screening glycemia criterion by a small margin (defined as margin of error for FPG ± 3 mg/dL or HbA1c ± 0.1%), the fasting plasma glucose (or HbA1c) can be repeated once. The repeat measure should be entered into the EDC screening local laboratory form and used to determine if the participant meets the criteria to proceed to the baseline visit. The repeat test should be done within a short period to ensure that the time elapsed between the original screening date and the baseline visit is less than 6-weeks (to stay within the schedule shown in MOP 4).

What if a participant misses a glycemia criterion at baseline by a small margin (e.g. HbA1c by 0.1%)? Can I repeat only the HbA1c or do I have to repeat the entire visit?

If a participant misses a baseline glycemia criterion by a small margin (defined as margin of error for FPG ± 3 mg/dL, HbA1c ± 0.1% or 2hPG ± 5 mg/dL), the entire baseline visit (FPG, HbA1c and 2hPG) may be repeated once. Repeat testing should be done within a short period to ensure that the time elapsed between the original screening date and the baseline visit is less than 6-weeks (to stay within the schedule shown in MOP 4).

Q6: A potential participant is known to have an A1c of ~6%. At the screening (or baseline) visit, this volunteer missed the HbA1c criterion by a margin larger than allowed, e.g. lower by 0.2%; however, there is a good explanation. The volunteer donated blood 8 weeks prior, can the volunteer return to repeat the screening/baseline visit?

A: The participant may return to repeat the screening/baseline glycemia measures; however, such exceptions should be rare and supported by an explanation that needs to be documented in the source documents. The CC will carefully monitor such exceptions. It is important to keep in mind that the repeat test should be done within a short period to ensure that the time elapsed between the

original screening date and the baseline visit is less than 6-weeks (to stay within the schedule shown in MOP 4), otherwise the entire screening visit must be repeated.

⇒ Participants should be reminded at all visits, starting at the screening visit, to not donate blood during the 8 weeks prior to a study visit. In addition, during the visit reminder calls participants should be asked if they have experienced any condition in the prior 8 weeks that may affect glucose tolerance (e.g. infection, blood donation or transfusion).

Q7: If a person recently had labs drawn prior to the screening visit, can the results be used for the screening labs?

A: Yes, only under the following circumstances:

- The laboratory tests were run at the same local laboratory used for the study.
- The laboratory tests were done within 4 weeks of the screening visit and 6 weeks of the baseline visit.
- The plasma glucose drawn in clinical practice was done while fasting >8 hours overnight.

Q8: A potential participant reported at prescreening that she had a vertical sleeve gastrectomy in 2011 - would she be excluded because of this surgery?

A: **Yes, participant is excluded**. According to the protocol, bariatric surgery – including vertical sleeve gastrectomy - is an exclusion criterion.

Q9.a: A potential participant reports that she was diagnosed with type 2 diabetes about 9 months ago. At that time, her hemoglobin A1c was 7.6%; however, she changed her lifestyle, lost weight and last month her A1c was 6.3%. Should I screen her?

Q9.b: Another participant was diagnosed with type 2 diabetes 3 years ago. At that time, his hemoglobin A1c was 9.1% and was on insulin and metformin. He has been on no diabetes medications for the 16 months and his A1c was 6.1% last month. Should I screen him?

A: **Yes**, both participants may be considered for a screening visit. D2d excludes people with diabetes at present (based on glycemic criteria or current use of medications) or if they have not been on diabetes pharmacotherapy within the past year. Past diabetes, by itself, is <u>not</u> exclusion.

Q10: A potential participant, who otherwise qualifies, had pituitary surgery more than 20 years ago and has been maintained on 3 mg of prednisone daily for secondary adrenal insufficiency since surgery without any change in the dose of prednisone for more than 10 years. He is also on 75 mcg of levothyroxine for secondary hypothyroidism and no other medications. The patient is stable and there have been no episodes of Addisonian crises requiring stress doses of glucocorticoids for more than 10 years. Physiologic dose of glucocorticoid replacement is not an exclusion criterion, correct?

A: **Correct**, this participant should <u>not be excluded</u> simply on the basis of stable adrenal insufficiency, as his condition does not affect assessment of glycemia. Only participants who require supra-physiologic doses of glucocorticoids are excluded.

19.8 Concomitant Medications

Q11: If a participant has a glucocorticoid injection into a joint or epidural space, how long do we need wait before coming in for a visit that requires glycemic testing (e.g. screening, baseline)?

A: The visit should be scheduled not earlier than 1 week after the injection.

Q12: If a participant is taking fish oil supplements to lower their triglycerides, should we record it on the Concomitant Medication form?

A: **No**. Data on supplements that the participant buys over the counter should not be recorded on the Concomitant Medication form.

Q13: If a person is taking gabapentin (Neurontin) for a non-seizure disorder (e.g. neuropathy), do they need to be on a stable dose for 6 months?

A: Yes, protocol exclusion criteria 14, requires participants to be on stable doses of anticonvulsants fo 6 months prior to screening. The indication for treatment does not matter.
