IMPAACT 2002 Version 1.0 Frequently Asked Questions

SCREENING BLOCKS AND RANDOMIZATION PROCEDURES

1. Are we able to add a block of participants into the Subject Enrollment System (SES) after the initial phase of adding the potential candidates that we identified as likely eligible?

Yes, once sites are close to screening all of the participants that were originally submitted, they may submit new participants into the Screening Log to receive additional randomization blocks. Sites are asked not submit additional participants 1 or 2 at a time, rather instead wait to submit a list of ~10-12 for a new randomization block.

2. For participants that screen fail but could be eligible later, how should the site put them back into the que for randomization?

If a participant is a screen failure but the site thinks that they may be eligible later, the participant must be submitted again to be re-randomized. The site must first go through all of the participants that were originally submitted, in order of the initial randomization blocks, before a screen fail participant can be randomized again and re-approached.

SCHEDULE OF EVALUATIONS

3. For the COMB-R sites, per the MM Manual, treatment decisions are based on response to treatment, and are determined by QIDS-C score. The SOE and the CRF Schedule do not list QIDS-C evaluation as required under the interim visit column. When is the QIDS-C required?

The MM Manual was not updated in this area. The QIDS-C is *not* required after the initial baseline assessment and treatment thereafter is based on the QIDS-SR not the QIDS-C.

Currently, there are no plans to update the manuals. If there are discrepancies between the protocol and the manuals, please follow the protocol. If the situation is unclear, please query the team.

4. For the COMB-R sites, per the SOEs, the QIDS-SR is only required when the participant meets with the site prescriber; however, per the CRF schedule the QIDS-SR form is required at every interim visit. When should the QIDS-SR be conducted?

The QIDS-SR should be conducted at <u>every MM interim visit</u> and at the scheduled 6 and 12 week interim visits.

5. For the COMB-R sites, the QIDS-SR did not warrant concern during an interim visit with a participant, However, based on clinical observation and judgment of the CBT therapist, presenting clinical symptoms appeared much more severe than as indicated by the QIDS-SR. Based on the CBT therapist's concern, the participant was evaluated by the MM prescriber. QIDS-C was administered per the MM Manual and the participant scored significantly higher. MM evaluation was incorporated into the interim visit and participant's medication dose was maximized as per treatment algorithm. How should sites document this in terms of the CRFs? Should the QIDS-C form be reported for this visit?

The therapist was correct to use clinical judgement since the QIDS-SR did not match with what was observed in the session and asking for MM evaluation was appropriate. The MM form for the interim visit should be completed. <u>The protocol does not require the QIDS-C at subsequent visits (as it is only required at the initial study visit)</u> However, conducting it is not a deviation and does not need to be reported on the CRFs.

6. For the COMB-R sites, if a participant has a separate appointment for medication management (MM) is that considered an interim visit? Or is it only an interim visit if also have psychotherapy at the same visit?

If the visit is not part of Week 1 or Week 6 (for example, if the visit is conducted at Week 3) then it should be documented as an interim visit, even if it is only medication management. Psychotherapy does not have to be conducted at the same time as MM.

7. What process should sites follow if we need to request a visit outside the window?

Generally, protocol teams do not grant permission to conduct a visit outside of the protocol-specified window. If it is necessary to conduct or complete a study visit outside of the visit window, the team encourages you to conduct the visit as soon as possible and document why this occurred.

For any study visits or procedures conducted outside of the protocol-specified window for a given visit, sites must provide a description of the deviation, document the reasons why it occurred, and any corrective and preventative actions taken in the participant's study chart and the site's study specific deviation log. The protocol team's response to any messages regarding the deviation should continue to be included in the documentation.

Additional guidance on protocol deviations, including the policy requirements for protocol deviations considered reportable by the IMPAACT Network can be found here: http://impaactnetwork.org/DocFiles/MOP/ProtDevs_08MAR17.pdf.

8. For the "collect/review locator information" on the Schedule of Evaluations (SOE), there is no corresponding CRF. How should this be documented?

Per protocol, the locator information for each participant should be reviewed at each study visit to confirm that it is accurate and up-to-date. This information should be documented in the participant's files, consistent with your site's SOPs. Additionally, the CRF update memo (dated 22 May 2017) added an optional Sensitive Data (F0101) Form which sites may use.

9. What if a participant consented more than 30 days before completing screening procedures and enrolling into the study?

Per protocol Section 6.1, while screening procedures must be completed within 30 days of enrollment, it is not explicitly stated that consent must also occur within this 30-day period. In general, we would defer to sites to follow your local IRB procedures regarding provision of consent, which may include the circumstances in which re-consent would be required. Unless the protocol specifies otherwise, informed consent is generally not expected to be repeated within six months of initial signing. Prior to enrollment, the site staff will confirm consent verbally – and if needed can review the elements of consent before enrollment.

10. During our Screening/Enrollment visit, the therapist administered the QIDS-C. However, the Medication Management Manual (MM Manual) describes the administration of the QIDS-C being performed by the prescribing clinician. Is it acceptable for the therapist to administer the QIDS-C?

Per protocol Section 5.3.1, a licensed mental health clinician must complete the QIDS-C at Screening.

11. During the Screening/Enrollment visit, we realized we would not be seeing any of the responses to the ASSIST which was administered via ACASI. Should sites be assessing substance abuse risks using our own clinical tools rather than administering another ASSIST to perform this type of assessment?

Yes, sites should assess substance use as per your usual clinical procedures.

12. If the QIDS-SR score and presenting clinical symptoms are not a concern during an interim visit, do sites need to proceed with the medical monitoring visit?

No, if the QIDS-SR and clinical symptoms do not indicate a need, the medical monitoring does not need to be conducted at interim visits; however, it does need to be conducted at Weeks 6, 12 and 24, regardless of the QIDS-SR score and clinical symptoms.

INCLUSION AND EXCLUSION CRITERIA

13. A participant recently reported she is pregnant. We reviewed inclusion and exclusion criteria in IMPAACT 2002 protocol and pregnancy is not listed as an exclusion criteria. Is this participant still eligible for the study?

Pregnancy is not an exclusion criteria for IMPAACT 2002; as long as this participant meets all other inclusion and exclusion criteria, she is considered eligible.

14. A participant is getting therapy outside of the study. Is this person ineligible because they are receiving therapy from a non-study therapist?

It would depend on the therapy. If it is a support group that meets once a month, that could be allowed because it is different from being in treatment. But if the participant is in therapy that would meet any of the CBD checklist items, then they would be ineligible unless they are willing to switch to a study therapist. Please contact the protocol team (IMPAACT.CORE2002@fstrf.org) if it is unclear.

15. A patient reported being diagnosed with bipolar (which is exclusionary), though the site psychiatrist is questioning that diagnosis and whether it was accurate. If the site psychiatrist does not confirm the bipolar diagnosis, could this patient be considered eligible?

If your site psychiatrist does not feel that the diagnosis is accurate, then you can approach and screen the patient. Further clinical screening at the time of the QIDS-C administration will determine whether the bipolar diagnosis is accurate. If the patient is subsequently enrolled, then the response for #21 "Does the participant have a known or self-reported history of any psychotic disorder and/or bipolar disorder" in the eligibility checklist in the Subject Enrollment System would be "No" since you determined the patient does not meet the criteria for bipolar.

16. Does only the clinician's QIDS score determine participant eligibility?

Yes, per inclusion criterion 4.1.6 the clinician's QIDS score (via Quick Inventory of Depressive Symptomatology – Clinician) determines participant eligibility and the participant completes the QIDS-SR via ACASI at Baseline.

TRAINING

17. Where can we access training materials?

All participating site staff were required to take place in both the General IMPAACT 2002 Study Startup Training and Arm-Specific Training held in December 2016. The materials from the General Startup Training can be found on the IMPAACT 2002 webpage: http://impaactnetwork.org/studies/IMPAACT2002.asp.

Arm-specific training for COMB-R and ESC sites consisted of webinar trainings for both Site Therapists and Licensed Prescribers. We are happy to provide the slides from this training upon request. Please contact Kate Lypen (klypen@fhi360.org) or Anna LeViere (aleviere@fhi360.org).

For any new site staff who will be joining IMPAACT 2002, please provide written confirmation that they have reviewed the training materials and request that they send any questions to the protocol team.

18. For ESC sites, does the person providing therapy need to be a licensed provider, or could they be a social worker with a lot of experience providing therapy to HIV-infected depressed youth? We have two individuals at our clinic who provide regular therapeutic care and who have logged the number of hours required for a license, but have not yet received the actual license.

A therapist without a license is acceptable as long as the therapist is currently providing psychotherapy at your clinic, is licensure eligible (meaning has a clinical degree, acquired experience hours) and has access to supervision by a licensed mental health professional at the site. Please contact the protocol team (IMPAACT.CORE2002@fstrf.org) regarding training requirements for staff.

SOURCE DOCUMENTATION

19. Regarding source documentation for pregnancy, are specific labs required to determine participant is currently not pregnant or can we use participant's self-report (no suspicion of pregnancy) if labs are not available.

Site may conduct pregnancy testing as indicated per standard of care; however, pregnancy testing is not required per protocol. Participant self-report may be utilized for source documentation.

20. What should sites be doing for source documentation that ACASI was administered?

The SVW0289 tracking form asks if the ACASI was administered. Complete that question on the tracking form and include a note in the patient's chart documenting that the ACASI was administered to provide source documentation.

21. At ESC sites, how should the site mental health clinician document counseling sessions?

Sites should document whatever information they need to for their clinical record as they would normally do, and the therapist should complete the ESC Therapy Checklist.

DATA COLLECTION AND CASE REPORT FORM CONSIDERATIONS

22. For COMB-R sites, how should the CBT adherence checklist be completed if a client was present, agreed to start the session but very soon after asked to stop and go back home? Should the therapist check that the participant refused, or check the skills that were used?

Check the skills that were used and those completed. Indicate that the session ended early due to the patient asking to discontinue the session. If the participant returns, you can complete the rest of the content for that session.

23. For the COMB-R sites, the CBT Adherence Checklist (QLW0280) asks about the length of the individual session and total length of the visit. What should be included in the total length of visit? For example, should the time to complete the QIDS-SR be included in the time for the individual session or in the total length of the visit? If the participant also saw the Prescriber for medical management, should that time be included in the total length of visit?

The length of session should reflect the length of the **CBT session**. Please exclude the MM session and the time it took to complete the QIDS-SR. Question #4 "total duration of visit" on this form is not necessary, and may be removed from the CRF at a later time; please ignore for now.

24. For COMB-R sites, for the QIDS-SR CRF form QLW0277:

- **Does the CBT clinician need to ask the QIDS-SR questions during the interim visits (face-to face-interview) or does the participant need to complete the questionnaire on his/her own?**

  The clinician does not complete the QIDS-SR; the participant should. The only interim visits in which needs to be completed are the MM visits, not the CBT visits.

- **If the participant must complete the questionnaire on their own, can the clinician help participants if they have any questions, or if they prefer can clinician read the questions to them?**

  If the participant has difficulty with comprehension, their questions about a word or phrase can be answered. If it is anything else, they should be encouraged to "give it your best guess."

- **Does the clinician sign the CRF as source documentation?**

  Source documentation is site specific. Please consult your site's SOPs.

25. For the COMB-R sites, after enrollment into the CBT arm, a participant has been completely non-adherent with study visits. The participant called this morning to say that she is ready to start coming and asked if she could be seen today. We are technically in Week 3 for this participant and have missed the Week 1 visit window by 5 days. Under which week should this visit to be performed?

The best thing to do will be to conduct all of the week one activities when that participant comes in. For the data, key this as the Week 1 visit given that you will be keying the expected Week 1 CRFs. This will prevent the need to exempt the Week 1 forms in delinquency, as well. If you receive any warnings in your upd8 report, please just submit a response in Resolve and the Data Managers will address.

26. For the COMB-R sites, a mental health (psychotherapy) counseling session and a Medication Management session usually occur on the same day for the same visit. However, due to research participant and medication management clinician availability, the medication management portion of the visit is sometimes scheduled on the day prior to or after the mental health counseling session. Is this ok to do? Which date should be used when submitting data via E-data?

Yes, this is fine and expected to occur. Please use the date the visit actually occurred for all forms. Please key the ADM0040: Visit Status Report for each visit to document that two visits occurred

27. For the COMB-R sites, for the antiretroviral medication, on form CMW0074: When reporting the need to maximize dose, (e.g. participant was initiated on Lexapro 10mg, but after MM it was determined that participant will receive Lexapro 20mg), do we need to stop Lexapro (status 1) and re-start medication on the same form with a different status or a different reason for prescription?

Medications in which the dose is raised would be listed as "4-ongoing" in Status. The protocol team is deciding how best to record the updated dose and that information will be shared with sites

28. For the COMB-R sites, when participants are coming in for their individual sessions, (e.g. during interim visits), and the QIDS-SR is being administered on paper should it be completed before or after the counseling session?

Sites should administer the QIDS-SR before the session, so that the clinician can see the scores.

29. For the COMB-R sites, how should missing components (i.e. "Prefer not to answer") be scored for the QIDS-SR, on the QLW0277 form?

Missing values (i.e., "Prefer not to answer") are coded as "8"s. These numerical values should not be incorporated into the scoring algorithm. For components that are based on selecting the highest score of two or more "item" scores, if one of the items is missing (i.e. Prefer not to answer=8), select the highest score of the non-missing items. If all items are missing, consider the component score to be missing.

For computing the Total QIDS-SR Score: If one or two of the nine component scores are missing, the QIDS-SR can still be scored as follows.

- First, assign the missing components values equal to the average of the non-missing component scores.
- The Total QIDS Score is the sum of the nine components, after missing values have been replaced by the average of the non-missing component scores.

If more than two component scores are missing, the QIDS cannot be scored and the Total Score should be coded as missing. In this case, the Protocol Data Managers will instruct sites on how to enter missing values into e-Data for the relevant component and Total scores

For additional guidance and examples, please see the memo titled "Guidance for Scoring the QIDS-SR in Instances with Missing Data." Under the Study Training Materials Section of the IMPAACT 2002 webpage: http://impaactnetwork.org/studies/IMPAACT2002.asp.

30. Where can we access the Subject Enrollment System (SES) and what variables do we enter?

Once you are logged into the FSTRF System, there is a 'Subject Enrollment' link under the Systems column.that will take you directly to the SES. Additional information on how to access the Data Management Center IMPAACT Portal, including the Subject Enrollment System, can be found in the IMPAACT 2002 Manual of Procedures: http://impaactnetwork.org/DocFiles/IMPAACT2002/IMPAACT%202002%20MOP%20v1.1%2028JAN17.pdf.

31. Do we need to submit signs/symptoms, diagnosis, and medication CRFs at each interim visits if there have been no changes to medical history but if there are ongoing issues and medications?

While medical history should be reviewed/assessed at interim visits, if there are no new or updated diagnoses, signs/symptoms or medications to report, the individual CRFs (PE0412, PE0421, PE6833, PE6853 and CMW0047) will not be required. The SVW0289 will only trigger delinquency to look for the additional CRFs if new or updated events/medications are noted since the last visit.

32. On form SVW0289- Study Event Tracking: Questions 4-7 (ex: Participant experienced any new, ongoing or resolved greater than Grade 3 at this visit or since the last visit? Experienced any new, ongoing or resolved diagnoses greater than Grade 3?). At entry, there are new diagnosis, symptoms, and medications that are recorded on the appropriate CRFs. This CRF however, asks specifically if there are grade 3 or above and to answer YES or NO. Do we answer NO and still continue to complete the diagnosis, symptoms and medication CRFs?

The following forms - PE6833 (Signs and Symptoms), PE6853 (Diagnoses), and PE0421 (Medications) - are required at Entry whether you answer "Yes" or "No" to questions #4-7 on the SWV0289 so that participant history may be obtained. Refer to the CRF update memo (dated 22 May 2017) for further clarification.

33. For participants who complete Screening/Entry in the same visit and do not need to come back for a 1 Week Visit, would it be possible to create a new form that would allow sites to record this? Otherwise, sites will be required to contact the DMC to exempt them from the 1 Week form when these visits are combined.

The Visit Tracking (TRK0181) Form is required at Week 0 for all participants and is designed to capture whether the Week 0 and Week 1 visits were conducted separately (on different days) or as a combined (same day) visit. Refer to the CRF update memo (dated 22 May 2017) for additional information.

34. On Form PE0046- CDC Revised HIV Classification: If a participant's CDC HIV classification improves from the most severe classification stage would you like that to be reflected on the CRF or should the most severe classification prevail?

Per the CRF, if there has been a change in the participant's CDC HIV Classification, sites should enter "1-Yes" for Question #2, and indicate the participant's current CDC HIV Classification for Question #3.

35. On Form PE6833- Signs and Symptoms: Would you like all psychiatric symptoms associated with diagnosis of depression reported? This would include symptoms that are already captured by the QIDS-C.

No, symptoms of depression do not need to be listed.

36. Are any questionnaires conducted on paper at any visit during the study?

All **participant completed** questionnaires are conducted through the ACASI, with the exception of the QIDS-SR which is completed on paper at weeks 1,6, 12, and interim visits for COMB-R sites only, and the QLW0283 (Sociodemographics questionnaire) which is completed on paper at week 0.

37. If we conduct Week 0 and Week 1 visits on the same day, which week should be selected for the ACASI?

The ACASI should be entered as Week 0; will then skip to Week 6 and won't enter anything from Week 1.

38. Should participants complete ACASI assessments before or after counseling sessions?

Either way is acceptable.

39. Is there a way for sites to test the ACASI prior to implementation?

Yes, please contact the Protocol Data Managers and they will provide you with a test link.

40. On the SVW0289 tracking form, for the question about how many interim visits were scheduled and how many were kept, should sites record the number of visits between Visit A and Visit B, excluding the current visit?

That is correct, do not include the current visit in this tally.