RISE

SOP for Handling Participant Side Effects

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Based off Healthcare Provider Side Effect/Adverse Event Manual/SOP

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Purpose:

This SOP is for Research Assistants (RAs) in the RISE study, and it describes procedures for identifying, documenting, and reporting side effects (SE).

1. **Side Effect Checklist Overview (SEC; see full survey in Appendix A)**
    a. Participants (PPTs) in the RISE Above Smoking project are given over-the-counter dual nicotine replacement therapy (NRT) to help them in their quit attempt
    b. To enhance PPT safety, symptoms and side effects experienced by study PPTs will be monitored throughout the study and reported to the study physician when needed
    c. Participants will complete a baseline Side Effect Checklist ("SE Checklist v2.0"; SEC) at Intake and repeat assessments at all visits according to how they have felt over the last week
    d. Severity of all side effects will be rated on the following scale:
        i. None (Code 0): no concerns
        ii. Mild (Code 1): symptom present but does not interfere with daily activities
        iii. Moderate (Code 2): symptom interferes with some activities
        iv. Severe (Code 3): no normal activities are possible
        v. From here on, this SOP will refer to mild SEs as Code 1, moderate as Code 2, and severe as Code 3
    e. If particular symptoms are endorsed by the PPT, study staff will email the study physician who will then determine . . .
        i. if any action should be taken by the PPT (e.g., changing the dosage or discontinuing study NRT; discontinuing the quit attempt, etc).
        ii. whether the symptoms/side effects are related to the study medication and thus, whether they need to be reported to the IRB and other entities
    f. Remember, any side effect may be related to medication; it may be a Serious Adverse Event; it may require reporting to the study physician, research coordinator, and PI

2. **Side Effect Tracking**
    a. RAs willcheck the Side Effect Tracking form at each visit to see if any symptoms/side effects need to be reported to the study physician
    b. The form looks like this:

Record ID	257-4
Participant information: **I am NOT** **a real participant** **[phone_screen_arm_1][phone_number_main]**	
Max Side Effect Intensity reported by patient was:	2 View equation If a Code 3, this is a possible SAE and must be reviewed by the HCP immediately.
Code 2 Side Effect Endorsements (symptom interferes with some daily activities) Code 2 events limited to: -cardiac symptoms (irregular heartbeat or palpitations, increased heart rate, chest pain), -dermatologic symptoms (skin swelling, skin rash or redness (not sunburn)), -depressed mood, -specific gastrointestinal symptoms (vomiting, indigestion), and -specific sleep problems (insomnia, abnormal dreams)	
Code 3 Side Effect Endorsements (no normal activities are possible) -any symptom	
Insomnia **In: _____** **V1: _____** **V2: and interferes with some activities** **V3: _____** **V4: and interferes with some activities** **V5: _____**	○ None ○ Does not interfere with daily activities ○ Interferes with some activities ○ No normal activities are possible reset The HCP can recode the symptom using the radio buttons above
STAFF: Are there any symptoms listed above for the current visit? * must provide value	○ No ○ Yes reset If NO, submit the form as complete. If YES, save as unverified and send the link to HCP/PI per the EvarQuit SE and SAE manual.
HCP/PI Response Other comments	

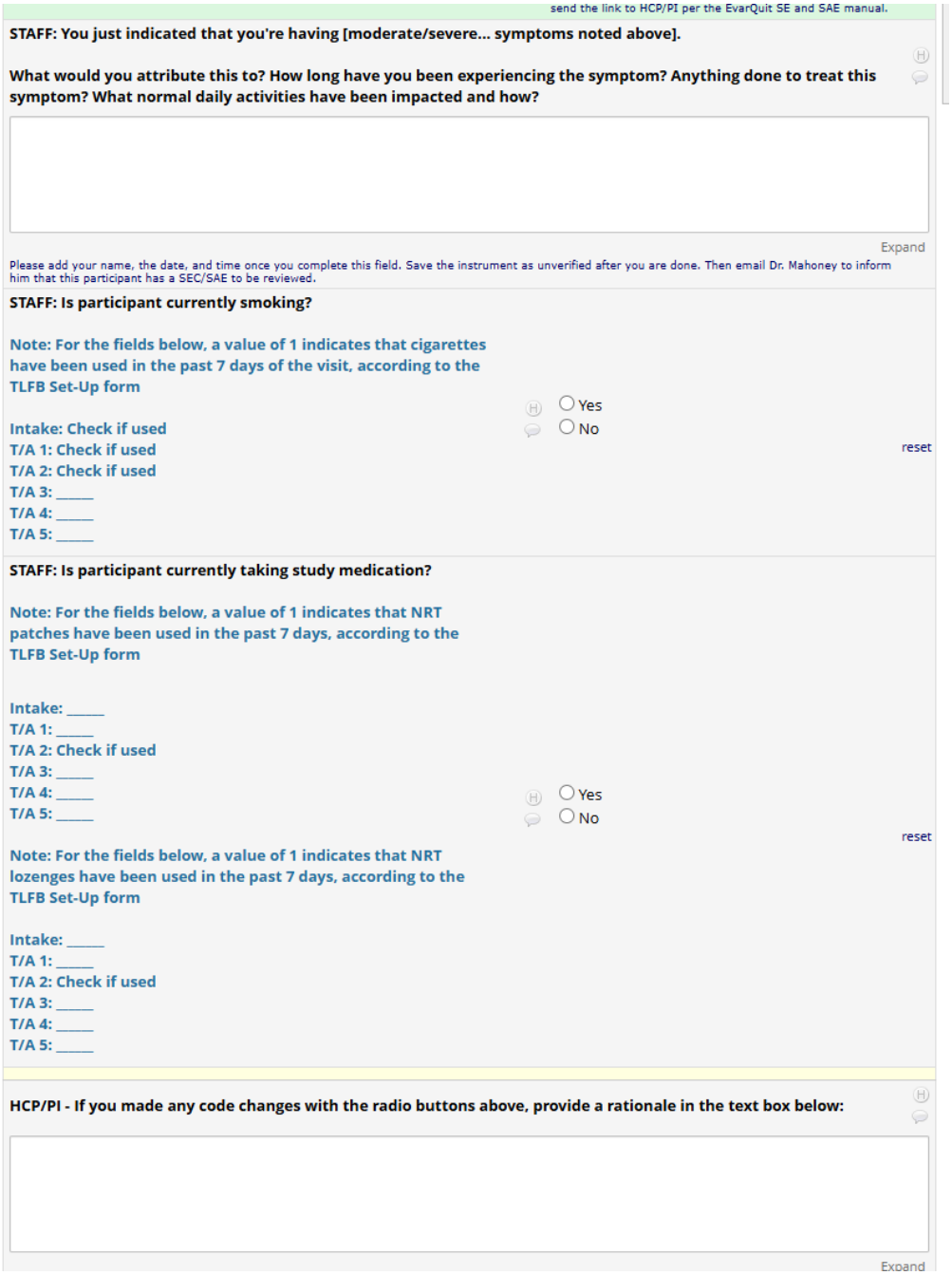
c. In the YELLOW banner at the top, you will see the PPT's name
d. **"Max Side Effect Intensity reported by patient was:"** this field will tell you the highest Coded symptom the PPT endorsed
e. "**Code 2 Side Effect Endorsements**" tells you which side effects must be reported IF they are Code 2
f. "**Code 3 Side Effect Endorsements**" tells you that ALL side effects that are Code 3 must be reported

g. In the **GREEN** banner halfway down the form you will see any symptoms/side effects endorsed by the PPT at this visit (as well as for other completed visits) and the Code for each one

h. Below the GREEN banner, in the GRAY banner, RAs should answer the question "**STAFF: Are there any symptoms listed above for the current visit?**"

   i. If "No" there is nothing more required

   ii. If "Yes", additional fields show up that need to be completed by the RA and the study physician (see below)


send the link to HCP/PI per the EvarQuit SE and SAE manual.

STAFF: You just indicated that you're having [moderate/severe... symptoms noted above].

What would you attribute this to? How long have you been experiencing the symptom? Anything done to treat this symptom? What normal daily activities have been impacted and how?

Expand

Please add your name, the date, and time once you complete this field. Save the instrument as unverified after you are done. Then email Dr. Mahoney to inform him that this participant has a SEC/SAE to be reviewed.

STAFF: Is participant currently smoking?

Note: For the fields below, a value of 1 indicates that cigarettes have been used in the past 7 days of the visit, according to the TLFB Set-Up form

Yes
No

Intake: Check if used
T/A 1: Check if used
T/A 2: Check if used
T/A 3: _____
T/A 4: _____
T/A 5: _____

reset

STAFF: Is participant currently taking study medication?

Note: For the fields below, a value of 1 indicates that NRT patches have been used in the past 7 days, according to the TLFB Set-Up form

Intake: _____
T/A 1: _____
T/A 2: Check if used
T/A 3: _____
T/A 4: _____
T/A 5: _____

Yes
No

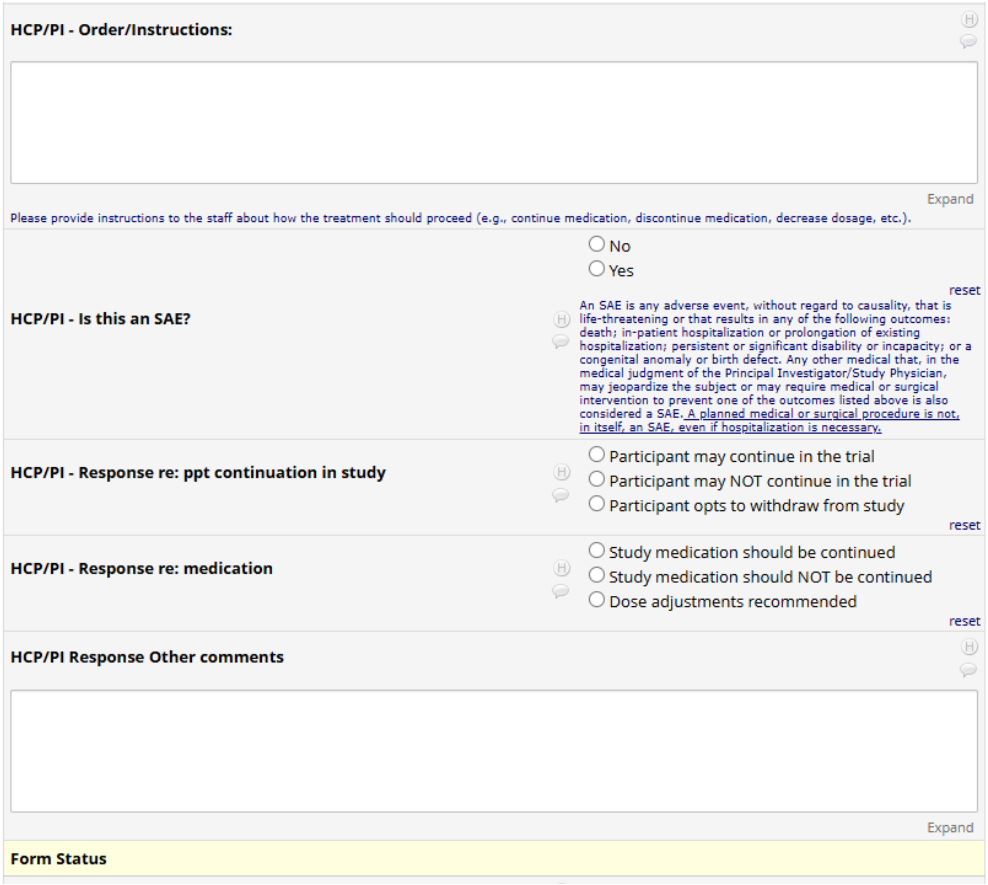
reset

Note: For the fields below, a value of 1 indicates that NRT lozenges have been used in the past 7 days, according to the TLFB Set-Up form

Intake: _____
T/A 1: _____
T/A 2: Check if used
T/A 3: _____
T/A 4: _____
T/A 5: _____

HCP/PI - If you made any code changes with the radio buttons above, provide a rationale in the text box below:

Expand



i. If the PPT endorsed a reportable symptom or symptoms, you must get more information about each one
    i. Follow the directions in REDCap in the "Side Effect Tracking" form
    ii. Say: **"You just indicated that you're having [moderate/severe… symptoms noted above]."**
    iii. Ask the following questions and document the answers in the box:
        1. **What would you attribute this to?**
        2. **How long have you been experiencing the symptom?**
        3. **Anything done to treat this symptom?**
        4. **What normal daily activities have been impacted and how?**
    iv. Answer the questions that appear below the box
        1. **Is participant currently smoking?**
        2. **Is participant currently taking study medication?**
    v. Save the form "Unverified"

3. **<u>Procedures for Code 1 Events</u>**
    a. A Code 1 event means that a symptom is present, but it does not interfere with daily activities
    b. No emails are required for Code 1 events

4. **Procedures for Code 2 Events**
    a. A Code 2 event means that a symptom interferes with some daily activities
    b. Some Code 2 symptoms do not need to be reported; but, if ANY of the symptoms below are endorsed AND they interfere with some activities (Code 2), you MUST report it to the study physician, research coordinator, and PI
        i. Irregular heartbeat or palpitations
        ii. Increased heart rate
        iii. Chest pain
        iv. Depressed mood
        v. Vomiting
        vi. Indigestion
        vii. Skin swelling
        viii. Rash or skin redness (not sunburn)
        ix. Insomnia
        x. Abnormal dreams
    c. To report a Code 2 event to the study physician, PI, and research coordinator, use the email template below (which is filled out with an example; you'll need to update the info in the template with the info for your PPT):

        Subject: Code 2 at T/A 4 - Please respond within 48 hours (RISE PPT XXX-XXXX)
        Body:

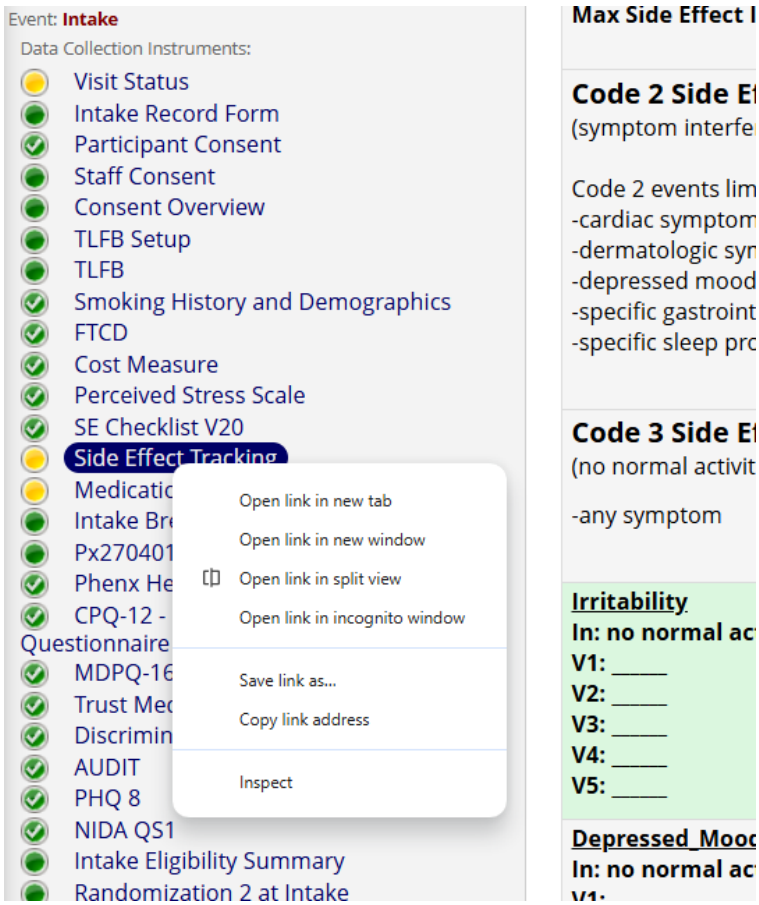
        "Hi Dr. Mahoney,
        At T/A 4 today, RISE participant 198-1000 reported the following previously reported symptoms at severity level 2:
        - **Insomnia**
        - **Increased Heart Rate**

        They also reported the following new symptom at severity level 2:
        - **Vomiting**

        The participant is currently smoking and is not using the study medication.
        Link to Redcap:
        https://redcap.buffalo.edu/redcap/redcap_v14.7.3/DataEntry/index.php?pid=2648&id=198-1000&event_id=9186&page=side_effect_tracking
        Please let me know if - after your review - further action should be taken, or if we can provide any further information.
        Thanks!
        [RA Name]"

        i. Enter the visit in the Subject line to aid in searching for side effect reports in email
        ii. Enter the PPT # at the end of the Subject line using the format above
        iii. If the symptom/side effect was reported at the Intake visit, there is no need for the second sentence "These symptoms were/were not reported at a previous visit; they were previously rated as severity = ____."

iv. To include a link to the relevant REDCap form:
    1. Open the Side Effect Tracking REDCap form
    2. Hover mouse over the name of the form on the left side of the page
    3. Right click and select "Copy link address"
    4. Paste that link into the email



d. The study physician, or PI will reply within the designated timeframe and the RA will follow any instructions given
    i. IF no reply is received within 48 hours, notify the research coordinator so they can follow up with the study physician

5. **<u>Procedures for Code 3 Events</u>**
    a. A Code 3 event means that no normal activities are possible because of that symptom
    b. All Code 3 events should be considered urgent and should be reported to the study physician, research coordinator, and PI immediately following the visit; follow-up will be within 24 hours
    c. If the PPT reports being in distress, you can advise them to contact their primary care physician or to call 911 if needed

d. To report a Code 3 event to the study physician, research coordinator, and PI, use the email template below (which is filled out with an example; you'll need to update the info in the template with the info for your PPT):

Subject: Code 3, please respond within 24 hours (RISE PPT #XXX-XXXX)
Body:

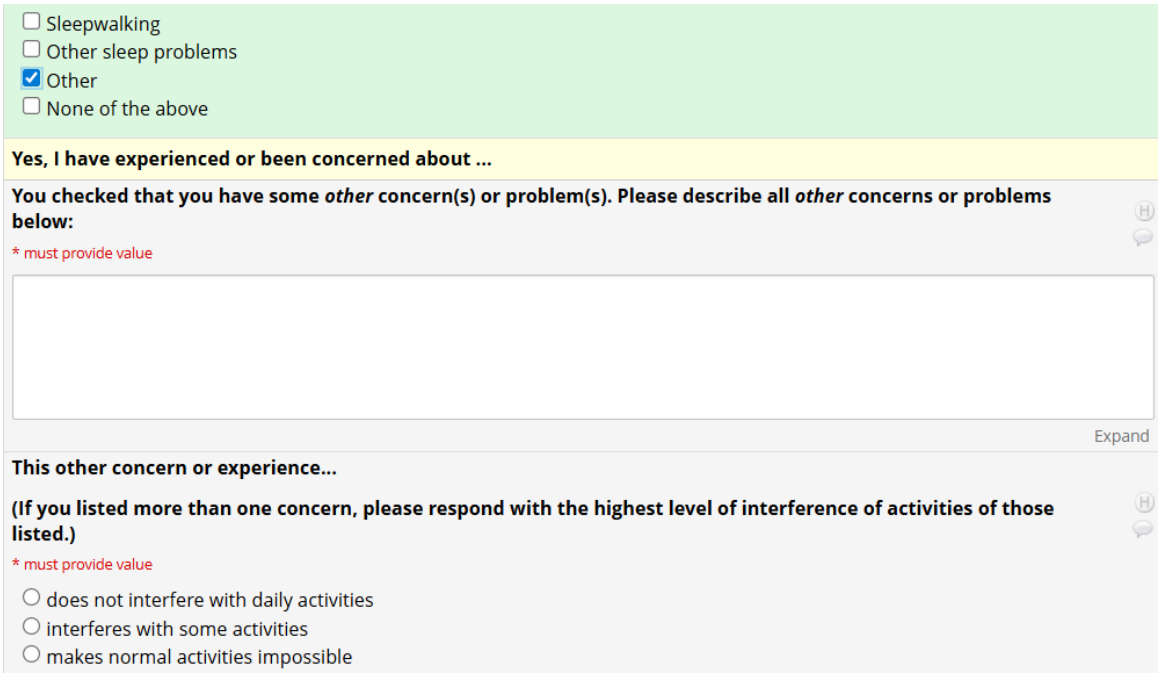
"Hi Dr. Mahoney,
At T/A 5 today, RISE participant 198-1000 reported the following new symptom at severity level 3:

- **Dry mouth**

The participant is currently smoking and is not using the study medication.
Link to Redcap:
https://redcap.buffalo.edu/redcap/redcap_v14.7.3/DataEntry/index.php?pid=2648&id=198-100&event_id=9186&page=side_effect_tracking
Please let me know if - after your review - further action should be taken, or if we can provide any further information.
Thanks!
[RA Name]"

e. If unsure how to proceed, reach out to the research coordinator at your site for guidance
f. **Study physician/site PI …**
    i. may follow up directly with the PPT to gather additional information
    ii. will evaluate the information presented in the email/notification, along with any further additional information received from contact with the PPT and, based upon clinical judgment, may change the code that the event received (either increasing or decreasing in severity)
    iii. may change the SEC data accordingly; any modifications will be tracked
        1. Note that it is not necessary for the SEC data to be changed but it is an option

6. **Procedures for handling "Other" side effects**
    a. If a PPT checks the "Other" box on the SEC, a notes box and a severity rating box pop up



b. Notes box: the PPT is directed to describe all "other" concerns/problems here
c. Severity rating: the PPT is directed: "If you listed more than one concern, please respond with the highest level of interference of activities of those listed."
d. The RA will question the PPT and obtain additional information about all reported "Other" symptoms.
    i. This should be documented in the staff notes box of the "Side Effect Tracking" form (if you learn about the side effect(s) when the PPT fills out the SEC at a visit) or of the "Ad Hoc AEs" form (if you learn about a side effect in between visits OR if the side effect occurred outside of the time period assessed by the SEC at a visit (i.e., the prior 7 days)
    ii. RA should probe the exact nature of the issue reported; also probe:
        1. severity
        2. duration (e.g., new vs. continuing)
        3. whether the symptom has become worse since treatment began
        4. how much each symptom interfered with daily activities
    iii. If any "Other" symptoms are coded as 2 or 3, follow instructions below to report them to the study physician, research coordinator, and PI

7. **Reporting symptoms and side effects outside of the Side Effect Checklist**
    a. There are a few circumstances in which you may need to report side effects to the study physician, research coordinator, and PI without using the SEC and Side Effect Tracking form
        i. If side effects are reported between visits

1. For example, a PPT is between T/A visits 2 & 3 and they call to say they are having vivid dreams and that they plan to take their NRT patch off when sleeping and put it back on in the morning.
2. They called outside of a scheduled visit so there will be no SEC, BUT you still need to inform the study physician, research coordinator, and PI that it happened

ii. If side effects occurred outside of the time period assessed by the SEC at a visit (i.e., the prior 7 days)

1. For example, a PPT reports at T/A 3 during TLFB that they experienced indigestion every time they used an NRT lozenge over the first 5 days after receiving them so they stopped using them
2. Those 5 days on which the PPT experienced this side effect happened before the 7-day period assessed by the T/A 3 SEC so the PPT didn't report them, BUT you still need to inform the study physician, research coordinator, and PI that it happened

b. In either circumstance outlined above, the RA will complete an Ad Hoc AEs form (**see full form in Appendix B)**
c. The Ad Hoc AEs form is very similar to the Side Effect Tracking form, but it is not connected to the SEC
d. You should probe the exact nature of the issue reported (see Section 6.d.ii above)
e. Document the symptom/side effect information in the form and follow instructions in Sections 4-6 of this SOP to notify the study physician, research coordinator, and PI if the symptom was coded 2 or 3 by the PPT

APPENDIX A: SIDE EFFECT CHECKLIST

In the LAST WEEK, have you experienced or been concerned about each of the following things?

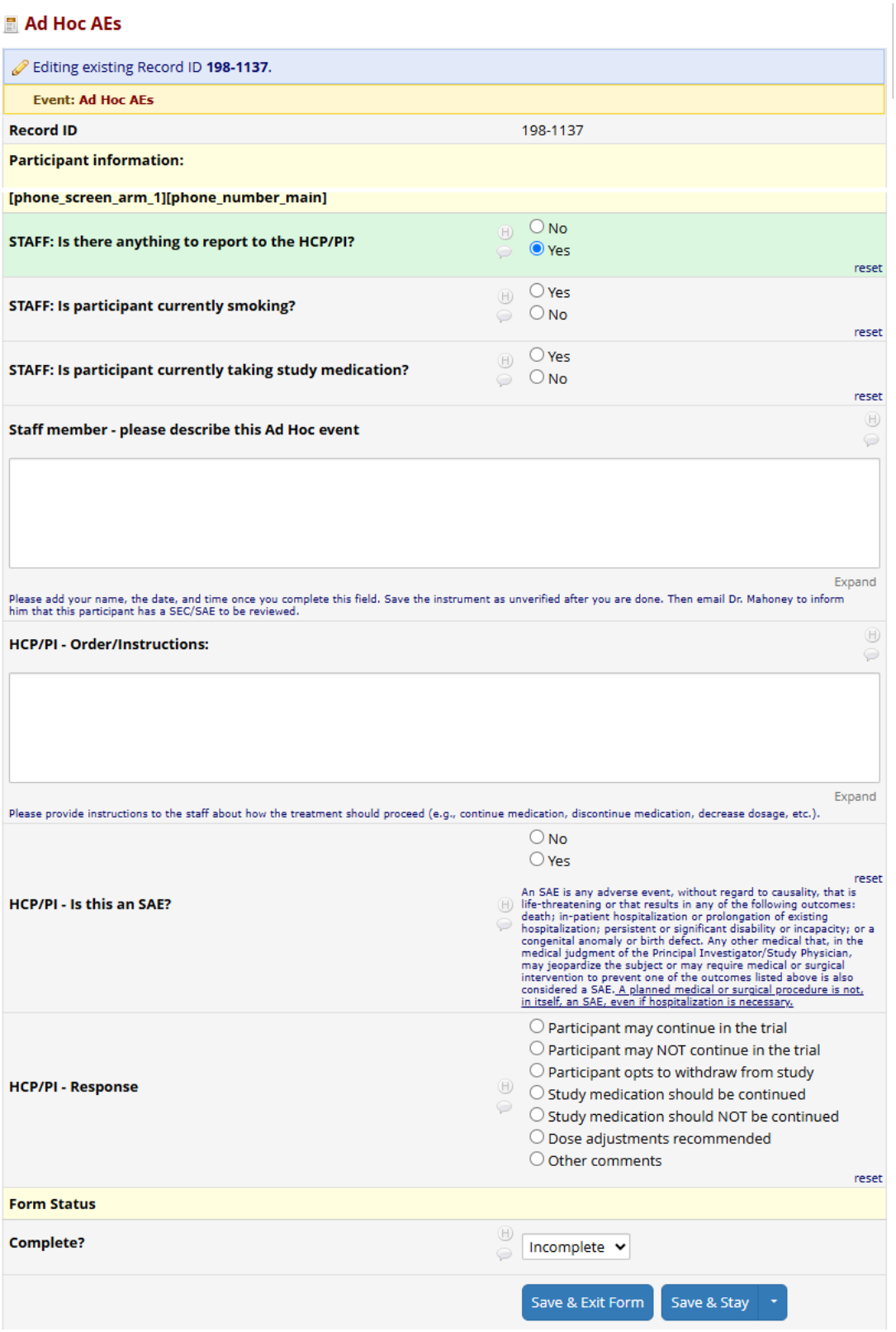
Check all that apply:

Irritability
Agitation
Hostility
Irregular heartbeat or palpitations
Increased heart rate
Chest pain
Depressed mood
Nausea
Vomiting
Abdominal pain
Constipation
Diarrhea
Dry mouth
Indigestion
Gas or flatulence
Anxiety
Skin swelling
Rash or skin redness (not sunburn)
Headache
Dizziness
Insomnia
Abnormal dreams
Sleepwalking
Other sleep problems
Other
None of the above

For each symptom endorsed above, the PPT is asked to rate how much it interferes with daily activities:

- Yes, I have experienced or been concerned about … (symptom)
    - but does not interfere with daily activities
    - and interferes with some activities
    - no normal activities are possible

APPENDIX B: Ad Hoc AEs form (this form can be found in the instrument column at the far right of the Record Home Page – see picture below for example)



Ad Hoc AEs

Editing existing Record ID **198-1137.**

Event: Ad Hoc AEs

Record ID	198-1137
Participant information:	
[phone_screen_arm_1][phone_number_main]	
STAFF: Is there anything to report to the HCP/PI?	○ No ◉ Yes reset
STAFF: Is participant currently smoking?	○ Yes ○ No reset
STAFF: Is participant currently taking study medication?	○ Yes ○ No reset
Staff member - please describe this Ad Hoc event	Expand Please add your name, the date, and time once you complete this field. Save the instrument as unverified after you are done. Then email Dr. Mahoney to inform him that this participant has a SEC/SAE to be reviewed.
HCP/PI - Order/Instructions:	Expand Please provide instructions to the staff about how the treatment should proceed (e.g., continue medication, discontinue medication, decrease dosage, etc.).
HCP/PI - Is this an SAE?	○ No ○ Yes reset An SAE is any adverse event, without regard to causality, that is life-threatening or that results in any of the following outcomes: death; in-patient hospitalization or prolongation of existing hospitalization; persistent or significant disability or incapacity; or a congenital anomaly or birth defect. Any other medical that, in the medical judgment of the Principal Investigator/Study Physician, may jeopardize the subject or may require medical or surgical intervention to prevent one of the outcomes listed above is also considered a SAE. A planned medical or surgical procedure is not, in itself, an SAE, even if hospitalization is necessary.
HCP/PI - Response	○ Participant may continue in the trial ○ Participant may NOT continue in the trial ○ Participant opts to withdraw from study ○ Study medication should be continued ○ Study medication should NOT be continued ○ Dose adjustments recommended ○ Other comments reset
Form Status	
Complete?	Incomplete

Save & Exit Form | Save & Stay

Record Home Page

The grid below displays the form-by-form progress of data entered for the currently selected record. You may click on the colored status icons to access that form/event. If you wish, you may modify the events below by navigating to the Define My Events page.

Choose action for record

Legend for status icons:

- Incomplete
- Incomplete (no data saved)
- Unverified
- Partial Survey Response
- Complete
- Completed Survey Response
- Many statuses (mixed)
- Many statuses (all same)

Record ID **257-7**

Data Collection Instrument	Phone Screen	Tracking	Intake	T/A V1	T/A V2 (TQD)	T/A V3	T/A V4 (EOT)	T/A V5 (3Mth)	Ad Hoc AEs
Study Status		●							
Visit Status	●		●	●	●	●	●	●	
Contact Log	●								
Contact Info	●								
Phone Screen	●								
Phone Screen Eligibility Summary	●								
Randomization for Intake	●								
Intake Info	●								
Intake Record Form			●						
Participant Consent (survey)			●						
Staff Consent			●						
Consent Overview			●						
T/A 1 Record Form				●					
T/A 2 Record Form					●				
T/A 3 Record Form						●			
T/A 4 Record Form							●		
T/A 5 Record Form								●	
TLFB Setup			●	●	●	●	●	●	
TLFB			●	●	●	●	●	●	
Medication Accountability Form						●	●		
Smoking History and Demographics (survey)			●						
FTCD (survey)			●						
QSU Phenx (survey)				●	●	●	●	●	
MNWS Phenx (survey)				●	●	●	●	●	
TOEs and AbstSE (survey)				●	●	●			
Cost Measure (survey)			●	●	●	●	●	●	
SE Checklist V20 (survey)			●	●	●	●	●	●	
Side Effect Tracking			●	●	●	●	●	●	
Ad Hoc AEs									●
Medications			●						
Intake Breath CO			●						