

Attachment F

DISCUSSION GUIDE

“An Exploratory Assessment of Substances Used as Adjuncts or Alternatives to Prescription Opioids”

I. Welcome and Warm-Up (10 minutes)

[RECORDING STARTS HERE]

Hi, I am MODERATOR'S NAME. I work with Mark Herring Associates (also known as MHA), a research firm based in Philadelphia. We are conducting this study on behalf of the Food and Drug Administration. FDA wants to hear about the experiences of people who have used certain substances along with or as a substitute for a prescription opioid pain reliever. During your recruitment interview, you indicated that you have used [NAME OF DRUG/SUBSTANCE; NOTE: for benzodiazepines and gabapentinoids, the specific one(s) should be stated here] along with or as a substitute for a prescription opioid. Is that correct?

I'd like to review a few things with you before we start our interview.

To participate in this interview, you signed a consent form and should have been given a copy, so I want to make sure you received that document.

[If yes, Interviewer will say: let's review a few important points from the form]

[If no, interviewer will provide a copy of the consent form as a reminder, then the interviewer will say: let's review some important points from the form.]

Our interview will take no more than 60 minutes. You are one of approximately 140 people across the country participating in this study.

Your participation is voluntary. We do not expect that any of the interview questions will make you uncomfortable. However, you can refuse to answer any question and you can stop the interview at any time without penalty.

Your identity and information will be kept secure to the extent provided by law. Neither your full name nor your personal information will be linked to any of your responses. Your feedback will be combined with those of all the other participants in a summary report that will not identify you by name.

Only MHA will have access to your signed consent form. Any information that includes your name or other personal information will be kept in a locked file cabinet or on a password-protected computer that only authorized MHA project staff can use. No names or contact information will ever be provided to FDA, and no one from FDA or MHA will contact you after this interview is over.

In addition to these steps, we have obtained a Certificate of Confidentiality from FDA. This certificate provides extra protection for you. Because we have this certificate, we cannot be required to disclose any information collected about you as a part of this study in any lawsuit or other legal proceeding. This certificate also prevents your study information from being released without your consent.

When applicable for the first few interviews, notify respondent that the other interviewer will be observing in the room.]

This interview is being audio recorded. Later, the audio recording will be transcribed to help us accurately remember what you said as we're writing the report. Any information that might identify you will be removed before we send your transcript to the FDA. The de-identified transcript will be stored on password-protected computers at MHA for three years and at the FDA for five years after the conclusion of this research project. FDA will never have direct access to your audio recording or to your name.

As we begin, we wanted to start by asking why you sought treatment at this time.

II. Discussion of Opioid Use (10-12 minutes)

When we talk about “prescription opioids” in this conversation, we’re using that term to eliminate heroin and medications you may have been prescribed as part of your current addiction treatment. We’re interested in your opioid use, whether you received it from a health care provider or by other means.

You said during your screening interview that you had used a prescription opioid pain medicine during the 12 months before you came here for treatment

[NOTE: confirm name(s) and review the worksheet completed during screening process to make sure it’s accurate and verify there aren’t any other ones on the list that they hadn’t previously identified]

1. How did you first hear about prescription opioids? What did you hear about them?
2. Did you look for any additional information about prescription opioids before you started using them?
 - a. [If not] why not?
 - b. [If so] what additional information were you looking for?
 - i. Where did you look for it?
 - ii. Did you find the information you wanted? If so, where?
3. Why did you use prescription opioids the first time? Within the past 12 months, why did you use prescription opioids?
[NOTE: Allow participants to respond without prompting first; if necessary, probe for healthcare provider advice, personal choice, other reasons]
4. What positive effects or benefits did you think you would experience from using prescription opioids?
 - a. Where did you get the information about these positive effects or benefits?
 - b. What positive effects or benefits did you personally experience while using prescription opioids?
5. What side effects or risks associated with prescription opioids did you know about before you started using them? [If necessary, probe on serious side effects/risks such as tolerance, dependence, addiction, overdose, etc.]
 - a. Where did you get this information?
6. What negative effects did you personally experience while using prescription opioids? **[NOTE: If necessary, probe on serious side effects/risks noted above and on broader issues such as issues with relationships/family, loss of job or home, etc.]**
 - a. What did you do when you experienced these negative effects?
7. What made the positive effects of taking prescription opioids outweigh the negative effects or risks?

8. How did you first obtain prescription opioids?
[NOTE: Allow the person to answer spontaneously and probe the following only if needed: by prescription, bought on the street, from family/friends, online, or some other way]
9. [For those who say an HCP prescribed] When prescribing the opioid(s) to you, what did your healthcare provider tell you about it/them?
[NOTE: Use the following probes only as necessary]
- What were they used for?
 - How should they be used?
 - Other possible benefits [beyond 9a)?
 - Possible side effects or risks?
 - Which medicines or substances should be avoided when using opioids [and if so, which one(s)]?
10. Did you ever obtain opioids by any means other than a prescription?
 [IF SO]
- Please tell me a little about that.
 - How and why?
 - Over time, did your method of obtaining prescription opioids change?
 [Probe if needed: did your supplier change?]
11. [If respondent has mentioned more than one prescription opioid] Which prescription opioid did you use most often? **[NOTE:** ask following questions for opioid used most often]
- Over what period of time did you use this opioid?
 - Did you use it on a regular schedule or off and on?
 - If a regular schedule, what was that schedule?
 - How did you determine how often to use it?
 - Did the frequency of your use vary, and if so, how and why?
 - How much of the prescription opioid did you generally take at one time?
[NOTE: This could include number of pills and/or milligrams, so both should be specifically probed about if needed]
 - How did you determine how much to use at one time? [Probe if needed: Did you take the amount directed by your healthcare provider, or more or less than directed?]
 - Did this vary and if so, how and why?
 - How did you take it? **[NOTE:** explore use of pills versus injection, snorting etc., as appropriate] Did this vary over time and if so, how and why?
 - Did you take more of this drug as time went on? How much more? Why did you increase the dose?

12. You mentioned earlier that you started taking prescription opioids for [cite reasons stated in #3 above]. Did you take anything else to deal with that/those issue(s), and if so, what else did you take?

[NOTE: All respondents will have qualified for this study by using a prescription opioid and a benzodiazepine, gabapentinoid, kratom, or CBD as an adjunct or substitute; interviewers will complete only the one specific section below (from Sections III – VI) that qualified the respondent for the study]

Discussion of Benzodiazepines (15 minutes)

When you volunteered for this interview you said you used a/some prescription medicines called benzodiazepines in the 12 months prior to starting treatment. Is that correct? [NOTE: Show respondent the worksheet completed during screening process to make sure it's accurate and verify there aren't any others on the list that they hadn't previously identified].

For simplicity going forward in our conversation, I'll use the general term "benzodiazepines" or "benzos" to mean the specific ones you identified on this worksheet.

1. How did you first hear about benzodiazepines? What did you hear about them initially?
2. Did you look for any additional information about benzos before you started using them?
 - a. [If not,] why not?
 - b. [If so,] what additional information were you looking for?
 - i. Where did you look for it?
 - ii. Did you find the information you wanted? If so, where?
3. Why did you use benzos the first time? During the past 12 months, why did you use benzos?
[NOTE: Allow participants to respond without prompting first; if necessary, probe for healthcare provider advice, personal choice, other reasons]
4. What positive effects or benefits did you think you would experience from using benzos?
 - a. Where did you get the information about these positive effects or benefits?
 - b. What positive effects or benefits did you personally experience while using benzos?
5. What side effects or risks associated with benzos did you know about before you started using them? [NOTE: Allow them to respond first and if necessary, probe on serious side effects/risks such as respiratory depression, difficulty breathing, etc.,]
 - a. Where did you get this information?
 - b. What side effects or negative outcomes did you personally experience while using benzos? [Probe specifically on serious side effects/risks **AND** on broader issues such as issues with relationships/family, loss of job or home, etc.]
 - c. What did you do when you experienced these negative effects?
6. Tell me a little about how/why you made the decision to use both? What made the positive effects of taking benzos outweigh the negative effects or risks?

7. Other than opioids, when you started using benzos, what other prescription medicines, if any, were you already using for the same reason(s) you just mentioned?
8. How did you first obtain benzos?
[NOTE: Allow them to respond first and if it doesn't come up organically, probe: by prescription, bought on the street, from family/friends, online, some other way]
9. [For those who say an HCP prescribed]: When prescribing a benzo(s) to you, what did your healthcare provider tell you about it/them?
[NOTE: Use the following probes as necessary]
 - a. What the benzo(s) is/are used for?
 - b. How it/they should be used?
 - c. Other possible benefits [beyond 9a)?
 - d. Possible side effects or risks?
 - e. Which medicines or substances should be avoided when using a benzo(s) [and if so, which one(s)]?
10. Did you ever obtain benzos by any means other than a prescription?
[IF SO]
 - a. Please tell me a little about that.
 - b. How and why?
 - c. Over time, did your method of obtaining prescription benzos change?
[Probe if needed: did your supplier change?]
11. [If respondent has mentioned more than one benzo] Which benzo did you use most often? [Ask following questions for benzo used most often]
 - a. Over what period of time did you use this benzo?
 - b. Did you use it on a regular schedule or off and on?
 - i. If a regular schedule, what was that schedule?
 - c. How did you determine how often to use it?
 - d. Did the frequency of your use vary, and if so, how and why? **[NOTE: This could include number of pills and/or milligrams, so both should be specifically probed about if needed]**
 - e. How much of this benzo did you generally take at one time?
 - i. How did you determine how much to use at one time?
 - ii. Did this vary and if so, how and why?
 - f. How did you take it? **[NOTE: explore use of pills versus injection, etc. as appropriate]** Did this vary over time and if so, how/why?
12. How did your use of benzos relate to prescription opioids? Did you use benzos while you were taking a prescription opioid? Did you use benzos in place of or as a substitute for the prescription opioid(s)? **[NOTE: make sure we get a reasonable number of responses regarding both concomitant use and alternative use if respondents say both uses]**

13. [Interviewer: Ask only of participants who said they used benzos *while* taking prescription opioids]

- a. Which did you start taking first – benzo or opioid?
- b. Why did you use them together?
 - i. What did you think the positive effects or benefits would be?
 - ii. Where did you get the information about the benefits of combining benzos and a prescription opioid?
[Probe: specific sources, e.g., prescribers/HCPs, the Internet generally, online forums/social media specifically, family/friends, etc.]
- c. What positive effects or benefits did you personally experience while using both benzos and opioids?
[Probe if needed: What additional positive effects did you experience besides the ones you expected?]
- d. What side effects or risks did you think might occur from using both benzos and the prescription opioid(s)?
[NOTE: probe for about serious side effects/risks such as respiratory depression/difficulty breathing, loss of consciousness, overdose and death associated with concomitant use]
 - i. Where did you get the information about the side effects or risks of combining benzos and a prescription opioid? [NOTE: Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends, etc.)]
- e. What side effects or risks did you personally experience while using both a benzo(s) and a prescription opioid(s)? [NOTE: Probe if needed: What additional side effects/risks did you experience besides the ones you expected?]
- f. Tell me a little about how/why you made the decision to use both? What made the positive effects or benefits worth the side effects or risks?
- g. Were you using a benzo(s) with a prescription opioid(s) because that was the best combination to get the effects you wanted or because that is what you could get?
[NOTE: If because that was what was available]: What drug or substance would you have preferred to use with prescription opioid(s) instead of the benzo? Have you used that drug or substance before and if so, how did it/they compare to using a benzo at the same time as a prescription opioid?
- h. If the same healthcare provider prescribed the benzo(s) and the prescription opioid(s), what did this healthcare provider discuss with you about using these two medicines together?

14. [Interviewer: Ask only of participants who said they used benzos as an alternative/substitute for a prescription opioid]

- a. At what point in your use of a prescription opioid(s) did you substitute benzos? Why did you substitute?
- b. Tell me more about how you used benzos as a substitute for a prescription opioid(s).
[Probe if needed: Did you alternate back and forth, or did you completely stop taking the prescription opioid?]
- c. What did you think the positive effects or benefits would be when substituting benzos for the opioid(s)? Where did you get this information about substituting benzos for prescription opioids?
[Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends)]
- d. What positive effects or benefits did you personally experience when substituting benzos for the prescription opioid(s)?
- e. What side effects or risks did you think might occur when using benzos instead of prescription opioid(s)? Where did you get this information?
[Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends)]
- f. What side effects or risks did you personally experience when substituting benzos for the prescription opioid(s)?
- g. If benzos were prescribed, what did this healthcare provider discuss with you about using benzos instead of a prescription opioid?

III. Discussion of Gabapentinoids (15 minutes)

For simplicity, I'm going to use "gabapentin" to broadly refer to several drugs, including gabapentin, Neurontin, Gralise, Horizant, Lyrica, Lyrica CR and pregabalin.

You said when you volunteered for this interview that you used gabapentin in the 12 months prior to starting treatment. Is that correct? Which one were you taking?

1. How did you first hear about gabapentin? What did you hear about it?
2. Did you look for any additional information about gabapentin before you started using it?
 - a. [If not,] why not?
 - b. [If so,] what additional information were you looking for?
 - i. Where did you look for it?
 - ii. Did you find the information you wanted? [If so,] where?
3. Why did you use gabapentin the first time? During the past 12 months, why did you use gabapentin?

[NOTE: Allow participants to respond without prompting first, if necessary, probe for HCP advice, personal choice, other reasons]
4. What positive effects or benefits did you think you would experience from using gabapentin?
 - a. Where did you get the information about these positive effects or benefits?
 - b. What positive effects or benefits did you personally experience while using gabapentin?
5. What side effects or risks associated with gabapentin did you know about before you started using it? **[NOTE: Allow them to respond first and if doesn't come up organically, probe for serious side effects/risks such as respiratory depression, dependence, etc.]**
 - a. Where did you get this information?
 - b. What side effects or negative outcomes did you personally experience while using gabapentin? **[NOTE: Probe on serious side effects/risks and on broader issues such as relationships/family, loss of job or home, etc.]**
 - c. What did you do when you experienced these negative effects?
6. Tell me a little about how/why you made the decision to use both? What made the positive effects of taking gabapentin outweigh the negative effects or risks?
7. Other than opioids, when you started using gabapentin, what other prescription medicines, if any, were you already using for the same reason(s) you just mentioned?

8. How did you first obtain gabapentin?
[NOTE: Allow respondent to answer spontaneously; if necessary, probe: By prescription, bought on the street, from family/friends, online, some other way]
9. [For those who say an HCP prescribed it]: When prescribing gabapentin to you, what did your healthcare provider tell you about it? **[NOTE: Probe the following as necessary]**
 - a. What the gabapentin is used for?
 - b. How it should be used?
 - c. Other possible benefits [beyond 4]?
 - d. Possible side effects or risks?
 - e. Which medicines or substances should be avoided when using gabapentin [and if so, which one(s)]?
10. Did you ever obtain gabapentin by any means other than a prescription?
[IF SO]
 - a. Tell me a little about that.
 - b. How and why?
 - c. Over time, did your method of obtaining prescription gabapentin change?
[NOTE: Probe if needed: Did the supplier change?]
11. [If respondent mentions more than one form of gabapentin] Which form of gabapentin did you use most often [Ask following questions for form of gabapentin used most often]
 - a. Over what period of time did you use this type of gabapentin?
 - b. Did you use it on a regular schedule or off and on?
 - i. If a regular schedule, what was that schedule?
 - c. How did you determine how often to use it?
 - d. Did the frequency of your use vary, and if so, how and why?
 - e. How much gabapentin did you generally take at one time? **[NOTE: This could include number of pills and/or milligrams, so both should be specifically probed about if needed]**
 - i. How did you determine how much to use at one time?
 - ii. Did this vary and if so, how and why?
 - iii. How did you take it? **[NOTE: explore use of pills versus injection, etc. as appropriate]** Did this vary over time and if so, how/why?
12. How did your use of this gabapentin relate to prescription opioids? Did you use gabapentin while you were taking a prescription opioid? Did you use gabapentin in place of or as a substitute for the prescription opioid(s)? **[NOTE: make sure we get a reasonable number of responses regarding both concomitant use and alternative use if respondents say both uses]**
13. **[Interviewer: Ask only of participants who said they used gabapentin *while* taking prescription opioid(s)]**

- a. Which did you start taking first – gabapentin or the opioid(s)?
- b. Why did you use them together?
 - i. What did you think the positive effects or benefits would be?
 - ii. Where did you get the information about the benefits of combining gabapentin and a prescription opioid? [Probe: specific sources, e.g., prescribers/HCPs, the Internet generally, online forums/social media specifically, family/friends, etc.]
- c. What positive effects or benefits did you personally experience while using both gabapentin and opioids? [Probe if needed: What additional positive effects did you experience besides the ones you expected?]
- d. What side effects or risks did you think might occur from using both gabapentin and the prescription opioid(s)? [**NOTE:** probe about serious side effects/risks such as for respiratory depression/difficulty breathing, loss of consciousness]
 - i. Where did you get the information about the side effects or risks of combining gabapentin and a prescription opioid? [**NOTE:** Probe specific sources (prescribers/HCPs, online forums, family/friends, etc.)]
- e. What side effects or risks did you personally experience while using both gabapentin and the prescription opioid? [**NOTE:** Probe if needed: What additional side effects/risks did you experience besides the ones you expected?]
- f. Tell me a little about how and why you made the decision to use both gabapentin and a prescription opioid(s). What made the positive effects or benefits worth the side effects or risks?
- g. Were you using gabapentin with a prescription opioid(s) because that was the best combination to get the effects you wanted or because that's what you could get?
[**NOTE:** If because that was what was available:] What drug or substance would you have preferred to use with prescription opioid(s) instead of gabapentin? Have you used that drug or substance before and if so, how did it/they compare to using gabapentin at the same time as a prescription opioid?
- h. If the same healthcare provider prescribed the gabapentin and the prescription opioid(s), what did this provider discuss with you about using these two medicines together?

14. [Interviewer: Ask only of participants who said they used gabapentin as an **alternative/substitute** for a prescription opioid]

- a. At what point in your use of a prescription opioid(s) did you substitute gabapentin? Why did you substitute?
- b. Tell me more about how you used gabapentin as a substitute for a prescription opioid.
[NOTE: Probe if needed: Did you alternate back and forth, or did you completely stop taking the prescription opioid?]
- c. What did you think the positive effects or benefits would be when substituting gabapentin for the opioid? Where did you get this information about substituting gabapentin for prescription opioids?
[NOTE: Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends)]
- d. What positive effects or benefits did you personally experience when substituting gabapentin for the prescription opioid(s)?
- e. What side effects or risks did you think might occur when using gabapentin instead of the prescription opioid? Where did you get this information? [NOTE: Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends)]
- f. What side effects or risks did you personally experience when substituting gabapentin for the prescription opioid(s)?
- g. If gabapentin was prescribed, what did this healthcare provider discuss with you about using gabapentin instead of a prescription opioid?

IV. Discussion of Kratom (15 minutes)

You said when you volunteered for this interview that you used kratom in the 12 months prior to starting treatment. Is that correct?

1. How did you first hear about kratom? What did you hear about it?
2. Did you look for any additional information about kratom before you started using it?
 - a. [If not,] why not?
 - b. [If so,] what additional information were you looking for?
 - i. Where did you look for it?
 - c. Did you find the information you wanted? If so, where?
3. Why did you use kratom for the first time? During the past 12 months, why did you use it? [**NOTE:** Allow participants to respond without prompting first: for personal choice, friend's advice, other reasons]
4. What positive effects or benefits did you think you would experience from using kratom?
 - a. Where did you get the information about these positive effects or benefits?
 - b. What positive effects or benefits did you personally experience while using kratom?
5. What side effects or risks associated with kratom did you know about before you started using it? [**NOTE:** Allow them to respond first and if doesn't come up organically, probe serious risks, e.g. risk of addiction and withdrawal]
 - i. Where did you get this information?
 - ii. What side effects or risks did you personally experience while using kratom? [**NOTE:** Probe on serious risks and broader issues such as issues with relationships/family, loss of job or home, etc.]
 - iii. What did you do when you experienced these negative effects or risks?
6. What made the positive effects of taking kratom outweigh the negative effects or risks?
7. Other than opioids, when you started using kratom, what other prescription medicines, if any, were you already using for the same reason(s) you just mentioned?
8. How did you first obtain kratom? [**NOTE:** Allow them to respond first, and if doesn't come up organically probe: Online, bought on the street, from family/friends, some other way?]
9. Over time, did your method of obtaining kratom change? Tell me a little about that. [**NOTE:** probe whether supplier changed]

10. Over what period of time did you use kratom?
 - a. Did you use it on a regular schedule or on and off?
 - i. [If a regular schedule,] what was the schedule?
 - b. How did you determine how often to use it?
 - c. Did the frequency of your use vary? If so, how and why?
 - d. How much kratom did you generally use at one time?
 - i. How did you determine how much to use at one time?
 - ii. Did this vary? If so, how and why?
 - e. How did you use it? [**NOTE:** Explore use of pills, capsule or extract, chewed leaves, tea, food, or smoked, etc., as appropriate] Did this vary over time and if so, how/why?

11. How did your use of kratom relate to prescription opioids? Did you use kratom while you were taking a prescription opioid? Did you use kratom in place of or as a substitute for the prescription opioid? [**NOTE:** make sure we get a reasonable number of responses regarding both concomitant use and alternative use if respondents say both uses]

12. [**Interviewer: Ask only of participants who said they used kratom while taking prescription opioids]**

 - a. Which did you start taking first - kratom or the prescription opioid?
 - b. Why did you use them together?
 - i. What did you think the positive effects or benefits would be?
 - ii. Where did you get the information about the benefits of combining kratom and a prescription opioid? [**NOTE:** Probe: specific sources (e.g., the Internet generally, online forums/social media specifically, family/friends, advertisements, HCPs, etc.)]
 - c. What positive effects or benefits did you personally experience? [**NOTE:** Probe if needed: What additional positive effects did you experience besides the ones you expected?]
 - d. What side effects or risks did you think might occur from using both kratom and the prescription opioid?

[**NOTE:** probe for awareness/knowledge about drug/drug interactions, respiratory depression, addiction, etc.]

 - i. Where did you get the information about the side effects or risks of combining kratom and a prescription opioid? [**NOTE:** Probe if needed: specific sources such as healthcare provider, online forums, family/friends, pharmacists, etc.]
 - e. What side effects or risks did you personally experience while using both kratom and the prescription opioid? [**NOTE:** Probe on serious side effects/risks and others such as relationship/family issues, job issues, etc.]
 - f. Tell me a little about how/why you made the decision to use both? What made the positive effects or benefits worth the side effects or risks?

- g. Were you using kratom because that was the best combination with prescription opioid(s) to get the effects you wanted or because that is what you could get?

[NOTE: If because that was what was available]: What drug or substance would you have preferred to use with prescription opioid(s) instead of kratom? Have you used that drug or substance before and, if so, how did it/they compare to using kratom at the same time as the prescription opioid?

13. [Interviewer: Ask only of participants who said they used kratom as an alternative/substitute for a prescription opioid]

- a. At what point in your use of a prescription opioid(s) did you substitute kratom? Why did you substitute?
- b. Tell me more about how you took kratom as a substitute for a prescription opioid.
[NOTE: Probe if needed: Did you alternate back and forth, or did you completely stop taking the prescription opioid?]
- c. What did you think the positive effects or benefits would be of substituting kratom for the opioid? Where did you get this information about substituting kratom for prescription opioids? [NOTE: Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends)]
- d. What positive effects or benefits did you personally experience when substituting kratom for the prescription opioid(s)?
- e. What side effects or risks did you think might occur when using kratom instead of the prescription opioid? Where did you get this information?
- f. What side effects or risks did you personally experience when substituting kratom for the prescription opioid(s)?
- g. [NOTE: Ask only if the participant said that kratom was suggested by a healthcare provider:] What did the medical professional who suggested kratom discuss with you about using it instead of a prescription opioid?

V. Discussion of CBD (15 minutes)

You said when you volunteered for this interview that you used cannabidiol, or CBD, in the 12 months prior to starting treatment. Is that correct?

1. How did you first hear about CBD? What did you hear about it?
2. Did you look for any additional information about CBD before you started using it?
 - a. [If no:] Why not?
 - b. [If so:] What additional information were you looking for?
 - i. Where did you look for it?
 - c. Did you find the information you wanted? If so, where?
3. Why did you use CBD for the first time? Within the past 12 months, why did you use CBD? **[NOTE: Allow participants to respond without prompting first; if necessary, probe: personal choice, friends or family members, pharmacist, other healthcare provider advice, other reasons]**
4. What positive effects or benefits did you think you would experience from using CBD?
 - a. Where did you get the information about these positive effects or benefits?
 - b. What positive effects or benefits did you personally experience while using CBD?
5. What side effects or risks associated with CBD did you know about before you started using it? **[NOTE: Allow them to respond first and if doesn't come up organically, probe for serious side effects/risks such as respiratory depression, dependence, etc.]**
 - a. Where did you get this information?
 - b. What side effects or risks did you personally experience while using CBD?
 - c. What did you do when you experienced these negative effects?
6. Did the positive effects of taking CBD outweigh the negative effects?
7. Other than opioids, when you started using CBD, what other prescription medicines, if any, were you already using for the same reason(s) you just mentioned?
8. How did you first obtain CBD?
[NOTE: Allow them to respond first, and if it doesn't come up organically, probe: over the counter at a pharmacy or store, bought on the street, from family/friends, online, some other way]
9. Over time, did your method of obtaining CBD change? Tell me a little about that.

10. Over what period of time did you use CBD?
 - a. Did you use it on a regular schedule or on and off?
 - i. If a regular schedule, what was that schedule?
 - b. How did you determine how often to use it?
 - c. Did the frequency of your use vary? If so, how and why?
 - d. How much CBD did you generally use at one time?
 - i. How did you determine how much to use at one time?
 - ii. Did this vary? If so, how and why?
 - e. How did you use it? [**NOTE:** explore use of pills, capsules, edibles, vaping, creams, lotions, oils, tinctures, etc., as appropriate] Did this vary over time and if so, how and why?

11. How did your use of CBD relate to prescription opioids? Did you use CBD while you were taking a prescription opioid(s)? Did you use CBD in place of or as a substitute for a prescription opioid(s)? [**NOTE:** make sure we get a reasonable number of responses regarding both concomitant use and alternative use if respondents say both uses]

12. [**Interviewer: Ask only of participants who said they used CBD while taking prescription opioids]**

 - a. Which did you start taking first – CBD or the prescription opioid?
 - b. Why did you use them together?
 - i. What did you think the positive effects or benefits would be?
 - ii. Where did you get the information about the benefits of combining CBD and a prescription opioid? [**NOTE:** Probe: specific sources e.g., the Internet generally, online forums/social media specifically, prescribers/HCPs, family/friends, advertisements, etc.]
 - c. What positive effects or benefits did you personally experience? [**NOTE:** Probe if needed: What additional positive effects did you experience besides the ones you expected?]
 - d. What side effects or risks did you think might occur from using both CBD and the prescription opioid? [**NOTE:** probe for awareness/knowledge about drug-drug interactions, etc.]
 - i. Where did you get the information about the side effects or risks of combining CBD and a prescription opioid? [**NOTE:** Probe if needed: specific sources such as healthcare provider, online forums, family/friends, pharmacists, etc.]
 - e. What side effects or risks did you personally experience while using both CBD and the prescription opioid?
 - f. Tell me a little about how/why you made the decision to use both? What made the positive effects or benefits worth the side effects or risks?
 - g. Were you using CBD with a prescription opioid(s) because that was the best combination to get the effects you wanted or because that is what you could get? [**NOTE:** If because that was what was available:] What

drug or substance would you have preferred to use with prescription opioid(s) instead of CBD? Have you used that drug or substance before and if so, how did it/they compare to using CBD at the same time as a prescription opioid?

13. **[Interviewer: Ask only of participants who said they used CBD as an alternative/substitute for a prescription opioid]**
- a. At what point in your use of a prescription opioid(s) did you substitute CBD? Why did you substitute?
 - b. Tell me more about how you took CBD as a substitute for a prescription opioid. **[NOTE: Probe if needed: Did you alternate back and forth, or did you completely stop the prescription opioid?]**
 - c. What did you think the positive effects or benefits would be of substituting CBD for the opioid? Where did you get this information about substituting CBD for prescription opioids? **[NOTE: Probe if needed: specific sources (prescribers/HCPs, online forums, family/friends)]**
 - d. What positive effects or benefits did you personally experience when substituting CBD for the prescription opioid(s)?
 - e. What side effects or risks did you think might occur when using CBD instead of the prescription opioid? Where did you get this information? **[NOTE: Probe if needed: specific sources – prescribers/HCPs, online forums, family/friends]**
 - f. What side effects or risks did you personally experience when substituting CBD for the prescription opioid(s)?
 - g. **[NOTE: Ask only if participant said that CBD was suggested by a healthcare provider:]** What did the medical professional who suggested CBD discuss with you about using it instead of a prescription opioid? Have you used that drug or substance before and, if so, how did it/they compare to using kratom at the same time as the prescription opioid?

VI. Additional Substances Used (10 minutes)

1. What other substances have you used? [Quickly create a list of any additional substances each participant identifies]

[NOTE: As time permits, ask the following questions for a few of the most important substances, giving priority to amphetamine, methamphetamine and other stimulants such as Adderall and Ritalin, if identified. See the additional list FDA provided as a reference for stimulant names]

- a. How did you use this substance with respect to prescription opioid(s), e.g. while you were using them, as an alternative to them, or were opioids an alternative to this substance?
- b. Why did you use this substance?
- c. How long did you use this substance? Did you use it consistently during this time, or were you using it on and off?
- d. What were the positive effects/benefits of using it?
- e. Did you experience any side effects or other problems while using it?
- f. How much of this substance did you use at one time?
- g. How often did you use it? Were you taking this substance on a regular schedule or using it when you felt you needed it?
- h. How did you use it? **[NOTE:** explore use of pills, capsules, edibles, vaping, creams, lotions, oils, tinctures, etc., as appropriate] Did this vary over time and if so, how/why?

[NOTE: After reviewing each agent individually to the extent that's possible within the time limits, ask the following summary questions:]

2. What combinations of all the substances we've discussed have you tried?
3. Which combination of substances did you like best? Why?
4. Which combination did you like the least? Why?
5. How did you move from one substance to another and why? **[NOTE:** Probe if needed: which substance did you start with and why, and then which substance did you add to it or which substance did you use as a replacement or substitute and why?]
6. How long have you been using each of these substances?

VII. Receiving Treatment (10 minutes)

1. Before coming to this treatment center, did you try to stop taking prescription opioids on your own? **[NOTE:** IF SO:]
 - a. How did you attempt to quit? **[NOTE:** If needed, probe on cold turkey/stopped entirely, decreased dose or frequency, substituted other substances and if so, what, etc.]
 - b. How long did that/each of those attempt(s) last?
 - c. What led to reoccurrence?

2. Have you sought help in the past?
[NOTE: IF SO:]
 - a. What kind(s) of help? [NOTE: If needed, probe specifically about medication-assisted treatment such as methadone, buprenorphine, and suboxone; behavioral interventions such as counseling, etc.]
 - b. What led to reoccurrence?
 - c. What difficulties did you experience after receiving this treatment?
[NOTE: probe about the following if they don't come up organically: stigma, employment difficulties, family difficulties, cravings]
3. Are there substances you are afraid you might want to use in the future? If so, what substances and why?
4. After you complete your treatment, how do you expect to deal with reason(s) for substance use?

VIII. Thank and Conclude (5 minutes)

1. Do you have anything else you want to add before we end this interview?
2. Thank respondent for his/her participation.
3. Distribute token of appreciation.
4. Remind respondent about contact information on consent form and tell them that if they ever have questions or concerns about medications generally they can contact the FDA at druginfo@fda.hhs.gov or by phone toll-free at (855) 543-3784
5. Wish the respondent well in his/her treatment/future.