Exhibit C
PNRR SOP for Patient History Questionnaire (PHQ)

PATIENT HISTORY QUESTIONNAIRE (PHQ)

NOTE: Instructions for PNRR Study Coordinators are marked in blue ink.

- The Patient History Questionnaire has to be filled out by each PNRR study participant at enrollment, and the provided information is part of the initial data set.
- During follow up visits a "FOLLOW-UP Questionnaire" should only be filled out, if 12 months have elapsed since the last time the patient filled out a questionnaire
- The FOLLOW-UP Questionnaire is a shortened version of the PHQ, ending with Section III.

After the patient has completed the questionnaire, the study coordinator should check the answers and make sure that answers were provided to all questions and if some questions were not answered by the patient, the study coordinator shall contact the patient and obtain the missing answers.

Patient Instructions (in questionnaire):

Please take a moment to read these instructions before completing the Patient History Questionnaire for the Peripheral Neuropathy Research Registry (PNRR).

- ***Please read each question carefully and answer as thoroughly as possible.***
- ***If you are unsure how to fill out any part of this form, please do not hesitate to ask for help and guidance.***

Section I. PATIENT INFORMATION

Question: ***What year were you born?*** _____: year patient was born

Question: ***What is your sex?***

Possible Answers:

☐ **Male**: genetic sex of patient is male
☐ **Female**: patient's genetic sex is female

Question: ***Are you Hispanic or Latino?***

Possible answers:

☐ **Yes:** patient is of Cuban, Mexican, Puerto Rican, South or Central American or other Spanish culture or origin, regardless of race
☐ **No:** patient is <u>not</u> of Cuban, Mexican, Puerto Rican, South or Central American or other Spanish culture or origin.

Exhibit C
PNRR SOP for Patient History Questionnaire (PHQ)

Question*: What is your race?*

Possible answers:

- ☐ **American Indian / Alaska Native**: patient is a descendent of any of the original peoples of North or South America (including Central America) and maintains tribal affiliation or community attachment
- ☐ **Asian**: patient is of Far Eastern, Indian or Southeast Asian descent
- ☐ **Black or African American**: patient is a descendent of any of the black racial groups of Africa
- ☐ **Native Hawaiian or other Pacific Islander**: patient has origins in Hawaii or other Pacific Island
- ☐ **White**: patient is of European, Middle Eastern or North African descent
- ☐ **More than one race**: patient is of mixed race

Section II. CURRENT SYMPTOMS

Information for Study Coordinator:

- **All questions should be answered evaluating the neuropathy (symptoms). If a patient experiences pain associated with another medical condition, the questions in section II of the questionnaire should be answered describing only the neuropathic. The study coordinator should make a note of the other painful condition in NOTES data entry field of the PEF.**
- **The patient should describe their CURRENT symptoms, as experienced within the last 7 days. If a patient experiences pain sometimes, but not in the past 7 days, the patient should be instructed to still describe his/her pain as long as pain is experienced on a regular basis.**
- **If the patient is on pain medication, the symptoms should be described as experienced (while on pain medication).**
- **If the pain levels fluctuate, the "average" pain level should be described.**

Patient Instructions:

- ***Please provide answers to these questions regarding symptoms due to your peripheral neuropathy only (e.g. pain, numbness, tingling, burning, weakness, balance, etc.)***
- ***Please refer to your "average" pain during the past 7 days. Do not refer to any extreme levels of pain such as "most" painful or "least" painful***

0. ***When did you notice the first symptoms associated with your peripheral neuropathy?***
Number of years since patient noticed the first PN symptoms, recorded with one decimal, e.g. 3.5

1. ***PAIN: Do you have pain?***

Possible Answers:

- ☐ **Yes**: patient has painful neuropathy
- ☐ **No**: patient's neuropathy is not painful

► If you do NOT have pain, skip to **Question 2** (on Page 8)

Exhibit C
PNRR SOP for Patient History Questionnaire (PHQ)

a. ***Where is your pain located? Mark <u>all</u> areas that apply.***

Patient to identify the areas of neuropathic pain.

Possible answers:

- ☐ **Left foot**: neuropathic pain anywhere below left ankle
- ☐ **Right foot**: neuropathic pain anywhere below right ankle
- ☐ **Left leg**: neuropathic pain anywhere between ankle and groin of left leg
- ☐ **Right leg**: neuropathic pain anywhere between ankle and groin of right leg
- ☐ **Left arm**: neuropathic pain anywhere between shoulder and wrist of left arm
- ☐ **Right arm**: neuropathic pain anywhere between shoulder and wrist of right arm
- ☐ **Left hand**: neuropathic pain anywhere below (distal of) left wrist
- ☐ **Right hand**: neuropathic pain anywhere below (distal of) right wrist
- ☐ **Torso/trunk**: patient experiences pain on torso/trunk, which is the main part of the body excluding the extremities, head and neck
- ☐ **Face**: neuropathic pain on face
- ☐ **Back**: neuropathic pain on back only (not on front of torso/trunk)
- ☐ **Neck**: neuropathic pain located in neck area

If patient marks Torso/trunk, face, back or neck, the study coordinator should make sure that this pain is neuropathy related and not associated with another medical condition.

b. ***Is your pain:***

Possible Answers:

- ☐ **Always present**: patient experiences pain every day
- ☐ **Sometimes present**: patient experience pain regularly, but not every day
- ☐ **Rarely present**: patient experiences pain no more than once a week
- ☐ **Don't know**: patient is unable to provide answer

c. ***How long ago did your pain start?***

Possible Answers:

- ☐ **Within the last week**: neuropathic pain started within the past 7 days
- ☐ **2 to 4 <u>weeks</u> ago**: neuropathic pain started within the last month
- ☐ **1 to 6 <u>months</u> ago**: neuropathic pain started within the last 6 months
- ☐ **7 to 12 <u>months</u> ago**: neuropathic pain started within the last year
- ☐ **1 to 5 <u>years</u> ago**: neuropathic pain started more than 1 year, but less than 5 years ago
- ☐ **6 to 10 <u>years</u> ago**: neuropathic pain started more than 5 years, but less than 10 years ago
- ☐ **11 to 20 <u>years</u> ago**: neuropathic pain started more than 10 years, but less than 20 years ago
- ☐ **As long as I can remember**: neuropathic pain started more than 20 years ago

Patient Instruction:
For the next set of questions, place an "X" through the number that <u>best describes</u> your pain.

d. ***Please use the scale below to tell us how <u>intense</u> your pain is.***

Pain Scale Interpretation:

- ☐ **0**: no pain
- ☐ **1, 2, 3**: mild pain, not impacting daily activities
- ☐ **4, 5, 6**: moderate pain, mildly impacting daily activities
- ☐ **7, 8, 9**: severe pain, impacting daily activities
- ☐ **10**: the most intense pain sensation imaginable

e. ***Please use the scale below to tell us how <u>sharp</u> your pain feels. Words used to describe sharp feelings include "like a knife," "like a spike," "jabbing," or "like jolts."***

Pain Scale interpretation:

- ☐ **0**: pain does not feel sharp
- ☐ **1, 2, 3**: pain feels a little bit sharp
- ☐ **4, 5, 6**: pain feels moderately sharp
- ☐ **7, 8, 9**: pain feels very sharp
- ☐ **10**: the most sharp sensation imaginable ("like a knife")

f. ***Please use the scale below to tell us how <u>hot</u> your pain feels. Words used to describe very hot pain include "burning" and "on fire."***

Pain Scale interpretation:

- ☐ **0**: pain does not feel hot
- ☐ **1, 2, 3**: pain feels a little bit hot
- ☐ **4, 5, 6**: pain feels moderately hot
- ☐ **7, 8, 9**: pain feels very hot
- ☐ **10**: the most hot sensation imaginable ("on fire")

g. ***Please use the scale below to tell us how <u>dull</u> your pain feels. Words used to describe very dull pain include "like a dull toothache," "dull pain," "aching," and "like a bruise."***

Pain Scale interpretation:

- ☐ **0**: pain does not feel dull
- ☐ **1, 2, 3**: pain feels a little bit dull
- ☐ **4, 5, 6**: pain feels moderately dull
- ☐ **7, 8, 9**: pain feels very dull
- ☐ **10**: the most dull sensation imaginable

h. ***Please use the scale below to tell us how <u>cold</u> your pain feels. Words used to describe very hot pain include "like ice" and "freezing."***

Pain Scale interpretation:

- ☐ **0**: pain does not feel cold
- ☐ **1, 2, 3**: pain feels a little bit cold
- ☐ **4, 5, 6**: pain feels moderately cold
- ☐ **7, 8, 9**: pain feels very cold
- ☐ **10**: the most cold sensation imaginable ("freezing")

i. ***Please use the scale below to tell us how <u>sensitive</u> your skin is to light touch or clothing. Words used to describe sensitive skin include "like sunburned skin" and "raw skin."***

Pain Scale interpretation:

- ☐ **0**: skin is not sensitive to touch
- ☐ **1, 2, 3**: skin is a little bit sensitive to touch
- ☐ **4, 5, 6**: skin is moderately sensitive to touch
- ☐ **7, 8, 9**: skin is very sensitive to touch
- ☐ **10**: the most sensitive sensation imaginable ("raw skin")

j. ***Please use the scale below to tell us how <u>itchy</u> your pain feels. Words used to describe itchy pain include "like poison oak" and "like a mosquito bite."***

Pain Scale interpretation:

- ☐ **0**: pain does not feel itchy
- ☐ **1, 2, 3**: pain feels a little bit itchy
- ☐ **4, 5, 6**: pain feels moderately itchy
- ☐ **7, 8, 9**: pain feels very itchy
- ☐ **10**: the most itchy sensation imaginable ("like poison oak")

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k. ***Which of the following statements best describes the time quality of your pain?***

Possible answers:

- ☐ **I feel background pain <u>all the time</u> and occasional flare-ups (break-through pain) <u>some of the time</u>.**
  - **Describe the background pain:** _____ Patient to describe background pain using adjectives such as burning, tingling, cold, hot, dull, itchy, etc.
  - **Describe the flare-up (break-through) pain:** _____ Patient to describe flare-up pain using adjectives such as burning, tingling, cold, hot, dull, itchy, etc.

- ☐ **I feel a single type of <u>pain all the time</u>.**
  - **Describe this pain:** _____ Patient to describe their pain symptoms using adjectives such as burning, tingling, cold, hot, dull, itchy, etc.
- ☐ **I feel a single type of pain only sometimes. Other times I am pain free.**

- **Describe this occasional pain:** _____ Patient to describe their pain symptoms using adjectives such as burning, tingling, cold, hot, dull, itchy, etc.

Study Coordinator needs to check that pain descriptions are provided.

If more than one choice is marked, Study Coordinator should discuss with patient which of the three options is the most fitting.

l. ***Now that you have told us the different physical aspects of your pain, the different types of sensations, we want you to tell us overall how unpleasant your pain is to you. Words used to describe very unpleasant pain include "miserable" and "intolerable." Remember, pain can have a low intensity, but still feel extremely unpleasant, and some kinds of pain can have a high intensity but be very tolerable. With this scale, please tell us how unpleasant your pain feels.***

Pain Scale interpretation:

☐ **0**: pain is not unpleasant
☐ **1, 2, 3**: pain feels a little bit unpleasant
☐ **4, 5, 6**: pain feels moderately unpleasant
☐ **7, 8, 9**: pain feels very unpleasant
☐ **10**: the most unpleasant sensation imaginable ("intolerable")

m. ***We want you to give us an estimate of the severity of the deep versus surface pain. We want you to rate both location of pain (deep and surface) separately. We realize this can be difficult to make these estimates, and most likely it will be a "best guess," but please give us your best estimate.***

i. ***How intense is your deep pain?***

Pain Scale interpretation:

☐ **0**: no deep pain
☐ **1, 2, 3**: deep pain is mild
☐ **4, 5, 6**: deep pain is moderate
☐ **7, 8, 9**: deep pain is severe
☐ **10**: the most intense deep pain sensation imaginable

ii. ***How intense is your surface pain?***

Pain Scale interpretation:

☐ **0**: no surface pain
☐ **1, 2, 3**: surface pain is mild
☐ **4, 5, 6**: surface pain is moderate
☐ **7, 8, 9**: surface pain is severe
☐ **10**: the most intense surface pain sensation imaginable

n. ***Do you experience abnormal perceptions of pain or discomfort from a normally non-painful stimulus? For example, do you experience tingling, burning, discomfort or some other abnormal sensation when lightly touched?***

Possible answers:

- ☐ **Yes**: patient has experienced at least one abnormal perception of pain or discomfort in the past seven days from an otherwise non-painful stimulus
- ☐ **No**: patient did not experience an abnormal perception of pain or discomfort from an otherwise non-painful stimulus in the past seven days
- ☐ **Don't Know**

o. ***Are you taking medication for your neuropathic pain?***

Possible Answers:

- ☐ **Yes**: patient takes medication for neuropathic pain
- ☐ **No**: patient does not take pain medication
  - ► If you do NOT take medication, skip to **Question 2** (next Page)

p. ***How efficient is your pain medication?***

- ☐ Not effective
- ☐ Somewhat effective
- ☐ Very effective
- ☐ Was once effective but no longer helps

q. ***Do you have side effects from your pain medication?***

Possible Answers:

- ☐ Sleepiness, drowsiness (somnolence)
- ☐ Dizziness
- ☐ Weight gain
- ☐ Nausea, upset stomach
- ☐ Sexual dysfunction
- ☐ Other: _____
- ☐ No side effects

r. ***Have you taken other medications for your neuropathic pain in the past, and if so please tell us why you stopped taking those medications:***

- The name of the discontinued pain medications should be listed, using either the pharmaceutical drug name or the brand name as listed in the RXNorm medication dictionary. If the option is available, both the pharmaceutical drug name and the brand name should be provided.
- For pain medication that was taken only once a day, the daily dosage should be listed, followed by the letters "QD." For example: "81 mg QD."

- For pain medications which are taken more than once each day, the medication for each dosage should be listed, followed by the frequency. Example: for a patient taking 300 mg gabapentin three times a day, the data entry should be "300 mg TID."
  A list of the medication frequency codes (e.g., TID for three times daily) is provided in Attachment 1

Name of medication	Dosage of medication	Reason you stopped / switched
		☐ Side effects ☐ Insurance coverage ☐ No longer effective ☐ Other: _____

Patient Instructions:

For the following questions, please refer only to those symptoms you have experienced due to your peripheral neuropathy during the past 7 days.

2. ***NUMBNESS: Do you have numbness (loss of sensation)?***

Possible Answers:

☐ **Yes**: patient has areas of numbness
☐ **No**: patient does not experience numbness
► If you do NOT have numbness, skip to **Question 3**.

a. *Where is your numbness (loss of sensation) located? Mark all areas that apply.*

Patient to identify the areas of neuropathic pain.

Possible answers:

☐ **Left foot**: area of numbness located below left ankle
☐ **Right foot**: area of numbness located below right ankle
☐ **Left leg**: area of numbness located between ankle and groin of left leg
☐ **Right leg**: area of numbness located between ankle and groin of right leg
☐ **Left arm**: area of numbness located between shoulder and wrist of left arm
☐ **Right arm**: area of numbness located between shoulder and wrist of right arm
☐ **Left hand**: area of numbness located below (distal of) left wrist
☐ **Right hand**: area of numbness located below (distal of) right wrist
☐ **Torso/trunk**: area of numbness located on torso/trunk, which is the main part of the body excluding the extremities, head and neck
☐ **Face**: area of numbness located on face
☐ **Back**: area of numbness located on back only (not on front of torso/trunk)

☐ **Neck**: area of numbness located in neck area

If patient marks Torso/trunk, face, back or neck, the study coordinator should make sure that the numbness is neuropathy related and not associated with another medical condition.

b. ***Is your numbness (loss of sensation):***

Possible Answers:

☐ **Always present**: patient experiences numbness every day
☐ **Sometimes present**: patient experience numbness regularly, but not every day
☐ **Rarely present**: patient experiences numbness no more than once a week
☐ **Don't know**: patient is unable to provide answer

c. ***How long ago did your numbness (loss of sensation) start?***

Possible Answers:

☐ **Within the last week**: numbness started within the past 7 days
☐ **2 to 4 weeks ago**: numbness started within the last month
☐ **1 to 6 months ago**: numbness started within the last 6 months
☐ **7 to 12 months ago**: numbness started within the last year
☐ **1 to 5 years ago**: numbness started more than 1 year, but less than 5 years ago
☐ **6 to 10 years ago**: numbness started more than 5 years, but less than 10 years ago
☐ **11 to 20 years ago**: numbness started more than 10 years, but less than 20 years ago
☐ **As long as I can remember**: numbness started more than 20 years ago

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3. ***Do you experience spontaneous abnormal sensations (with or without loss of sensation)? Some people might describe these as "pins and needles," "tingling," or "like part of a limb fell asleep."***

Possible Answers:

☐ **Yes, all the time**: patient experiences spontaneous abnormal sensations on average at least once a week or more frequently
☐ **Yes, occasionally**: patient experiences spontaneous abnormal sensation less than once a week on average
☐ **No, never**: patient does not have spontaneous abnormal sensations

4. ***WEAKNESS: Do you have weakness (loss of strength or power)?***

Possible Answers:

☐ **Yes**: patient experienced symptoms of weakness within the past week
☐ **No**: patient did not experience symptoms of weakness within the past week

► If you do NOT have weakness, skip to **Question 5**.

a. ***What is your weakness (loss of strength or power)? What are the types of activities you have difficulty with? Mark all that apply.***

Possible Answers:

- ☐ **Feet and ankles (trip easily)**
- ☐ **Foot drop**
- ☐ **Proximal legs (difficulty going upstairs, getting out of a chair or toilet)**
- ☐ **Fine motor tasks with hands (difficulty buttoning, zipping a zipper)**
- ☐ **Decreased grip strength**
- ☐ **Proximal arms (difficulty lifting heavy objects, shampooing hair)**
- ☐ **Other:** _____

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5. ***Do you experience tight, painful contractions of your muscles? These are sometimes referred to as "cramps" or "charley horse."***

Possible Answers:

- ☐ **Yes, frequently:** painful muscle contractions are experienced twice a month or more frequently
- ☐ **Yes, sometimes**: painful muscle contractions are experience less than twice a month, but more than six times a year
- ☐ **Yes, but very rarely**: painful muscle contractions are experiences less than 6 times a year.
- ☐ **No, never**: patient does not have painful muscle contractions

► If you do NOT have painful contraction, skip to **Question 6** (next Page).

a. ***Are your tight, painful contractions of your muscles controlled with medications?***

Possible Answers:

- ☐ **Yes**: painful muscle contractions are controlled with medication
- ☐ **No, medication does not work**
- ☐ **I do not take medication for my muscle cramps**

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6. ***BALANCE: Do you have trouble with your balance or difficulties walking because of poor balance?***

Possible Answers:

- ☐ **Yes**: patient has impaired balance or difficulties walking
- ☐ **No**: patient does not experience balance impairment

► If you do NOT have trouble with your balance, skip to **Question 7**

a. ***Is your trouble with balance:***

Possible Answers:

- ☐ **Always present**: patient has balance issues every day
- ☐ **Sometimes present**: impaired balance only under certain conditions or not every day
- ☐ **Rarely present**: patient notices impaired balance occasionally; no more than once a week
- ☐ **Don't know**

b. ***Do you use any assistive devices when walking? Mark <u>all</u> that apply.***

Possible Answers:

- ☐ **Yes, I use a walker**
- ☐ **Yes, I use orthotics**
- ☐ **Yes, I use a wheelchair**
- ☐ **Yes, I use a cane**
- ☐ **No, I am bedbound**
- ☐ **No, I do not use any assistive devices when walking**

c. ***Have you had any falls?***

Possible Answers:

- ☐ **Yes, almost every day**
- ☐ **Yes, more than once a week**
- ☐ **Yes, about once per month**
- ☐ **Yes, more than once over the last year**
- ☐ **Yes, less than once per year**
- ☐ **No, I have not fallen**

7. **<u>AUTONOMIC:</u>** ***Now we want to know a little bit about your autonomic system. Your autonomic system regulates things like heart rate, blood pressure, sweating, bowel function and sexual function.***

a. ***Do you experience spells of lightheadedness or dizziness as if you were going to faint?***

Possible Answers:

- ☐ **Yes**: patient experiences spells of lightheadedness or dizziness
- ☐ **No:** patient does not experience lightheadedness or dizziness

► If you do <u>NOT</u> have dizziness, skip to **Question 7b** (below)

If answered with yes:

***i. Do your spells of lightheadedness or dizziness get worse after the following activities? Mark <u>all</u> that apply*.**

Possible Answers:

- ☐ **After standing up quickly**
- ☐ **After a hot bath or shower**
- ☐ **After standing for a long time**
- ☐ **After a large meal**
- ☐ **Other:**_____

ii. Have you ever fainted or "passed out?"

Possible Answers:

- ☐ **Yes, at least once per month**
- ☐ **Yes, several time per year**
- ☐ **Yes, about once per year**
- ☐ **Yes, less than once per year**
- ☐ **Yes, but very rarely**
- ☐ **No, I have never fainted**

b. ***Do you have abnormal sweating? Mark <u>all</u> that apply.***

Possible Answers:

- ☐ **Yes, I sweat more after eating**
- ☐ **Yes, I sweat less in a warm environment**
- ☐ **Yes, I have other abnormal sweating, please explain** _____
- ☐ **No**

c. ***Do you experience dryness of your eyes or mouth?***

Possible Answers:

- ☐ **Yes**
- ☐ **No**

d. ***Do you have abnormal bowel movements? Mark <u>all</u> that apply.***

Possible Answers:

- ☐ **Yes, I have diarrhea**
- ☐ **Yes, I have constipation**
- ☐ **No**

e. ***Do you have difficulties with urination? Mark <u>all</u> that apply.***

Possible Answers:

- ☐ **Yes, I often experience a sudden, immediate need to go to the bathroom (urgency)**
- ☐ **Yes, I have the urge to go to the bathroom frequently (frequency)**
- ☐ **Yes, I lose control of my bladder (incontinence)**
- ☐ **Yes, I have trouble emptying my bladder or initiating urination**
- ☐ **No, I don't have difficulties with urination**

f. ***MEN ONLY: Has your sexual function changed recently? Mark <u>all</u> that apply.***

Possible Answers:

- ☐ **Yes, I have been having difficulties with having erections**
- ☐ **Yes, I have been having difficulties having ejaculation**
- ☐ **No**

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8. ***<u>SLEEP</u>: Have you experienced sleeping difficulties?***

Possible Answers:

- ☐ **Yes**: patient has some sleeping difficulties
- ☐ **No**: no sleeping problems

► If you do <u>NOT</u> have sleeping difficulties, skip to **Question 9**.

a. ***Do you have difficulty falling asleep or staying asleep at night from pain due to your peripheral neuropathy?***

Possible Answers:

- ☐ **Yes**
- ☐ **No**

b. ***Do you have an urge to move your legs at night, accompanied or caused by unpleasant sensations?***

Possible Answers:

- ☐ **Yes**
- ☐ **No**

c. ***Are your sleeping difficulties controlled with medications?***

Possible Answers:

- ☐ **Yes**
- ☐ **No, medication does not work**
- ☐ **I do not take sleeping aid medication**

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9. ***Which symptom bothers you the most? Please mark only <u>one</u>.***

Possible Answers:

- ☐ **Pain**
- ☐ **Numbness (loss of sensation)**

- ☐ **Weakness (loss of strength or power)**
- ☐ **Balance or difficulty with walking**
- ☐ **Other:** _____

If patient selected more than one answer for Question 9, the study coordinator shall discuss this with the patient to determine which symptom is the most bothersome for the patient and correct the answer for Question 9 accordingly.

Section III. MEDICATIONS, VITAMINS, AND SUPPLEMENTS

Patient instructions:

Please list all medications, vitamins, and supplements that you are currently taking.

Medication, Vitamin, or Supplement:

- The names of all current medications should be listed, using either the pharmaceutical drug name or the brand name as listed in the RXNorm medication dictionary. If the option is available, both the pharmaceutical drug name and the brand name should be provided. Vitamins should be listed by either by using the chemical name or by listing the vitamin name as listed in the RXNorm medication list. If available, both the chemical name and the vitamin name should be provided.
- Supplements: all taken supplements should be listed using the generic description of the supplement, for example "turmeric oil"
- Supplements that are not included in the RXNorm medication list, can be entered by requesting unrestricted medication data entry fields. The number of supplements not found in the RXNorm list should be entered, using the "**How many supplements did the patient list which are not on the RXNorm list?**" The requested number of data entry fields will then be created by REDCap.

Dosage:

- For medication taken only once a day, the daily dosage should be listed, followed by the letters QD (Latin: *quaque die*). For example, "81 mg QD."
- For medications taken more than once each day, the medication for each dosage should be listed, followed by the frequency. For example, a patient taking 500 mg Metformin twice a day, the dosage information should be entered as "500 mg BID." A list of the medication frequency codes (e.g., BID for twice a day) is provided in Attachment 1.
- For multivitamins and supplements, it is acceptable to enter the information in form of volume measurements, e.g., "1 capsule QD."

Study coordinator to check provided medication list against patient's medical records. Missing medications and dosages should be added to the PNRR data set.

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Section IV. MEDICAL HISTORY

Question for FOLLOW-UP ONLY:

Have you had any new medical issues, diagnoses, or surgeries since your last PNRR visit?

Possible Answers:

- ☐ **Yes**: patient has reports new medical issues or surgeries
- ☐ **No**: no new medical issues or surgeries
  - ► If you have NOT had new medical issues, diagnoses, or surgeries since your last PNRR visit, Questionnaire is complete.

10. ***Please mark all that apply:***

- ☐ **Amyloidosis**
- ☐ **Anorexia**
- ☐ **Cancer**

  Have you ever received chemotherapy?
  - ☐ Yes
  - ☐ No
  - ☐ Don't know

  Name of drug(s): _____

  Study coordinator to contact Oncologist if patient is not able to provide name of drug(s). At minimum, drug(s) known to cause nerve damage should be listed.

- ☐ **Cardiac disease**
- ☐ **Celiac Disease**
- ☐ **Crohn's disease**
- ☐ **Diabetes Mellitus**
  - ☐ Type I: total lack of insulin or do not produce enough insulin
  - ☐ Type II: cannot use insulin efficiently
- ☐ **Elevated cholesterol**
- ☐ **Elevated triglycerides**
- ☐ **Fibromyalgia**
- ☐ **Hepatitis**
  - ☐ Hepatitis A
  - ☐ Hepatitis B
  - ☐ Hepatitis C

  Have you ever received Interferon treatments?
  - ☐ Yes
  - ☐ No
  - ☐ Don't know
- ☐ **HIV**

  Have you ever received ddI, d4T, or ddc?
  - ☐ Yes
  - ☐ No
  - ☐ Don't know

Have you ever received protease inhibitor?

- ☐ Yes
- ☐ No
- ☐ Don't know

- ☐ **Irritable bowel disease**
- ☐ **Kidney disease**
- ☐ **Leprosy**
- ☐ **Liver disease**
- ☐ **Lyme disease**
- ☐ **Mixed connective tissue disease**
- ☐ **Peripheral vascular disease**
- ☐ **Rheumatoid arthritis**
- ☐ **Sarcoidosis**
- ☐ **Scleroderma**
- ☐ **Shingles**
- ☐ **Sjögren's syndrome**
- ☐ **Syphilis**
- ☐ **Systemic lupus erythematosus (SLE)**
- ☐ **Thyroid disease**
  - ☐ Hyper – patient had iodine treatment or takes methimazole medication
  - ☐ Hypo – patient takes levothyroxine sodium (Synthroid) medication
  - ☐ Don't know
- ☐ **Ulcerative colitis**
- ☐ **Vitamin B1 deficiency**
- ☐ **Vitamin B6 deficiency**
- ☐ **Vitamin B6 over-dosage**
- ☐ **Vitamin B12 deficiency**

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11. ***Did you have any vaccinations, infections, or the flu <u>1 to 3 months</u> before the onset of your neuropathy?***

Possible Answers:

- ☐ **Yes, I had the flu**
- ☐ **Yes, I had an infection(s) ► if YES, which one(s)? _____**
- ☐ **Yes, I had vaccination(s) ► if YES, which one(s)? _____**
- ☐ **No**
- ☐ **Don't know**

12. ***If you have other medical or infectious conditions, please list below:***

All medical conditions should be listed here – independent if they are effecting neuropathy or not. Study Coordinator should check medical records and physician notes to ensure that all medical and infectious conditions are captured in the database.

13. ***If you have had major surgery, please list the type of surgery and when it was performed:***

- **Definition for "major surgery":** a surgery that required anesthesia or an overnight stay at a health care facility
- **Year of surgery**: calendar year the surgery was performed

14. ***As a child, did you have difficulties or delays in development?***

Possible Answers:

☐ **Yes**
☐ **No** ►If you did NOT have delays, skip to **Section V** (next Page).

a. ***As a child did you have difficulty with (mark all that apply):***

Possible Answers:

☐ **Riding a bicycle**
☐ **Roller skating / ice skating**
☐ **Running**
☐ **Keeping up with peers in physical activities**
☐ **Don't know**

b. ***At what age did you begin having developmental delays?*** _____ ***(years)***

Section V. SOCIAL AND OCCUPATIONAL HISTORY

15. ***What is your current occupation?*** _____

16. ***What is your past occupation?*** _____

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17. ***Have you had (now or in the past) any occupational exposure to excessive amounts of hazardous chemicals? Mark all that apply.***

Possible Answers:

☐ **Yes, herbicides, pesticides or fungicides**
☐ **Yes, heavy metals, such as lead, mercury, arsenic or others**
☐ **Yes, solvents such as N-hexane, perchloroethylene, trichloroethylene, carbon disulfide or others**
☐ **No**

Most patients do not remember the brand name of the substance(s) they came in contact with. If they do not remember the exact name, the "function" should be listed. For example: "pesticides routinely used in apple orchards;" "solvents used for photo development."

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18. ***Have you ever smoked? If you have never smoked, mark "No" and skip to Question 18.***

Possible Answers:

☐ **Yes, I currently smoke**

If YES, how many packs per day? AND For how many years?

- ☐ Less than 1 pack
- ☐ More than 1 pack
- ☐ Less than 10 years
- ☐ More than 10 years

☐ **Yes, I have smoked in the past, but I do not currently smoke**

If YES, how many packs per day? AND For how many years?

- ☐ Less than 1 pack
- ☐ More than 1 pack
- ☐ Less than 10 years
- ☐ More than 10 years

At what age did you stop smoking? _____(years)

☐ **No**

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19. ***Have you ever drunk alcohol? If you do not drink alcohol, mark "No" and skip to Question 20*** *(below). For this question, one drink is equal to one glass of wine, one bottle of beer, or one mixed drink.*

Possible Answers:

☐ **Yes, I currently drink**

If YES, how many drinks per day? AND For how many years?

- ☐ Less than 2 drinks
- ☐ More than 2 drinks
- ☐ Less than 10 years
- ☐ More than 10 years

☐ **Yes, I have drunk alcohol in the past, but I do not currently drink**

If YES, how many drinks per day? AND For how many years?

- ☐ Less than 2 drinks
- ☐ More than 2 drinks
- ☐ Less than 10 years
- ☐ More than 10 years

At what age did you stop drinking? _____(years)

☐ **No**

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20. ***Have you ever used recreational drugs? If you have never used recreational drugs, mark "No" and skip to Question 20.*** *For this question, "recreational drugs" refer to any drugs taken for a psychoactive rather than medical purpose, such as marijuana, cocaine, or methamphetamine.*

Possible Answers:

☐ **Yes, I currently use recreational drugs**

If YES, which drug(s) do you use? AND For how many years?

☐ _____ ☐ Less than 10 years

☐ _____ ☐ More than 10 years

☐ **Yes, I have used recreational drugs in the past, but I do not currently use recreational drugs**

If YES, which drug(s) do you use? AND For how many years?

☐ _____ ☐ Less than 10 years

☐ _____ ☐ More than 10 years

At what age did you stop using recreational drugs? _____ (years)

☐ **No**

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21. ***What is your marital status?***

Possible Answers:

☐ **Single**
☐ **Married**
☐ **Widowed**
☐ **Separated**
☐ **Divorced**

22. ***Which best describes your living situation?***

Possible Answers:

☐ **I live alone**
☐ **I live with my spouse / partner**
☐ **I live with my parent(s) / sibling(s)**
☐ **I live with a roommate**
☐ **I live with my children**

Exhibit C
PNRR SOP for Patient History Questionnaire (PHQ)

Section VI. FAMILY HISTORY

In Section VI, the patients are asked about their family history in regard to neuropathy and other diseases, and then list each family member and their disease. One of the questions asked is the age of the family member at the time of diagnosis. Often the patient does not remember the exact age and indicates that the diagnosis was made "in 50s" or "mid 60s" or a similar statement.

If only the decade is indicated, the first year of the decade should be entered. For example, for "50s" the number 50 should be entered.

If "mid 50s" is used as the age indication, the value "55" should be entered into the database.

23. ***Do you have family members with peripheral neuropathy?***

Possible Answers:

☐ **Yes**: other (blood-related) family members have neuropathy

☐ **No**: no other (blood-related) family member has neuropathy
►If you did NOT have any family members with peripheral neuropathy, skip to **Question 24.**

☐ **Don't know**: patient does not know if any relatives have neuropathy
►Skip to **Question 24**.

Please tell us more about your family members with peripheral neuropathy. In the table below, list their relationship to you, type of neuropathy, and the age at which they were diagnosed with autoimmune disease. *See example.*

- **Relationship to you**: relationship to relative with peripheral neuropathy from view of patient.
- **Type of neuropathy:** type of neuropathy (if known), e.g., diabetic neuropathy, otherwise "unknown" or just neuropathy
- **Age at diagnosis:** estimated age at diagnosis or exact age if known.

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24. ***Do you have family members with autoimmune disease?*** *Examples of autoimmune diseases include rheumatoid arthritis, vasculitis, systemic lupus erythematosus, Sjögren's disease, Hashimoto's thyroiditis, ulcerative colitis and Crohn's disease.*

Possible Answers:

☐ **Yes**: one or more (blood-related) family members have autoimmune disease.

☐ **No**: no (blood-related) family member has an autoimmune disease.
►If you did NOT have any family members with autoimmune disease, skip to **Question 25.**

☐ **Don't know**: patient does not know if any relatives have autoimmune diseases.
►Skip to **Question 25**.

Please tell us more about your family members with autoimmune disease. In the table below, list their relationship to you, type of autoimmune disease, and the age at which they were diagnosed with autoimmune disease. *See example.*

- **Relationship to you**: relationship to relative with autoimmune disease from view of patient.
- **Type of autoimmune disease:** name of autoimmune disease.
- **Age at diagnosis:** estimated age at diagnosis or exact age if known.

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25. ***Do you have any family members with the following diseases or conditions: DIABETES, HIGH TRIGLYCERIDES or HIGH CHOLESTEROL?***

Possible Answers:

☐ **Yes**: one or more (blood-related) family members have either diabetes mellitus, elevated triglycerides or elevated cholesterol

☐ **No**: no (blood-related) family member has diabetes or elevated triglycerides or cholesterol
►If you did NOT have any family members these diseases/conditions, skip to **Question 26.**

☐ **Don't know**: patient does not know if any relative has diabetes or elevated triglycerides or elevated cholesterol
►Skip to **Question 26**.

Patient Instruction: Please tell us more about your family members with these diseases/ conditions. In the table below, list their relationship to you, type of disease/condition, and the age at which they were diagnosed with that disease or condition. *See example.*

- **Relationship to you**: relationship to relative with medical condition from view of patient.
- **Type of disease / condition:** if a relative has more than one condition, all applicable conditions should be listed in one line, e.g., diabetes and high cholesterol
- **Age at diagnosis:** estimated age at diagnosis or exact age if known. If patient has more than one medical condition, the age at diagnosis for each condition should be listed, e.g. 62 and 68

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26. ***Do you have any other family history of disease?***

Possible Answers:

☐ **Yes**: one or more (blood-related) family members have another disease

☐ **No**: no (blood-related) family member has another disease

☐ **Don't know**: patient does not know if any relative has another disease

Exhibit C
PNRR SOP for Patient History Questionnaire (PHQ)

Please tell us more about your family history of disease. In the table below, list their relationship to you, type of disease, and the age at which they were diagnosed with that disease. *See example.*

- **Relationship to you**: relationship to relative with medical condition from view of patient.
- **Type of disease / condition:** if a relative has more than one disease, they should be all listed in one data entry field
- **Age at diagnosis:** estimated age at diagnosis or exact age if known. If a relative has more than one disease, the age at diagnosis for each disease should be listed, in the same order they are listed in the "type of disease / condition" data entry field.

Date Submitted:
Date should be entered when data entry was **completed** (= assumed final).

Form Status:

- **Incomplete:** not all data is entered yet
- **Unverified:** all data is entered, but waiting for confirmation for some data (for example, when waiting for confirmation about primary diagnosis pending lab results, the form should be considered unverified)
- **Complete:** all information is verified, no additional edits are anticipated

Exhibit C
PNRR SOP for Patient History Questionnaire (PHQ)

ATTACHMENT 1: Medication Frequency Codes

Frequency Code	Frequency Description
BID	Twice a day
BIW	Twice a week
CI	Continuous infusion
HS	At bedtime
OTO	One time only
PRN	As needed
QH	Every hour
Q12H	Every 12 hours
Q2WK	Every 2 weeks
Q3WK	Every 3 weeks
Q4WK	Every 4 weeks
Q6WK	Every 6 weeks
Q4H	Every 4 hours
Q6H	Every 6 hours
Q8H	Every 8 hours
QD	Once a day
QID	4 times a day
QIW	4 times a week
QMO	Once a month
QOD	Every other day
QWK	Every week
STAT	Immediately
TID	3 times a day
TIW	3 times a week
OT	Other, specify
QPM	Each evening
QAM	Each morning