PHYSICIAN EXAMINATION FORM (PEF)

- **ALL DATA ENTRY FIELDS OF THE PHYSICIAN EXAMINATION FORM MUST BE POPULATED.**
- **All abnormalities reported in the Physician Examination Form should be related or caused by Peripheral Neuropathy. Participants with confounding medical conditions, visible in the PEF data should not be enrolled in PNRR.**

INCLUSION / EXCLUSION CRITERIA:

The enrolling physician should use the inclusion and exclusion criteria to determine if a potential participant with peripheral polyneuropathy is eligible for enrollment into the PNRR study.

INCLUSION CRITERIA	EXCLUSION CRITERIA
Participants with idiopathic polyneuropathy, for which other common causes of PN have been excluded	Participants with predominantly demyelinating polyneuropathies
Participants with diabetic neuropathies, as determined by the enrolling physician	Participants with any identified cause of neuropathy besides diabetes
Participants with idiopathic or diabetic length- or non-length dependent small fiber neuropathy	Participants diagnosed with second confounding neurological condition
Participants with symptoms exclusively in the peripheral nervous system	Participants with upper neuron involvement

NOTE: if underlying cause of neuropathy is identified for a participant during future testing and after participant was enrolled in PNRR, then the enrollment category for participant should be changed to "Other" and underlying etiology should be identified in the open text field.

NOTE: All information recorded as part of the Physician Examination Form are considered part of the Minimum Data Set (MDS) and must be recorded for a new study participant to count as fully enrolled.

GENERAL INFORMATION

1. **Physician:** name of examining physician (last name only)
2. **Subject ID:** PNRR subject ID assigned to research participant upon enrollment
3. **Year of Visit:** calendar year the exam was performed
4. **Year of birth:** year participant was born
5. **Sex:** genetic sex of participant – male or female
6. **Weight:** weight measured on the day of exam in kilograms (kg)
7. **Height:** last measured height in centimeters (cm)

Note: *Body Mass Index (BMI) will be automatically calculated from weight and height data and will be displayed in the database*

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8. Type of Peripheral Neuropathy (PN):

Evaluation if participant experiences pain associated with the peripheral neuropathy or not.

NOTE: the physician should determine if the neuropathy should be classified as painful or non-painful based on examination. The classification if participant has painful or non-painful PN should NOT be based on the participants answer in regard to neuropathic pain in the PHQ.

Choices/Values:

- **Painful:** participant has neuropathic pain or discomfort from PN
- **Non-Painful:** participant does not report neuropathic pain or discomfort from PN

9. Primary Diagnosis

a. Idiopathic PN: no underlying etiology could be identified for participant. Participants enrolled as idiopathic must have negative laboratory testing for most common causes of PN on record.

b. Diabetic PN: shall be chosen as the enrollment category if the enrolling physician determines that hyperglycemia in form of diabetes mellitus (DM) or prediabetes (PreD) is cause of PN.

NOTE: *if participant has long-standing PN and was only recent diagnosis of DM or PreD, then participant should be enrolled as idiopathic with DPN as secondary diagnosis.*

Severity of hyperglycemia
Type of DM should be specified for each participant enrolled as diabetic PN:

- **Type 1** – diabetes mellitus type 1
- **Type 2** – diabetes mellitus type 2
- **Prediabetes** – in form of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)

c. Other (REDcap only, not listed on PEF-CRF): for participants originally enrolled as diabetic or idiopathic PN, for which a cause of their PN is identified after participant was enrolled in PNRR, should be re-classified as "Other". The identified cause of PN should be listed in the open text fields that pops-up when "Other" is chosen as enrollment category.

10. Secondary Diagnosis:

If participant has a secondary medical condition known to cause or known to accelerate the natural history of PN (symptom progression), the condition should be listed as a secondary diagnosis.

Example*, for a participant with long standing diabetes who was recently diagnosed with renal insufficiency as a complication from DM, renal insufficiency should be listed as secondary diagnosis as it accelerates PN progression and needs to be put into consideration during some data analysis projects.*

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MUSCLE EXAMINATION

Upper Extremities:

11. **Finger extension**
12. **Finger flexion**
13. **First Dorsal Interosseous (FDI)**
14. **Abductor Digiti Minimi (ADM)**
15. **Abductor Pollicis Brevis (APB)**

Lower Extremities:

16. **Ankle dorsiflexion**
17. **Ankle plantar flexion**
18. **Great toe dorsiflexion**
19. **Great toe plantar flexion**

The exact examination routine how muscular strength for each muscle group is determine shall be at the discretion of the evaluating physician. The results from the examination shall be recorded in a simplified Medical Research Council (MRC) scale.

Table 1: PNRR Reference Scale for Muscular Strength evaluations

PNRR Scale	MRC Scale	Description
5	5/5-	Normal muscular strength
4	4+/4/4-	Active movement against gravity with reduced movement against resistance
3	3+/3/3-	Active movement against gravity but not against resistance
2	2+/2/2-	Movement against gravity eliminated, but movement can be performed in gravity neutral position
1	1	Only flicker of movement, very limited range of motion
0	0	No movement

20. **Muscular Strength Evaluation for Utah Early Neuropathy Score (UENS) – <u>REDCap only</u>**

Toe Extension (Great toe dorsiflexion): the muscular strength of toe extension (a.k.a. toe dorsiflexion) is part of the UENS, and recorded muscular strength must be converted from MRC into UENS scale for this data entry field.

UENS Scale	MRC Scale	Description
0	5/5-	Normal muscular strength
2	4+/4/4-/3+/3/3-/2+/2/2-/1/0	Reduced muscular strength in toe extension

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DEEP TENDON REFLEXES

21. **Patellar**
22. **Achilles**

The method of examination is at the discretion of the examining physician.

The following Tendon Reflex Scale shall be used to transfer the examination results into the PNRR Physician Examination Form:

Table 2: PNRR Reference Scale for Tendon Evaluation

PNRR Database Scale	Tendon Reflex Rating Scale	Description of Reflex Response
0	0	Reflex absent with reinforcement
1	1	Reflex present but decreased in amplitude and velocity and only elicit with reinforcement
2	2/2+	Normal amplitude and velocity without reinforcement
1	3/3+	Increase in amplitude and velocity without any pathological symptoms
Not eligible for PNRR enrollment	4	Increase in amplitude and velocity, spreading to other sites and/or duplication of jerk or clonus

LOCOMOTION AND BALANCE

23. **Gait:**

Observation of regular walking pattern at the discretion of the physician. Only gait abnormalities related to Peripheral Neuropathy or chronic conditions should be considered when making assessment. Temporary conditions, such as sprained ankle should not be considered.

Choices/Values:

- **Normal:** normal gait in the opinion of the physician
- **Abnormal:** gait is abnormal in the opinion of the physician
- **Not Done:** gait was not evaluated

24. **Tandem gait:**

Toes of the back foot touch the heel of the front foot at each step. The participant's ability to perform tandem walk should be observed across the examination room for at least 5 steps

Choices/Values:

- **Able:** participant is able to perform tandem gait without problems.
- **Not Able:** participant unable to perform a minimum of five (5) steps in tandem gait
- **Not Done:** tandem gait was not evaluated

25. Toe walk:

Participant is asked to walk across the room on their tip toes. Participant needs to take at least five (5) steps to make evaluation of ability to perform toe walk. If heel touches the floor prior to completion of five steps, participant is unable to do toe walk.

Choices/Values:

- **Able:** participant is able to walk on tiptoes for a minimum of five (5) steps
- **Not Able:** participant unable to stay on toes only for five (5) steps
- **Not Done:** toe walk was not evaluated

26. Heel walk:

Participant is asked to walk on heel (with toes lifted off the ground) across the room for a minimum of five (5) steps without toes touching the floor.

Choices/Values:

- **Able:** participant is able to walk on heels
- **Not Able:** participant unable to remain on heels only five (5) steps
- **Not Done:** heel walk was not evaluated

27. Romberg:

Participant is asked to stand in middle of room and maintain standing position for at least ten (10) seconds after closing eyes. Romberg sign is considered present (positive test) when participant starts to sway back and forth.

Choices/Values:

- **Negative:** Romberg sign is absent, no upper body swaying
- **Positive:** Romberg sign is present, participant starts swaying after closing eyes
- **Not done:** Romberg was not evaluated

SENSORY EXAMINATION

28. Pinprick:

Sharp needle-like object (safety-pin) should be used for pinprick examination. Both right and left lower extremities should be evaluated for absent, reduced and normal pinprick sensation.

Pinprick Score	Short Description	Exact Description
0	Normal	Pinprick intact, normal sensation
1	Reduced	Pinprick reduced, but participant still able to feel sharpness of pin point as a prick. **Hypersensitivity** should also be reported as reduced pinprick
2	Absent	Pinprick is absent, participant feels only pressure, no more sensation of prick

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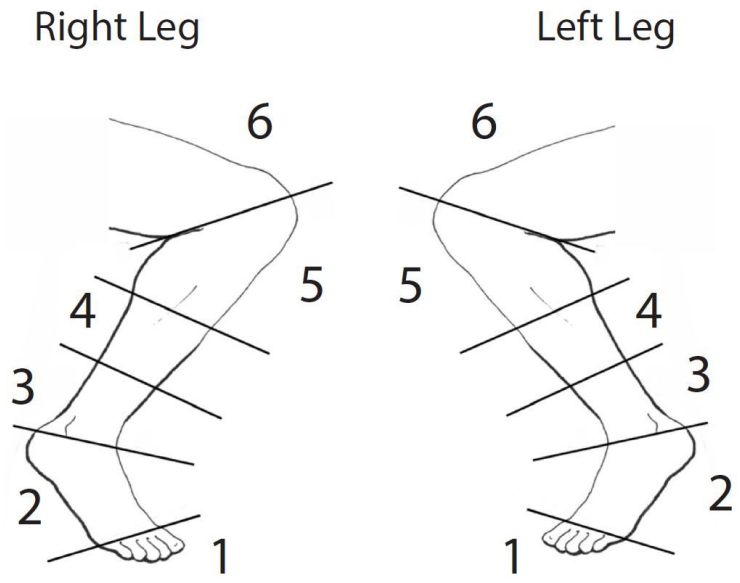
Pinprick needs to be evaluated separately for each of the six leg-segments specified below.

If pinprick changes from absent to reduced within one segment, then that segment should still be marked as 2= absent and the next higher segment should be marked 1= reduced. The same applies for change from reduced to normal pinprick sensation.

Leg Segment Number	Short Description	Exact Description
1	Toes	Pinprick in toes, distal of the Metatarsal-phalangeal joint (MPJ)
2	Foot dorsum	Pinprick in foot, between Metatarsal-phalangeal joint and Malleolus plane
3	Above Ankle	Above Malleolus plane up to approximately one third of the distance to the knee
4	Mid Shin	Mid-section (one third) of shin
5	Below Knee	Area below the knee, approximately one third of length of shin
6	Above Knee	Thigh above knee

Figure 1: Leg Segment Depiction



29. Joint position sense (JPS) or proprioception:

Proprioception evaluated at IP joint at hallux and for ankle joint; physician is moving joint in large and small movements while participant has to identify direction of movement while eyes are closed.

JPS Score	Short Description	Exact Description
0	Normal	Proprioception (joint position sense) is intact
1	Reduced	Participant can identify large manipulations, but not small ones; or participant has at least one wrong answer, but has identifying >70% of the manipulations correctly.
2	Absent	Participant unable to reliably identify joint movements

30. Vibration sense:

Rydel-Seiffer tuning fork (64 Hz) should be used for evaluation of vibration sense. The participant is asked to report when he/she no longer feels the "vibration" from the fork at the testing site. The physician shall read the value off the black triangle on the left damper as soon as the participant reports that he no longer can feel any vibration (scale 0-8).

After the tuning fork is put into motion its base shall be positioned at the following testing sites:

Toes: dorsum of hallux at IP joint
Ankle: internal or external malleolus
Knee: tibial tuberosity
Finger: dorsum of index finger, over DIP joint

Absolute values for each testing site (scale 0 to maximum 8).

Vibration Sense	Short Description	Exact Description
0	Normal	Reading equals normative value or higher
1	Reduced	Rydel-Fork Reading is below normative value, but higher than 0
2	Absent	Participant unable to detect tuning fork vibrations

Table 3: Normative values for Rydel-Seiffer tuning fork

Age	Upper Limbs	Lower Limbs
≤40	≥6.5	≥4.5
41-60	≥6.0	≥4.0
61-85	≥6.0	≥3.5
>85	≥5.5	≥3.0

31. Allodynia or Hypersensitivity:

Presence of allodynia or hypersensitivity at the toe level. Examining physician to touch participant's right and left foot at the toe level and asking if touch feels uncomfortable to participant.

Allodynia	Short Description	Exact Description
0	Absent	Participant does not report allodynia or hypersensitivity to touch
1	Present	Participant has allodynia/hypersensitivity

32. Feet Appearance:

Both feet should be evaluated for any abnormal appearances, such as infections (e.g. infected ulcers), fissures (e.g. cracked skin in particular on heel), any deformities (e.g. high arches, hammertoes, flat feet or hallux vagus), dry or discolored skin and excessive calluses, or any other abnormal foot appearances.

Values: **Normal:** foot appears normal, none of the specified abnormalities were present
Abnormal: foot appears abnormal, one or more of the specified abnormalities were present

If feet appearance is considered abnormal in the opinion of the enrolling physician, the type of abnormality should be captured:

- **Infection:** foot ulcers or athlete's foot (tinea pedis) are two examples of common infections
- **Deformities:** such as high arches (pes cavus), flat feet (pes planus), hammertoes or hallux
- **Dry skin, callus:** participant has dry skin on feet, soft or hard corns (clavus), or excessive callus
- **Fissures:** breakage, crackling or splitting of the callus around the heel

32. NOTES:

Any additional information that might be of interest to future data users should be entered here. In addition, if any of the requested evaluations were not performed due to injuries or medical conditions, those should be explained in the Notes as the missing information is then not considered a violation against the MDS requirements.

33. Date Data Entry Completed:
Date should be entered when data entry was **completed**.

34. Physician Examination Form (PEF) 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