INSTRUCTIONS:

- **THIS FORM SHOULD BE COMPLETED BY THE STUDY COORDINATOR OR PHYSICIAN BY INTERVIEWING THE SUBJECT AND/OR PRIMARY CAREGIVER.**
- **THIS FORM SHOULD BE COMPLETED AT BASELINE (AFTER DRUG WASHOUT, IF APPLICABLE, AND BEFORE THE INITIAL DOSE OF STUDY DRUG) AND AT EACH FOLLOW-UP STUDY VISIT.**
- **A PORTION OF THIS FORM WILL ALSO BE COMPLETED AT THE TIME OF THE QUARTERLY FOLLOW-UP TELEPHONE CALLS (QUESTIONS B1-B5 ONLY).**
- **AT EACH DATA COLLECTION TIMEPOINT, THE STUDY COORDINATOR MUST ASK THE SUBJECT ABOUT EVERY SYMPTOM LISTED ON THE FORM. THE DESCRIPTION OF EACH SYMPTOM (*lower case, italicized text*) MUST BE READ COMPLETELY AND EXACTLY AS WRITTEN. IF THE SUBJECT IS AN INFANT, READ THE DESCRIPTION IN THE {BRACKETS}.**
- **IF "OTHER" SYMPTOMS ARE REPORTED BY THE SUBJECT, THE STUDY COORDINATOR SHOULD REFER TO CTCAE CODE LIST P OR THE CTCAE BOOKLET TO DETERMINE THE PREFERRED SHORT NAME OF THE SYMPTOM AND THE SEVERITY.**
- **FOR THE BRACKETED WORDS IN CAPITAL LETTERS, SUBSTITUTE THE APPROPRIATE NAME OR INFORMATION – e.g., THE COORDINATOR SHOULD SAY THE SUBJECT'S NAME WHERE [PATIENT] APPEARS.**
- **THE COORDINATOR SHOULD CIRCLE THE CODE NUMBER THAT CORRESPONDS TO THE SUBJECT'S/PRIMARY CAREGIVER'S RESPONSE.**

***SYMPTOM FREQUENCY DEFINITIONS: THE DEFINITIONS BELOW WILL BE APPLIED TO EACH OF THE SYMPTOMS LISTED ON THIS FORM**

RARELY: *Almost never, not very often, hardly ever, or infrequently.*
SOMETIMES: *Occasionally, from time to time, or every now and again.*
OFTEN: *Repeatedly, over and over again, regularly, or a lot.*

****TIME PERIOD DEFINITIONS:**
BASELINE:

- If the subject required drug wash-out, then the timeframe is the time between the end of washout and the day of the interview. The interview MUST be completed prior to study drug initiation.
- If the subject did not require drug wash-out, then the timeframe is the 2 weeks prior to the day of the interview. The interview MUST be completed prior to study drug initiation.

STUDY VISIT 1: This includes the 6 months between randomization and the day of the 6-month study visit.

STUDY VISIT 2: This includes the 6 months between Study Visit 1 and the day of the 12-month study visit.

STUDY VISIT 3: This includes the 12 months between Study Visit 2 and the day of the 24-month study visit.

STUDY VISIT 4: This includes the 12 months between Study Visit 3 and the day of the 36-month study visit.

QUARTERLY FOLLOW-UP CALL: This includes each 3-month interval between Study Visits once a subject reaches the Study Drug Maintenance Phase.

PRE-INTERVIEW SCRIPT:
"During this interview I am going to ask about certain medical symptoms. I am going to ask you how often [YOU/SUBJECT] have/has experienced any of the following symptoms in the last [TIME PERIOD**] and if yes, how much it bothered [YOU/YOUR CHILD]."*

Section A: KEY IDENTIFYING INFORMATION

A1. Study Identification Number ___ ___ - ___ ___ ___ ___ ___ ___ - ___

A2. Study visit

BASELINE 0
STUDY VISIT 1 (Month 6) ..... 1 **(A3)**
STUDY VISIT 2 (Month 12)..... 2 **(A3)**
STUDY VISIT 3 (Month 24)..... 3 **(A3)**
STUDY VISIT 4 (Month 36)..... 4 **(A3)**
QUARTERLY FOLLOW-UP CALL ..... 7 **(A3)**
CALL FROM SUBJECT/FAMILY ..... 8 **(A3)**

a. What number screening is this? ___

A3. Date of form completion **(Date of phone call or interview)** ___ ___ / ___ ___ / ___ ___ ___ ___
M M D D Y Y Y Y

A4. Name of person completing form _____ ___ ___ ___
PRINT FULL NAME INITIALS

A5. Source of information

SUBJECT 1
CAREGIVER..... 2

Section B: SYMPTOM QUESTIONNAIRE

How often have/has [YOU/SUBJECT] had any feelings of dizziness with standing in the last [TIME PERIOD]? Dizziness is a feeling of instability, unsteadiness, lightheadedness, falling, or feeling like you are "about to fall" when moving from a lying or sitting position to a standing position.

IF DIZZINESS UPON STANDING IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF DIZZINESS UPON STANDING IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B. ASSESS WHETHER OR NOT THE SUBJECT HAD AN INTERCURRENT ILLNESS SUCH AS GASTROENTERITIS OR IF S/HE WAS EXPOSED TO AN UNUSUAL ENVIRONMENT SUCH AS EXTREME HEAT.

B1. Dizziness upon standing (Constitutional, other)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B2)**	
RARELY..... 1	TRANSIENT (LASTS < 5 SECONDS).. 1
SOMETIMES..... 2 →	INTERFERING WITH FUNCTION ONLY..... 2
OFTEN..... 3	INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

c. Is there an intercurrent illness or other cause for this symptom? YES .....1 NO.....2 **(B2)**

1. Specify _____

How often have/has [YOU/SUBJECT] had any feelings of dizziness in the last [TIME PERIOD]? Dizziness is the sensation of instability. It is a fairly non-specific term and can also be characterized as feeling "unsteady", lack of balance, and/or lightheadedness. [YOU/SUBJECT] may feel that you/s/he is "about to fall". {In younger subjects, the caregivers may note lack of balance when the subject is walking and/or falling down more often than usual.}

IF NO DIZZINESS IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF DIZZINESS IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B. ASSESS WHETHER OR NOT THE SUBJECT HAD AN INTERCURRENT ILLNESS SUCH AS GASTROENTERITIS OR IF S/HE WAS EXPOSED TO AN UNUSUAL ENVIRONMENT SUCH AS EXTREME HEAT.

B2. Dizziness – Other, not otherwise specified (General dizziness)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B3)**	
RARELY..... 1	WITH HEAD MOVEMENTS OR NYSTAGMUS ONLY 1
SOMETIMES..... 2 →	INTERFERING WITH FUNCTION ONLY..... 2
OFTEN..... 3	INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

c. Is there an intercurrent illness or other cause for this symptom? YES .....1 NO.....2 **(B3)**

1. Specify _____

How often have/has [YOU/SUBJECT] had any feelings of fainting (also called syncope) in the last [TIME PERIOD]? Syncope is a brief loss of consciousness because there is not enough blood flow to the brain. Sometimes people may feel lightheaded and then may slump to the side if sitting or drop to the floor. Some people call this "passing out" or "blacking out". FAINTING MUST BE DISTINGUISHED FROM MERELY "FALLING ASLEEP". **PLEASE MAKE EVERY EFFORT TO VERIFY LOSS OF CONSCIOUSNESS; THIS CAN BE DIFFICULT IF THE EVENT IS NOT WITNESSED. IN THESE CASES, THE SUBJECT MAY SAY THAT S/HE "FOUND MYSELF ON THE FLOOR", ETC.**

IF NO FAINTING IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF FAINTING IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B. ASSESS WHETHER OR NOT THE SUBJECT HAD AN INTERCURRENT ILLNESS SUCH AS GASTROENTERITIS OR IF S/HE WAS EXPOSED TO AN UNUSUAL ENVIRONMENT SUCH AS EXTREME HEAT UNUSUAL, PROLONGED STANDING, OR PAINFUL STIMULI.

B3. Fainting with loss of consciousness (Syncope)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B4)**	
RARELY..... 1	~~..... 1~~
SOMETIMES..... 2 →	~~..... 2~~
OFTEN..... 3	PRESENT..... 3
	LIFE-THREATENING CONSEQUENCES 4

c. Is there an intercurrent illness or other cause for this symptom? YES .....1 NO.....2 **(B4)**

1. Specify _____

How often have/has [YOU/SUBJECT] had any shortness of breath or difficulty breathing with [YOUR/HIS/HER] usual activities in the last [TIME PERIOD]?

IF NO SHORTNESS OF BREATH IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF SHORTNESS OF BREATH IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B. ASSESS WHETHER OR NOT THE SUBJECT HAD AN INTERCURRENT ILLNESS SUCH AS A RESPIRATORY INFECTION (e.g., BRONCHITIS; PNEUMONIA).

B4. Shortness of breath (Dyspnea)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL.....0 **(B5)**	
RARELY ..... 1 →	ON EXERTION, BUT CAN WALK 1 FLIGHT OF STAIRS WITHOUT STOPPING or {SHORTNESS OF BREATH, DIFFICULTY BREATHING OR CATCHING BREATH BUT NOT AFFECTING ABILITY TO FEED}..... 1
SOMETIMES..... 2 →	UNABLE TO WALK 1 FLIGHT OF STAIRS OR 1 CITY BLOCK WITHOUT STOPPING or {SHORTNESS OF BREATH, DIFFICULTY BREATHING OR CATCHING BREATH AFFECTING ABILITY TO FEED (TAKING LONGER TO FEED THAN EXPECTED, EATING LESS)}..... 2
OFTEN 3	WITH ACTIVITIES OF DAILY LIVING or {ACTIVITIES OF DAILY LIVING (AFFECTING ABILITY TO PLAY)}..... 3
	AT REST, INTUBATION/VENTILATOR INDICATED 4

c. Is there an intercurrent illness or other cause for this symptom? YES .....1 NO.....2 **(B5)**

1. Specify _____

How often have/has [YOU/SUBJECT] had any wheezing in the last [TIME PERIOD]? Wheezing is the high-pitched whistling sound of air moving through narrowed airways. Wheezing is most obvious when exhaling or breathing out, but may also be present when inhaling or breathing in. Wheezing often occurs in people who have asthma.

IF WHEEZING IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF WHEEZING IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B5. Wheezing (Bronchospasm)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL ..... 0 **(See below)**	
RARELY.....1	ASYMPTOMATIC 1
SOMETIMES .....2 →	SYMPTOMATIC, NOT INTERFERING WITH FUNCTION 2
OFTEN.....3	INTERFERING WITH FUNCTION 3
	LIFE THREATENING..... 4

If you are completing this form for a scheduled study visit, continue with question B6. Otherwise, if you are completing this form for a quarterly phone call or call from the subject or family, please SKIP questions B6-B26 and GO TO question B27 if the subject or family has/have "other" symptoms to report.

How often have/has [YOU/SUBJECT] had any heart palpitations in the last [TIME PERIOD]? Palpitations are the feeling of a rapidly or irregularly beating heart when at rest. A feeling of a rapidly beating heart is normal with exercise, but an irregular heart beat would be the feeling that your heart is beating faster than usual with exercise.

IF PALPITATIONS ARE NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF PALPITATIONS ARE REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B6. Palpitations (Cardiac arrhythmia)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL.....0 **(B7)**	
RARELY 1	PRESENT..... 1
SOMETIMES..... 2 →	PRESENT WITH ASSOCIATED SYMPTOMS 2
OFTEN 3	~~.....3~~
	~~..... 4~~

How often have/has [YOU/SUBJECT] had headache pain in the last [TIME PERIOD]? Headache is a term used to describe aching or pain that occurs in one or more areas of the head, face, or neck that is unrelated to trauma. {In younger subjects, the caregivers may note [SUBJECT] holding [HIS/HER] head as if in pain.}

IF HEADACHE IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF HEADACHE IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B7. Headache (Pain – Neurology – Head/Headache)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL.....0 **(B8)**	
RARELY 1	MILD PAIN, NOT INTERFERING WITH FUNCTION 1
SOMETIMES ..... 2 →	MODERATE PAIN, INTERFERING WITH FUNCTION ONLY..... 2
OFTEN 3	SEVERE PAIN, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

How often have/has [YOU/SUBJECT] had nasal congestion in the last [TIME PERIOD]? Nasal congestion is also known as nasal blockage, nasal obstruction, and stuffy nose. This can be caused by a viral infection, allergies, enlarged adenoids, or foreign bodies. A head cold is characterized by nasal congestion that is associated with sneezing, Rhinorrhea (runny nose), sore throat, and/or headache.

IF NASAL CONGESTION IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF NASAL CONGESTION IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B8. Nasal congestion, head cold (Upper Respiratory – Other)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B9)**	
RARELY 1	MILD 1
SOMETIMES ..... 2 →	MODERATE 2
OFTEN 3	SEVERE 3
	LIFE THREATENING, DISABLING ... 4

How often have/has [YOU/SUBJECT] had a cough that was not related to a cold or head cold in the last [TIME PERIOD]?

IF NO COUGH IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF COUGH IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B9. Cough

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B10)**	
RARELY..... 1	SYMPTOMATIC, NON-NARCOTIC MEDICATION ONLY INDICATED.....1
SOMETIMES..... 2 →	SYMPTOMATIC AND NARCOTIC MEDICATION INDICATED 2
OFTEN..... 3	SIGNIFICANTLY INTERFERING WITH SLEEP OR ACTIVITIES OF DAILY LIVING.....3
	~~.....4~~

How often have/has [YOU/SUBJECT] had chest pain in the last [TIME PERIOD]? Chest pain is discomfort or pain that is felt anywhere along the front of your body between the neck and bottom of the ribcage. {In younger subjects, the caregivers may note [SUBJECT] holding [HIS/HER] head as if in pain.}

IF NO CHEST PAIN IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF CHEST PAIN IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B10. Chest pain (Pain – Chest/Heart)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B11)**	
RARELY..... 1	MILD PAIN, NOT INTERFERING WITH FUNCTION 1
SOMETIMES..... 2 →	MODERATE PAIN, INTERFERING WITH FUNCTION ONLY..... 2
OFTEN..... 3	SEVERE PAIN, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

How often have/has [YOU/SUBJECT] experienced any changes in how food tastes in the last [TIME PERIOD]? Change in how food tastes is a change in the sense of taste (dysgeusia). Some foods may taste different than they used to, foods may not have much taste at all, or everything may taste the same. Do not include any changes in taste that happened when you had a cold or head cold. {In younger subjects, the caregivers may note [SUBJECT] losing interest in food they typically enjoy.}

IF NO CHANGE IN TASTE IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF CHANGE IN TASTE IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B11. Change in how food tastes (Taste Alteration – Dysgeusia)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B12)**	
RARELY 1	ALTERED TASTE BUT NO CHANGE IN DIET 1
SOMETIMES ..... 2 →	ALTERED TASTE WITH CHANGE IN DIET 2
OFTEN 3	~~..... 3~~
	~~..... 4~~

*How often have/has [YOU/SUBJECT] had any stomach pain or indigestion in the last [TIME PERIOD]? Stomach **pain** is **pain** that is felt in the abdominal (tummy) area (the area between your chest and groin). Indigestion is a vague feeling of stomach discomfort.*

IF NO STOMACH PAIN IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF STOMACH PAIN IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B12. Stomach pain or indigestion (Pain – Abdomen, NOS)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B13)**	
RARELY 1	MILD PAIN, NOT INTERFERING WITH FUNCTION 1
SOMETIMES ..... 2 →	MODERATE PAIN, INTERFERING WITH FUNCTION ONLY..... 2
OFTEN 3	SEVERE PAIN, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

How often have/has [YOU/SUBJECT] had any feelings of nausea in the last [TIME PERIOD]? Nausea is a feeling of unease and discomfort in the stomach with an urge to vomit.

IF NO NAUSEA IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF NAUSEA IS REPORTED, ask *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B13. Nausea

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL.....0 **(B14)**	
RARELY 1	LOSS OF APPETITE WITHOUT ALTERATION IN EATING HABITS 1
SOMETIMES 2	ORAL INTAKE DECREASED WITHOUT SIGNIFICANT WEIGHT LOSS 2
OFTEN 3	INADEQUATE ORAL CALORIC OR FLUID INTAKE, IV FLUIDS, TUBE FEEDING, TPN INDICATED ≥24 hrs 3
	LIFE-THREATENING CONSEQUENCES 4

How often have/has [YOU/SUBJECT] vomited in the last [TIME PERIOD]? Vomiting is the release of stomach contents through the mouth.

IF VOMITING IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF VOMITING IS REPORTED, ask *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B14. Vomiting

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B15)**	
RARELY 1	1 EPISODE/24 hrs 1
SOMETIMES 2	2-5 EPISODES/24 hrs, IV FLUIDS INDICATED <24 hrs..... 2
OFTEN 3	≥6 EPISODES/24 hrs, IV FLUIDS/TPN INDICATED ≥24 hrs..... 3
	LIFE-THREATENING CONSEQUENCES 4

How often have/has [YOU/SUBJECT] had diarrhea in the last [TIME PERIOD]? Diarrhea is defined by increased stool frequency and loose, watery bowel movements.

IF NO DIARRHEA IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF DIARRHEA IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B15. Diarrhea

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B16)**	
RARELY 1	INCREASE OF <4 STOOLS/DAY OVER BASELINE 1
SOMETIMES..... 2 →	INCREASE OF 4-6 STOOLS/DAY OVER BASELINE 2
OFTEN 3	INCREASE OF ≥7 STOOLS/DAY OVER BASELINE, INTERFERING WITH ACTIVITIES OF DAILY LIVING3
	LIFE THREATENING CONSEQUENCES 4

How often have/has [YOU/SUBJECT] had constipation in the last [TIME PERIOD]? Constipation is a condition in which stool becomes hard, dry, and difficult to pass, and bowel movements don't happen very often. Other symptoms may include painful bowel movements, and feeling bloated, uncomfortable, and sluggish.

IF NO CONSTIPATION IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF CONSTIPATION IS REPORTED, ask *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B16. Constipation

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B17)**	
RARELY 1	OCCASIONAL OR INTERMITTENT SYMPTOMS 1
SOMETIMES..... 2 →	PERSISTENT SYMPTOMS, REGULAR USE OF LAXATIVES 2
OFTEN 3	INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	LIFE THREATENING CONSEQUENCES 4

How often have/has [YOU/SUBJECT] noticed that [YOUR/THEIR] hands or feet becoming cold and turning blue or white in the last [TIME PERIOD]? This is also known as Raynaud's phenomena. This means that when hands and/or feet are exposed to cold, or other stimuli, the small blood vessels get smaller and close off, and this leads to pain and color changes in the skin.

IF RAYNAUD'S IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF RAYNAUD'S IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B17. Hands or feet becoming cold and turning blue or white (Vascular, Other – specify)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B18)**	
RARELY 1	MILD, NOT INTERFERING WITH FUNCTION 1
SOMETIMES..... 2 →	MODERATE, INTERFERING WITH FUNCTION ONLY..... 2
OFTEN 3	SEVERE, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	LIFE THREATENING, DISABLING ... 4

How often have/has [YOU/SUBJECT] had any muscle cramps or muscle pain or aches in the last [TIME PERIOD]? Muscle cramps are involuntary, painful shortening of muscles.

IF NO MUSCLE PAIN IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF MUSCLE PAIN IS REPORTED, ask *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B18. Muscle pain or cramps (Pain – Muscle or Cramps)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B19)**	
RARELY 1	MILD PAIN, NOT INTERFERING WITH FUNCTION 1
SOMETIMES..... 2 →	MODERATE PAIN, INTERFERING WITH FUNCTION ONLY..... 2
OFTEN 3	SEVERE PAIN, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

How often have/has [YOU/SUBJECT] had back pain in the last [TIME PERIOD]?

IF NO BACK PAIN IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF BACK PAIN IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B19. Back pain (Pain – Back)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B20)**	
RARELY 1	MILD PAIN, NOT INTERFERING WITH FUNCTION 1
SOMETIMES..... 2 →	MODERATE PAIN, INTERFERING WITH FUNCTION ONLY..... 2
OFTEN 3	SEVERE PAIN, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

How often have/has [YOU/SUBJECT] had swelling or puffiness around the eyes in the last [TIME PERIOD]? This swelling may be caused by excess fluid accumulation around the eyes that can cause the eyelids to be swollen shut.

IF SWELLING AROUND THE EYES REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF SWELLING AROUND THE EYES IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B20. Swelling around the eyes (Edema: Head/Neck)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B21)**	
RARELY 1	LOCALIZED TO DEPENDENT AREAS, NO IMPAIRMENT 1
SOMETIMES..... 2 →	LOCALIZED FACIAL OR NECK EDEMA WITH FUNCTIONAL IMPAIRMENT 2
OFTEN 3	GENERALIZED FACIAL OR NECK EDEMA WITH FUNCTIONAL IMPAIRMENT 3
	SEVERE WITH ULCERATION OR CEREBRAL EDEMA, TRACHEOTOMY OR FEEDING TUBE INDICATED 4

How often have/has [YOU/SUBJECT] had swelling of the feet in the last [TIME PERIOD]? This is excess fluid usually around the feet and ankles unrelated to trauma.

IF NO SWELLING OF THE FEET IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF SWELLING OF THE FEET IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B21. Swelling of the feet (Edema: Limb)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B22)**	
RARELY..... 1	5-10% INTER-LIMB DISCREPANCY IN VOLUME OR CIRCUMFERENCE, PITTING EDEMA..... 1
SOMETIMES..... 2	>10-30% INTER-LIMB DISCREPANCY IN VOLUME OR CIRCUMFERENCE, OBLITERATION OF SKIN FOLDS.... 2
OFTEN..... 3	>30% INTER-LIMB DISCREPANCY IN VOLUME, LYMPHORRHEA, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	PROGRESSION TO MALIGNANCY, AMPUTATION INDICATED, DISABLING..... 4

How often have/has [YOU/SUBJECT] had any changes in [YOUR/HIS/HER] mood in the last [TIME PERIOD]? A mood swing is an change of the emotional state and is often associated with frequent changes in mood.

IF MOOD CHANGES ARE NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF MOOD CHANGES ARE REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B22. Mood changes (Mood Alteration – **Specify**)

c. Specify (using CTCAE short name)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B23)**	
RARELY..... 1	MILD MOOD ALTERATION NOT INTERFERING WITH FUNCTION 1
SOMETIMES..... 2	MODERATE MOOD ALTERATION INTERFERING WITH FUNCTION, NOT ACTIVITIES OF DAILY LIVING..... 2
OFTEN..... 3	SEVERE MOOD ALTERATION INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	SUICIDAL IDEATION, DANGER TO SELF OR OTHERS..... 4

How often have/has [YOU/SUBJECT] had any changes in [YOUR/HIS/HER] behavior in the last [TIME PERIOD]? This describes a change in the way a [YOU/HE/SHE] functions or operates and includes altered responses to external stimuli.

IF BEHAVIOR CHANGES ARE NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF BEHAVIOR CHANGES ARE REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B23. Behavior changes (Personality/Behavioral)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B24)**	
RARELY..... 1 →	CHANGE, BUT NOT ADVERSELY AFFECTING SUBJECT OR FAMILY 1
SOMETIMES..... 2 →	CHANGE, ADVERSELY AFFECTING SUBJECT OR FAMILY 2
OFTEN..... 3	MENTAL HEALTH INTERVENTION INDICATED 3
	CHANGE HARMFUL TO OTHER OR SELF, HOSPITALIZATION INDICATED 4

How often have/has [YOU/SUBJECT] had trouble sleeping in the last [TIME PERIOD]? Trouble sleeping is the opinion or complaint of inadequate or poor-quality sleep because of one or more of the following: difficulty falling asleep; waking up frequently during the night with difficulty returning to sleep; waking up too early in the morning; or unrefreshing sleep.

IF TROUBLE SLEEPING IS NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF TROUBLE SLEEPING IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B24. Trouble sleeping (Insomnia)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B25)**	
RARELY..... 1	OCCASIONAL DIFFICULTY WITH SLEEPING..... 1
SOMETIMES..... 2 →	DIFFICULTY SLEEPING, INTERFERING WITH FUNCTION BUT NOT ACTIVITIES OF DAILY LIVING 2
OFTEN..... 3	FREQUENT DIFFICULTY SLEEPING, INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

How often have/has [YOU/SUBJECT] had nightmares in the last [TIME PERIOD]? A nightmare is a dream occurring during rapid eye movement sleep that arouses feelings of intense, unavoidable fear, terror, distress, or extreme anxiety that usually wakes up people in the middle of the night.

IF NIGHTMARES ARE NOT REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF NIGHTMARES ARE REPORTED, ask *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B.

B25. Nightmares (Constitutional Symptoms – Other)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B26)**	
RARELY..... 1	MILD.....1
SOMETIMES..... 2 →	MODERATE 2
OFTEN..... 3	SEVERE 3
	LIFE THREATENING, DISABLING....4

How often have/has [YOU/SUBJECT] had any feelings of tiredness in the last [TIME PERIOD]? This is a feeling of fatigue or lack of stamina.

IF NO TIREDNESS IS REPORTED, CIRCLE '0' (NONE/NOT AT ALL) THEN MOVE TO THE NEXT QUESTION. IF TIREDNESS IS REPORTED, ASK *How much does it bother [YOU/SUBJECT]?* FULLY READ ALL OPTIONS IN COLUMN B. ASSESS WHETHER OR NOT THE SUBJECT HAD AN INTERCURRENT ILLNESS SUCH AS A RESPIRATORY INFECTION.

B26. Tiredness or lack of energy (Fatigue)

a. How often have you had …?	**b. How much does it bother you?**
NONE/NOT AT ALL..... 0 **(B27)**	
RARELY..... 1	MILD FATIGUE OVER BASELINE ... 1
SOMETIMES..... 2 →	MODERATE OR CAUSING DIFFICULTY PERFORMING SOME ACTIVITIES OF DAILY LIVING..... 2
OFTEN..... 3	SEVERE FATIGUE INTERFERING WITH ACTIVITIES OF DAILY LIVING..... 3
	DISABLING..... 4

POST-INTERVIEW SCRIPT:

"During this interview I asked about specific medical symptoms. Have you experienced any other symptoms during this [TIME PERIOD] that we have not talked about?

- **IF "OTHER" SYMPTOMS NEED TO BE REPORTED BY THE SUBJECT, THE STUDY COORDINATOR SHOULD REFER TO CTCAE CODE LIST P OR THE CTCAE BOOKLET TO DETERMINE THE PREFERRED SHORT NAME OF THE SYMPTOM AND THE SEVERITY.**
- **IF ADDITIONAL SYMPTOMS DO <u>NOT</u> NEED TO BE REPORTED, THE COORDINATOR SHOULD END THE INTERVIEW:** *Thank your for answering these questions!*

Report all other symptoms. Photocopy and attach this page and/or subsequent pages to document more than 5 "other" symptoms.

B27. How many other symptoms does the patient report? (0-10)

____ **(if 0, skip to Z1)**

OTHER SYMPTOM #1

a. Other symptom name
(specify using CTCAE short name) _____

b. Other symptom code (CTCAE MedDRAcode) ___ ___ ___ ___ ___ ___ ___ ___

c. How often have you had …?	**d. How much does it bother you?**
NONE/NOT AT ALL.....0 **(Z1)**	
RARELY 1	GRADE 1 1
SOMETIMES ..... 2 →	GRADE 2 2
OFTEN 3	GRADE 3 3
	GRADE 4 4

B28. **OTHER SYMPTOM #2**

a. Other symptom name
(specify using CTCAE short name) _____

b. Other symptom code (CTCAE MedDRAcode) ___ ___ ___ ___ ___ ___ ___ ___

c. How often have you had …?	**d. How much does it bother you?**
NONE/NOT AT ALL.....0 **(Z1)**	
RARELY 1	GRADE 1 1
SOMETIMES ..... 2 →	GRADE 2 2
OFTEN 3	GRADE 3 3
	GRADE 4 4

B29. **OTHER SYMPTOM #3**

a. Other symptom name
(specify using CTCAE short name) _____

b. Other symptom code (CTCAE MedDRAcode) ___ ___ ___ ___ ___ ___ ___ ___

c. How often have you had …?	**d. How much does it bother you?**
NONE/NOT AT ALL.....0 **(Z1)**	
RARELY 1	GRADE 1 1
SOMETIMES ..... 2 →	GRADE 2 2
OFTEN 3	GRADE 3 3

	GRADE 4 4

B30. **OTHER SYMPTOM #4**

a. Other symptom name
(specify using CTCAE short name) _____

b. Other symptom code (CTCAE MedDRAcode) ___ ___ ___ ___ ___ ___ ___ ___

c. How often have you had …?	**d. How much does it bother you?**
NONE/NOT AT ALL.....0 **(Z1)**	
RARELY ..... 1 } →	GRADE 1 1
SOMETIMES ..... 2 } →	GRADE 2 2
OFTEN ..... 3 } →	GRADE 3 3
	GRADE 4 4

B31. **OTHER SYMPTOM #5**

a. Other symptom name
(specify using CTCAE short name) _____

b. Other symptom code (CTCAE MedDRAcode) ___ ___ ___ ___ ___ ___ ___ ___

c. How often have you had …?	**d. How much does it bother you?**
NONE/NOT AT ALL.....0 **(Z1)**	
RARELY ..... 1 } →	GRADE 1 1
SOMETIMES ..... 2 } →	GRADE 2 2
OFTEN ..... 3 } →	GRADE 3 3
	GRADE 4 4

Section Z: TIME TO COMPLETE FORM AND SIGNATURE

Z1. How long did it take to complete this form? ___ ___ ___ minutes

Signature of PI: _____ Date: _____

END OF FORM