**Section 1: “Neuroendocrine” Symptoms (based on Canadian Criteria; see instructions)**

[The following instruction should be placed before the following questions, whether individually or as a group.]

“Please mark if, during the course of the illness, the participant has experienced the following symptom(s) *to a significant degree*. (Do not mark yes if there has not been a significant increase in the symptom when comparing symptoms during the illness with symptoms before the illness. Also, do not mark yes if the symptom appears to be better explained by something that is unrelated to the illness, eg., notable weight loss due to intentional weight loss efforts):”

1. Subnormal body temperature (see instructions\*) Yes No \*Data looking at body temperature vary substantially in terms of conclusions regarding average body temperatures or what constitutes normal versus abnormal temperatures. It is suggested that it would be reasonable to mark “yes” if a participant tends, on measurements on different occasions, to exhibit oral temperatures less than 97.0 F (36.1 C). It is recommended that participants avoid drinking or eating hot or cold foods or fluids for at least fifteen minutes prior to temperature measurement.
2. Marked diurnal fluctuations: measured temperatures vary significantly through the day (see instructions\*)? Yes No \*Note: The evidence for this appears to be very limited and is not sufficient to support a definition of what constitutes marked diurnal variation. Further research is needed to validate this symptom and the appropriate threshold.
3. Alternating feelings of hot and cold (or, one part of the body feels hot while another feels cold)? Yes No

* If yes, indicate severity: Mild Moderate Severe;
* If yes, indicate frequency: Daily Monthly Occasionally

1. Recurrent feelings of feverishness? Yes No
2. Cold limbs (arms/legs/hands/feet)? Yes No
3. Abnormal sweating episodes? Yes No

* If yes, indicate severity: Mild Moderate Severe;
* If yes, indicate frequency: Daily Weekly Monthly Occasionally

1. Significant intolerance of heat? Yes No

* If yes, indicate severity: Mild Moderate Severe;

1. Significant intolerance of cold? Yes No

* If yes, indicate severity: Mild Moderate Severe;

1. Marked weight increase or loss? Yes No

* If weight gain, indicate how much weight gain \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_kg Over what time period? \_\_\_\_\_\_\_\_\_[length of time]
* If weight loss, indicate how much weight loss \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_kg Over what time period? \_\_\_\_\_\_\_\_\_[length of time]

Note: Weight gain or loss of less than 10% of body weight might not be considered “marked” unless it were over a short time period or otherwise unusual and apparently related to the illness. Question may be answered 'no' if a significant weight change appears usual, not associated with the illness.

1. Significant loss of appetite? Yes No [do not mark yes if loss of appetite seems to be due primarily to a gastrointestinal issue – ie, significant, ongoing nausea]

* If yes, indicate severity: Mild Moderate Severe;

1. Significant gain of appetite? Yes No

* If yes, indicate severity: Mild Moderate Severe;

1. Symptoms of illness worsen with stress? Yes No

**Section 2: Symptoms**

**In the past 6 months, has the participant experienced the following:**

| Symptom |  |
| --- | --- |
| * 1. Decreased appetite | Absent/minimal  Mild  Moderate  Severe |
| * 1. Increased appetite | Absent/minimal  Mild  Moderate  Severe |
| * 1. Abnormal/unintentional weight gain | Absent/minimal  Mild  Moderate  Severe |
| * 1. Weight gain, in the last 6 months (kgs) | Data to be filled out by site |
| * 1. Abnormal/unintentional weight loss | Absent/minimal  Mild  Moderate  Severe |
| * 1. Weight loss, in the last 6 months (kgs) | Data to be filled out by site |
| * 1. Decreased thirst | Absent/minimal  Mild  Moderate  Severe |
| * 1. Increased thirst | Absent/minimal  Mild  Moderate  Severe |
| * 1. Decreased urination | Absent/minimal  Mild  Moderate  Severe |
| * 1. Increased urination | Absent/minimal  Mild  Moderate  Severe |
| * 1. Are you intolerant of cold temperatures | Absent/insignificant  Mild  Moderate  Severe |
| * 1. Are you intolerant of hot temperatures | Absent/insignificant  Mild  Moderate  Severe |
| 1. Do your limbs (arms/legs/hands/feet) feel unusually cold | Absent/insignificant  Mild  Moderate  Severe |
| 1. Do your limbs (arms/legs/hands/feet) feel unusually hot | Absent/insignificant  Mild  Moderate  Severe |
| 1. Night sweats | Absent/minimal  Mild  Moderate  Severe |
| 1. Excessive daytime sweating | Absent/minimal  Mild  Moderate  Severe |
| 1. Unusual decrease in sweating or inability to sweat | Yes  No |
| 1. Hot flashes | Absent/minimal  Mild  Moderate  Severe |
| 1. Decreased sexual interest | Absent/insignificant  Mild  Moderate  Severe |
| 1. Hair thinning (excludes male-pattern baldness in males) | Absent/minimal  Mild  Moderate  Severe |

## GENERAL INSTRUCTIONS

This CRF contains data on neuroendocrine/hypothalamic symptoms that would be collected for an ME/CFS study. The term “neuroendocrine symptoms” was used in the 2003 Canadian guidelines for the diagnosis of ME/CFS. However, not all of these symptoms may be substantially mediated through endocrine pathways (eg, excessive sweating(1)).

Questions in the first section of this module reflect the symptoms listed as neuroendocrine in the Canadian Consensus Criteria (CCC) and may be used as a group in determining whether a participant meets the neuroendocrine criterion in the CCC. They may also be used as standalone questions in studies focused on further characterizing manifestations or patterns of illness. The instructions contained in quotation marks should be placed before these questions, whether individually or as a set. **NOTE:** *These questions are designed to associate symptoms with illness (eg, in the process of determining whether a patient meets criteria or in characterizing the pattern of illness experienced). Thus, the questions in Section A of the CRF should not be used to assess change in neuroendocrine symptoms as a result of exercise challenges or treatment trials and also should not be used to compare ME/CFS participants with other conditions or healthy control groups.*

Questions in the second section of this module may be selected as part of a review of systems and may be used for comparison between ME/CFS participants and other populations.

Important note: None of the data elements included on this CRF Module are considered Core (i.e., required for all ME/CFS studies to collect). All data elements are considered supplemental (i.e., non Core) and should only be collected if the research team considers them appropriate for their study.

## REFERENCES

Carruthers BM et al. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols. A Consensus Document. Journal of Chronic Fatigue Syndrome. 2003;11(1):7-115.

Hamilos DL, Nutter D, Gershtenson J, Redmond DP, Clementi JD, Schmaling KB, Make BJ, Jones JF. Core body temperature is normal in chronic fatigue syndrome. Biol Psychiatry. 1998; 43(4):293-302.