**Supplemental Digital Content 2.** Solicited systemic reactions: terminology, definitions, and intensity scales

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| **CRF term (MedDRA LLT)** | **Fever** | **Headache** | **Malaise** | **Myalgia** |
| **Diary card term** | Temperature | Headache | Feeling unwell | Muscle aches and pains |
| **Definition** | Elevation of temperature to ≥ 100.4°F (≥ 38.0°C) | Pain or discomfort in the head or scalp. Does not include migraine. | General ill feeling.  Malaise is a generalized feeling of discomfort, illness, or lack of well-being that can be associated with a disease state. It can be accompanied by a sensation of exhaustion or inadequate energy to accomplish usual activities. | Muscle aches and pains are common and can involve more than one muscle at the same time. Muscle pain can also involve the soft tissues that surround muscles. These structures, which are often referred to as connective tissues, include ligaments, tendons, and fascia (thick bands of tendons).  Does not apply to muscle pain at the injection site which should be reported as injection site pain. |
| **Intensity scale\*** | Grade 1: ≥ 100.4°F to ≤ 101.1°F or ≥ 38.0°C to ≤ 38.4°C | Grade 1: No interference with activity | Grade 1: No interference with activity | Grade 1: No interference with activity |
|  | Grade 2: ≥ 101.2°F to ≤ 102.0°F or ≥ 38.5°C to ≤ 38.9°C | Grade 2: Some interference with activity | Grade 2: Some interference with activity | Grade 2: Some interference with activity |
|  | Grade 3: ≥ 102.1°F or ≥ 39.0°C | Grade 3: Significant; prevents daily activity | Grade 3: Significant; prevents daily activity | Grade 3: Significant; prevents daily activity |

\*For all reactions but fever, subjects or parents / guardians will record the intensity level (Grade 1, 2, or 3) in the diary card. For fever, they will record the body temperature, and the classification as Grade 1, 2, or 3 will be assigned at the time of the statistical analysis