

## **INSTRUCTIONS FOR COMPLETING THE SAFTEE**

The SAFTEE is designed to collect information on adverse health events occurring during a specified time period of a clinical trial. The purpose of the SAFTEE technique, is to report adverse health events regardless of whether they are suspected to be drug related or not in order to reduce the under-reporting of unanticipated events compared to “known or expected” events.

SAFTEE General Inquiry (GI) is made up of three queries concerned with general health status.

### **Preferred Events Terms:**

SAFTEE uses a list of some 76 preferred-event terms. Raters are asked to use these terms preferentially to record the reported event rather than their own terms or the patient’s words to avoid variability. Alternate terms should be used only when a specific protocol requires it and should be standard across all the sites using the same protocol. For events marked by an asterisk, additional specifications are needed.

### **ALPHABETICAL LIST OF PREFERRED TERMS**

Abdominal pain	Dystonia* (specify where)	Muscle/bone/joint pain*
Accidental injury*	Ear ache	Nasal congestion
Akathisia	Early morning awakening	Nausea
Akinesia	Edema* (specify where)	Over-arousal*
Anxiety/nervousness	Eye irritation	Painful urination
Appetite decrease	Fever	Perceptual problems
Appetite increase	Flatulence	Poor hearing
Attempted suicide	Genital discomfort*	Premenstrual tension
Blurred vision	Gum problems*	Rapid heartbeat
Breast pain/swelling	Hair problems*	Rash/Skin irritation*
Changes in color (urine)	Headache*	Rigidity (muscle)
Chest pain	Hypersalivation	Sexual Dysfunction
Concentration difficulty	Increased frequency (urination)	Shortness of breath
Confusion	Increased libido	Sore throat
Constipation	Increased thirst	Sore tongue*
Coughing	Insomnia	Stomach/abdominal discomfort
Cramps	Headache	Stool discoloration
Decreased libido	Intercurrent illness*	Somnolence
Dental problems*	Interrupted sleep	Taste abnormality*
Depression	Irregular heartbeat	Tinnitus
Diarrhea	Irritability	Tiredness/fatigue
Difficulty falling asleep	Itching (specify where)	Tremor
Difficulty swallowing	Loss of consciousness*	Vomiting
Difficulty urinating	Medical or surgical procedure*	Weight gain
Discharge (nipples)	Memory problem	Weight loss
Dizziness/faintness	Missed menses/Menstrual	Wheezing
Drowsiness	Irregularity*	
Dry mouth	Mouth Ulcer	
Dyskinesia* (specify where)		

### **Examination Procedures:**

In administering the GI form, the examiner should ask each query of the patient allowing sufficient time for a response. When the patient responds positively when asked, the examiner should record necessary information about that event.

Throughout the examination, the examiner should ask the patient only about events occurring in the previous assessment interval (since last visit). The examiner should repeat the phrase reminding the patient of the interval each time to focus the patient on the appropriate time period.

For the initial visit, the assessment interval is 90 days prior the visit to cover the period of form 90.

### **Completion of the Recording Form:**

If an event is elicited with the first 3 open questions, and again under the list of symptoms, it should not be recorded twice, this should be indicated by checking the box labeled "PREV REC" on the second page.

SAFTEE provides for the recording of the following items of information on every elicited event.

- **Date of onset** should be used to record the month and day that the event first occurred since the last assessment. For the initial assessment the rater should record any event within 90 days prior the visit.
- **Duration** of any event is recorded in days. Events that last less than one day should be recorded as one day (e.g. an event that lasts 15 minutes in one occasion should be recorded as 1 day; an event that lasts 15 minutes in 3 different days should be recorded as 3 days.) The duration should not be greater than the interval between the assessments. For the first assessment the duration should not be greater than 90 days.
- **Pattern** is used to indicate whether the event occurred continuously, intermittently, or isolated.
- **Current status** is used to indicate whether the problem is ongoing or whether the patient has recovered or not.
- **Severity** is concerned with the intensity of the event and can be assessed through referencing the symptom severity guidelines, observation and/or through patient report subjective distress.
- **Drug related** is used by the examiner to assess the relationship of drug to event. This category provides the opportunity to indicate the reasons for suspecting a drug-related effect. If no such effect is suspected check "*Not Applicable*"
  - "*Dose response*" indicates that the intensity of the event is related to the dosage level.
  - "*Dechallenge/Rechallenge*" is used if the drug has been stopped and/or restarted with a concomitant improvement/exacerbation of the problem.
  - "*Timing of onset*" is used if the onset of the event has some regular relationships to drug administration (e.g. it always occurs one hour after taking the drug).
  - "*Seen in other patients in this trial*", "*Known drug effect*" and supported by "*laboratory data*" are other reasons for suspecting a drug relationship.
- **Action taken** refers to the clinician's response to a particular event.

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## Guidelines for Reporting Adverse Events on the SAFTEE

DEFINITION: An Adverse Event is any side effect, complaint, new intercurrent illness, exacerbation of a previous illness, injury that the subject experiences while involved in the research study. The event, if minimal, mild, moderate or severe, should be documented on the **SAFTEE** and described using standard medical terminology. If serious/life threatening, complete **the Serious Adverse Event Page** in the case report form and provide all required information. In addition, any hospitalizations, surgical or diagnostic procedures should be documented as well.

### COMMON SYMPTOM INDICATORS

**Severity:**                      *Minimal*                      *Mild*                      *Moderate*                      *Severe*

#### 1. NAUSEA:

<i>Minimal</i>	Single occurrence, lasting less than two hours; no change in eating habits
<i>Mild</i>	Multiple occurrences or duration longer than two hours; no change in eating habits
<i>Moderate</i>	Intake significantly less than MDR, but able to eat
<i>Severe</i>	No significant nutritional intake

#### 2. VOMITING:

<i>Minimal</i>	Stomach contractions, retching or heartburn without emesis
<i>Mild</i>	1 episode in any 24 hour period
<i>Moderate</i>	2-5 episodes in 24 hours or 1 episode per day on 5 or less days
<i>Severe</i>	6-10 episodes in 24 hours or more than one episode on more than 5 days

#### 3. DIARRHEA:

<i>Minimal</i>	Loose but not watery stools, without cramping or incontinence
<i>Mild</i>	Diarrhea without cramping or incontinence or 2 or fewer episodes day
<i>Moderate</i>	Diarrhea with cramping, no incontinence or 3 or more episodes per day
<i>Severe</i>	Diarrhea with incontinence and cramping or 6 or more episodes per day

#### 4. ABDOMINAL PAIN:

<i>Minimal</i>	Single occurrence of abdominal pain that is not distressing and does not limit activities
<i>Mild</i>	Multiple occurrences of abdominal pain that is not distressing and does not limit activities
<i>Moderate</i>	Single or multiple occurrences of abdominal pain that causes distress but does not limit activities
<i>Severe</i>	Abdominal pain or cramping of sufficient severity to limit activities

## 5. CHANGE IN APPETITE:

<i>Minimal</i>	Hunger increased or decreased without change in food intake or weight
<i>Mild</i>	Hunger increased or decreased with change in food intake and pre-study weight stable or < 5% reduction
<i>Moderate</i>	Hunger increased or decreased; change in food intake and 5%-10% weight loss or gain present without intention to diet or gain weight
<i>Severe</i>	Hunger increased or decreased; weight loss or gain of more than 10% of pre-study weight without intention to diet or gain weight

## 6. HEADACHE:

<i>Minimal</i>	Single occurrence of headache that is not distressing and does not limit activities
<i>Mild</i>	Multiple occurrences of headache that is not distressing and does not limit activities
<i>Moderate</i>	Single or multiple occurrences of headache that causes distress but does not limit activities
<i>Severe</i>	Headache with pain of sufficient severity to limit activities

## 7. DIZZINESS:

<i>Minimal</i>	Occasional transient subjective dizziness, lasting less than 1 minute per occurrence; no limitation of function and no objective findings
<i>Mild</i>	Subjective dizziness lasting greater than 1 minute; no objective findings and no impairment of function
<i>Moderate</i>	Dizziness with impairment of function or limitation of activities; nystagmus or increased body sway noted on exam
<i>Severe</i>	Dizziness with impairment of function, falling or syncope

## 8. FATIGUE:

<i>Minimal</i>	Subjective fatigue without increased need for rest; able to perform all activities of daily living (ADLs)
<i>Mild</i>	Subjective fatigue with increased need for rest; able to perform all activities of daily living (ADLs)
<i>Moderate</i>	Subjective fatigue with increased need for rest; able to perform ADLs only with effort;
<i>Severe</i>	Unable to perform ADLs; able to meet basic needs only with assistance

## 9. NERVOUSNESS/ANXIETY:

<i>Minimal</i>	Occasional nervousness/anxiety that does not cause distress or limit activities
<i>Mild</i>	Occasional nervousness/anxiety that is distressing but tolerable, but does not limit activities
<i>Moderate</i>	Occasional or persistent nervousness/anxiety that is distressing but tolerable and limits activities
<i>Severe</i>	One or more panic attacks or persistent nervousness/anxiety that is intolerable

## **10. INSOMNIA:**

<i>Minimal</i>	Sleep that is not restful, but without change in amount or pattern of sleep
<i>Mild</i>	More than between 1 and 3 occasion of unexplained difficulty falling asleep or of increased nocturnal awakenings, but without change in amount of sleep
<i>Moderate</i>	More than 3 occasions of unexplained difficulty falling asleep and nocturnal awakenings with significant reduction in sleep, but without daytime impairment of function
<i>Severe</i>	More than 3 occasions of unexplained difficulty falling asleep and nocturnal awakenings with significant reduction in sleep, with daytime impairment of function

## **11. SOMNOLENCE:**

<i>Minimal</i>	Occasional subjective tiredness but without change in daily activities
<i>Mild</i>	Persistent subjective tiredness, but without change in daily activities
<i>Moderate</i>	Persistent subjective tiredness; requiring resting or napping less than 2 hours during the day
<i>Severe</i>	Persistent tiredness that significantly limits daily activities, requiring napping or resting more than 2 hours daily; falling asleep during work, school or other activities

## **12. DEPRESSION:**

<i>Minimal</i>	Occasional depressed mood that does not cause distress or limit activities
<i>Mild</i>	Occasional depressed mood that is distressing but tolerable, but does not limit activities
<i>Moderate</i>	Occasional or persistent depressed mood that is distressing but tolerable associated with change in activities
<i>Severe</i>	Suicidal ideation or persistent depression that is intolerable and associated with change in activity

## **13. ITCHING:**

<i>Minimal</i>	Localized itching without need to scratch
<i>Mild</i>	Localized itching with scratching
<i>Moderate</i>	Generalized itching that is tolerable, does not interfere with sleep or activities
<i>Severe</i>	Generalized itching that is intolerable, interferes with sleep and/or activities

## **14. SKIN RASH:**

<i>Minimal</i>	Localized erythema or localized macular/papular eruption, lasting less than 48 hours and without symptoms
<i>Mild</i>	Localized erythema or localized macular/papular eruption lasting greater than 48 hours without symptoms
<i>Moderate</i>	Erythema or macular/papular eruption with pruritis or other associated symptoms involving more than one site on the body
<i>Severe</i>	Generalized (most of body affected) symptomatic macular, papular or urticarial or atypical eruption with or without mucous membrane involvement and with or without exfoliative dermatitis or ulcerating dermatitis

## **15. CHANGE IN LIBIDO:**

<i>Minimal</i>	Occasional increase or decrease in libido that does not engender distress or concern to the subject; no change in sexual activity or performance
<i>Mild</i>	More persistent libido increase or decrease that does not engender distress or concern to the subject; no changes in sexual activity or performance
<i>Moderate</i>	More persistent libido increase or decrease that does engender distress or concern to the subject; change in sexual activity or performance reported
<i>Severe</i>	Significant increase or total lack of interest in sex that is distressing or of concern to the subject; associated with changes in sexual activity or performance

## **16. MISSED MENSES:**

<i>Minimal</i>	Single occurrence of delayed menses (one cycle) that are otherwise regular
<i>Mild</i>	Single occurrence of absent menses (one cycle) that are otherwise regular
<i>Moderate</i>	Multiple occurrences of delayed or absent menses
<i>Severe</i>	Total amenorrhea

**Instructions for Documenting  
Significant Lab Abnormalities on the SAFTEE**

**Definition of Significant Lab Abnormalities:**

Significant lab abnormalities would be defined as receiving the following information from Quintiles:

Panic High (PH) or Panic Low (PL) – Potentially critical high or low results which warrants a phone call to the investigator site and the Sponsor.

Exclusion (EX) flag – indicates a patient’s results exceed the limits described in the protocol and warrants communication to the investigator site. This includes:

- ALT/AST > 5X Upper Normal Limit
- Total bilirubin > 10% above Upper Normal Limit
- Serum B-hCG positive
- Urine drug screen positive for anything other than cannabinoids

**Event:**

Check **Yes** if the abnormality meets the definition outlined above. Check **No** if the abnormality does not meet the definition outlined above.

**Date of Onset:**

Record the date that is on the Quintiles lab report.

**Duration**

Not applicable

**Pattern**

Not applicable

**Severity**

Not applicable.

**Drug Related:**

In most, if not all cases, the response to this item will be “Don’t Know”

**Action Taken:**

This refers to the clinician’s response to the particular event