# Ontology of **fever generation**

As related to Cytokine Release Syndrome (CRS)

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Fever, typically presenting at onset, is a hallmark feature of CRS.

DE-RISKING CYTOKINE RELEASE SYNDROME

*Digital Measures Development*

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# Ontology of **fever generation**

**Concepts** | **Properties** | **Values** *(or nested properties)*

**Fever generation**

*Also known as a rise in body temperature*

**Type**
Rate of change

**Definition**
A rise in core body temperature above the personal normal baseline that has not reached the threshold for defining a fever, established on CRS grading scales as 38°C

**Measure**
Change in body temperature from baseline temperature until reaching the threshold temperature

*Summary statistics*

- Rise in body temperature → Temperature (degrees Celsius, degree Fahrenheit) over time (hour, minutes, seconds), time frame (hours, minutes, seconds)

**Core body temperature**

- Baseline
- Current
- Threshold

→ Degree C or F

**Measurement interval**

- Interval between core body temperatures → Days, hours, minutes, seconds
- Time post-treatment
- Start/end → Initiation timestamp/termination, minimum and maximum duration of monitoring
- Minimum number of temperature recordings → Number of recordings

**Metadata**

- Individual-specific variables → Age, BMI, baseline health status (disease history, disease burden, etc.)
- Environmental variables → Location, indoor or outdoor, transition of indoor to outdoor (or vice versa), weather, etc.
- Context-of-use dependent → Pre-treatment, immunotherapy type, condition or therapeutic area (if relevant), therapeutic interventions
- Measurement modality → Technology type and model, evaluation method/algorithm, sensor placement

## Examples

**Core body temperature** Baseline

**Baseline**: Temperature at pre-infusion time, temperature over last two days.

**Definition**: Body temperature over a specified time frame for use as a comparator to future body temperature recordings. Defining the parameters of baseline temperature will lead to more precise determination of fever generation.

**Core body temperature** Threshold

**Threshold**: Definition of CRS grade fever (38 degrees C); 2 standard deviations from baseline.

**Definition:** The point at which the measurement signals reach a critical transition. Defining the parameters of threshold temperature will lead to earlier detection and an increased response window.

**Measurement interval**

**Interval between measures:** Every four hours (standard of care) with continuous monitoring.

**Duration:** 14 days (recommended observation period for CRS).

## Measure considerations and assumptions:

- Body temperature should be reflective of a core body temperature. Oral, axillary, and rectal body temperatures are considered to reflect core temperature.
- Context is key; while core body temperature is maintained within a narrow window, it fluctuates daily based on several factors, including circadian rhythm, exercises, environmental factors.
- Sensor placement (e.g., wear location) can influence the measurement, conversion, and prediction algorithms for core body temperature and fever generation, respectively.
- A rise in body temperature may be influenced by other factors including prophylactic treatment (e.g., antipyretics) and the cause of the fever (alternative adverse events).
- The interval between measures should balance ethical safety monitoring (not exceeding four hours), the duration of measurement collection, and the time required for physiological and technical capture capacity of change.
- The administration of temperature-suppressing medications should be labeled.

# More more CRS resources are available to support you.

Full ontology of early warning signs of CRS

**Ontology of fever generation**

Ontology of tachycardia

Ontology of hypotension

Ontology of hypoxia

Visit the project page

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