
VIT
VICTORY

Investigator Responsibilities

Role of Site Investigator

+ Full compliance with requirements of Good Clinical Practice (GCP)
+ Ensure subject safety is protected & well-managed
+ Conduct the study in compliance with the protocol

Investigator Responsibilities

Acknowledge and retain responsibility for study conduct

+ Personally conduct or supervise the clinical study
+ Ensure that all study staff are informed of their obligations (Delegation of Authority)
+ Maintain records of staff qualifications
+ Ensure that mechanisms are in place to ensure that site staff receive the appropriate information throughout the study
+ Ensure that appropriate medical coverage is identified for any planned absences (holiday, attending a conference, etc.)

Allow monitoring, auditing & regulatory inspections

+ Notify CERU asap of any planned regulatory inspections
+ Interact with the CERU monitor during monitoring visits

Delegation of Authority Logs

"The Investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties." (ICH section 4.1.5)

Each team member to must be trained on the study before performing any study related, delegated tasks.

Complete log and send to CERU **before** start of trial.

Delegation of Authority Logs

This log is used by the Qualified Investigator (i.e. Site Investigator) to indicate the Site Staff that have a material effect on the conduct of the Study and to whom the Investigator has delegated significant Study related duties/tasks. The signatures and details on this log will also facilitate tracking of edits/changes of the Site records. This log is to be kept by the Qualified Investigator and the Sponsor.

Name of Qualified Investigator: _____ Signature of Qualified Investigator: _____

Print Name	Signature	Initials	Study Role (Qualified Investigator*, sub-QI*, Research Coordinator (RC), Pharmacist, Technician, Dietitian	Key Delegated Tasks Reference numbers (see next page)	Dates	
					Start	End

Key Delegated Tasks

Reference Number	Key Delegated Tasks
1	Screening subjects for eligibility
2	Conducting informed consent discussions for eligible patients
3	Obtaining written informed consent
4	Patient enrollment/randomization and follow-up
5	Checking eligibility criteria
6	Daily monitoring of patient health, safety and study compliance
7	Data collection, includes: ❖ Case Report Form entries ❖ Case Report Form corrections ❖ Data query resolution
8	Source documentation maintenance, includes:

Highlighted Responsibilities

Site Investigator/sub-I delegate must make the following determinations and sign/date applicable documents, whether in the patient chart or on a study specific form, to indicate he/she made the assessment:

1. Confirmation of patient eligibility – including burn size (20% TBSA) and need for grafting
2. SAE Identification & Assessment
    + Ensure adherence to reporting requirements & timelines
    + Provide causality assessment
    + Determine relationship to investigational product

Sample Medical Chart Entry

This patient is enrolled in IRB study ID#, VItamin C in Thermal injuRY: The VICToRY Pilot Trial

Patient met all inclusion criteria and did not meet any exclusion criteria as confirmed with Dr. _____.

Consent obtained from _____ (*relationship to patient*) on *dd/mmm/yyyy* at *time* hrs. All questions & concerns addressed with patient/SDM at this time. Copy of consent was given to patient/SDM.

Date/time of entry: _____
Signature of Research Coordinator: _____

Serious Adverse Events (SAEs)

Any untoward medical event that:

+ Results in death
+ Is life-threatening
+ Requires hospitalization or prolongation of hospitalization
+ Results in significant or permanent disability/incapacity
+ Leads to a congenital anomaly/birth defect
+ Other serious medically important event (e.g. may require medical or surgical intervention)

Serious Adverse Events (SAEs)

Do not report Adverse Events

Only Report SERIOUS Adverse Events that are:

1. **Unexpected – regardless of relationship to intervention**

OR

2. **Related to Intervention – regardless of expectedness**

Only report deaths due to unexpected serious events

The relationship of the study intervention to the SAE must be determined by SI/sub-I

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SAE Relationship to Intervention

Refer to the definitions below when determining relatedness:

Not related: A serious adverse event that is clearly due to extraneous causes (disease, environment, etc.) and does not meet the criteria for drug relationship listed under “Possibly” or “Probably”.

Unlikely related: A serious adverse event that is more likely due to other causes than the study supplement.

Possibly related: Suggests that the association of this SAE with the study supplements is unknown and the event is not reasonably supported by other conditions.

Probably related: Suggests that a reasonable temporal sequences of this SAE with study supplement administration exists and the association of the event with the study supplement seems likely.

Glucose Measurements

+ Due to the similar molecular structure of vitamin C and glucose it is possible that capillary blood sugar point-of-care devices will report artificially high glucose measurements. To that end, we are mandating that glucose may only be measured with one of the following 3 systems:
  1. Core Lab
  2. POC arterial blood gas machine validated in the presence of high plasma concentrations of vitamin C
  3. Nova Biomedical StatStrip glucometer (validated accurate in the presence of high plasma concentrations of vitamin C)

Glucometers and Test Strips

- Nova Biomedical StatStrip glucometers
  - Are being provided to you for use in the study
  - Meters and strips will be shipped to you prior to activation

Glucose Testing Post Treatment

- High plasma concentration of vitamin C may be observed up to 7 days after the last dose of vitamin C is received.
- For patient's receiving oral hypoglycemics or insulin, one of the 3 validated methods must be used to measure glucose for 7 days after the last dose, or a minimum of 36 hours if the hospital device is validated with the approved method. If validated, the hospital device may be used from that point on as needed.
- Hospital method is ok in those patients that do NOT require oral hypoglycemics or intravenous insulin.

Subject Withdrawal

A patient may be withdrawn from IP at any time:

+ At Substitute Decision Maker or her/his own request
+ At the discretion of the investigator for safety, behavioral or administrative reasons

A patient may withdraw (or be withdrawn) from the study prematurely for the following reasons:

+ Serious Adverse Event related to intervention
+ Termination of the study by the sponsor
+ Other safety concerns (must be specified)

Discontinuation of IP

For individual subjects, the treating physician will have the right to discontinue study product if the enrolled patient develops:

+ **a new diagnosis of oxalate kidney stones**
+ **severe hemolysis**
+ **severe acid-base/ electrolyte imbalances**
+ **refractory hypoglycemia**

such that, in the opinion of the treating physician, ongoing use of study product would compromise patient safety.

We do not currently provide definitions, so please use local clinical standards.

These events will be recorded on the Events of Interest form. We request that you record their occurrence and the SI/sub-I rational for continuing or stopping IP.

G6PD Prevalence

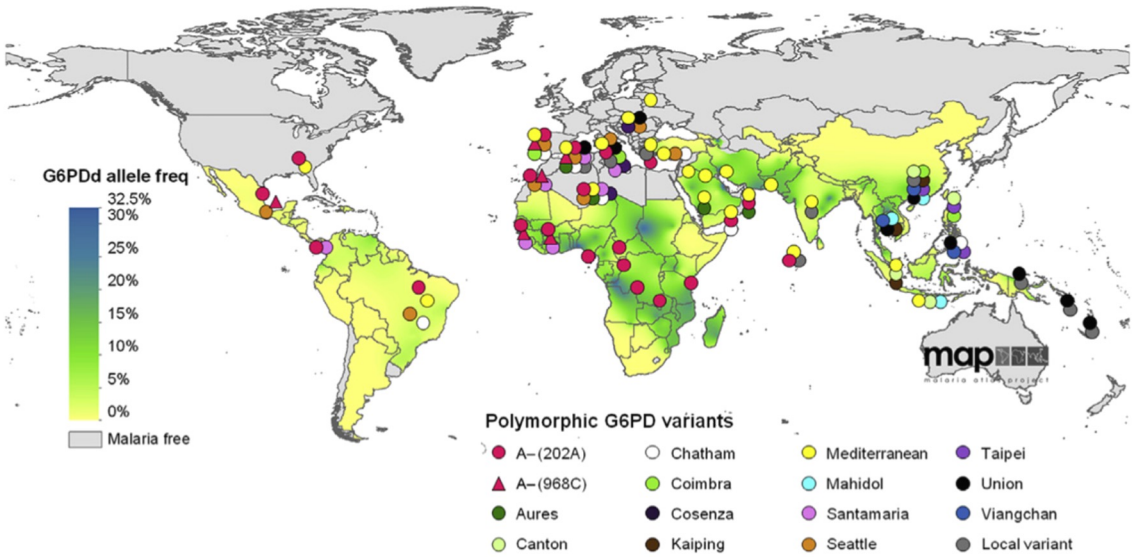
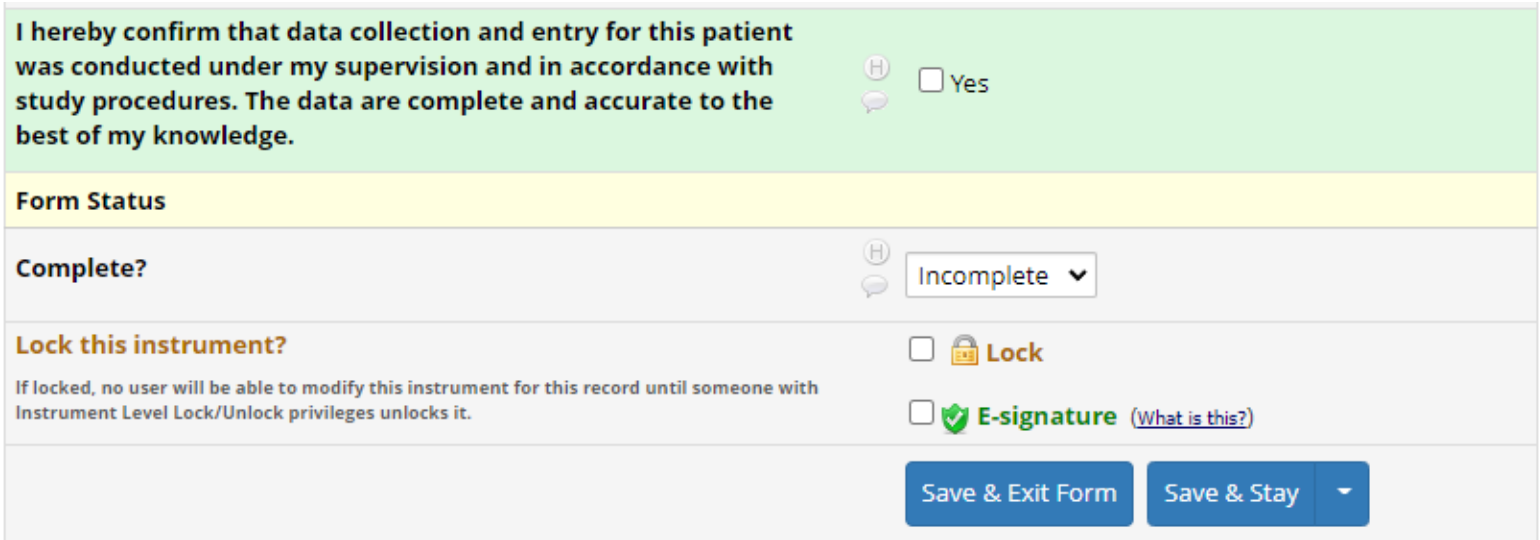


Fig. 4. Global distribution of G6PD deficiency. This map is a combination of 3 previous maps.[47,49,59] Color shades on the map indicate the median predicted allele frequency of G6PD deficiency in malaria-endemic and malaria-eliminating countries, according to the geostatistical model designed by Howes and coworkers.[49] Each colored circle illustrates the geographic distribution of 1 polymorphic *G6PD* allele present in more than 1 population. (triangles used for G6PD A– [968C, L323P] to distinguish it from *G6PD* A– [202A, V68M]; note that both of these mutations are always found associated with 376G, N126D). Dark gray circles indicate local polymorphic variants that have been detected only in 1 population. (*Data from* Refs.[47,49,59])

Site Investigator Confirmation Form

Once all data entry has been completed and queries resolved the site investigator will be asked to ‘sign’ the Site Investigator Confirmation form.



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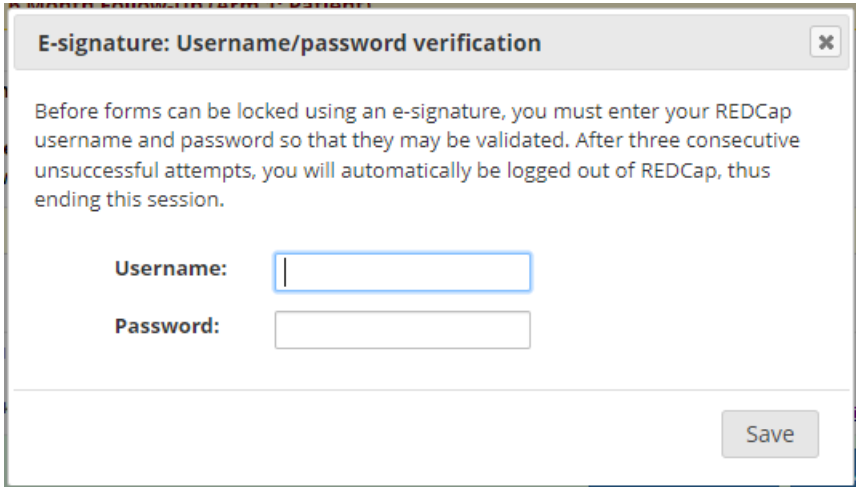
Site Investigator Confirmation Form

To ‘sign’ you will need to do the following:

+ Check ‘Yes’ that you agree with the statement.
+ Change the form status from ‘Incomplete’ to ‘Complete’.
+ Check ‘Lock’.
+ Check ‘E-signature’.
+ Click ‘Save
+ Enter your username and password in the popup window.



Questions

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