DATE: August 4, 2010

TO: Oral Insulin Study Group Members

FROM: TNCC

RE: Clarification on Reporting Serious Adverse Events for the Oral Insulin Study (TN-07)

This memo is being provided to sites to clarify reporting of serious adverse events for the Oral Insulin study. The following information is also detailed in section 10 of the Oral Insulin Manual of Operations:

Per section 6.1.2 of the Oral Insulin protocol, (p. 17-18), *"For this trial, an adverse event associated with the treatment or study procedures that suggests a significant hazard, contraindication, side effect or precaution (as described below) is to be reported as a serious adverse event (SAE). A serious adverse event (experience) or reaction is any untoward medical occurrence that:*

- *results in death,*
- *is life-threatening,*
- *requires inpatient hospitalization or prolongation of existing hospitalization,*
- *results in persistent or significant disability/incapacity, or*
- *is a congenital anomaly/birth defect.*

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered serious adverse events when, based upon appropriate medical judgment, they may jeopardize the patient and/or may require medical or surgical intervention to prevent one of the outcomes listed above."

The TNCC would like to clarify that any event that meets the definition of a serious adverse event as indicated above (whether or not related to treatment or study procedures) should be reported to the TNCC using the online system. It will be up to the medical monitor to make the final determination regarding the relationship of an adverse event to study treatment or procedures. A future amendment for the Oral insulin protocol will include this clarification.

The FDA has given TrialNet a waiver for reporting hospitalizations at diagnosis of type 1 diabetes. However, this pertains to FDA reporting only. Local IRBs maintain their own reporting requirements for such events. Therefore, all sites should continue to report these events to the TNCC using the online system. Sites should consult with their local IRB to determine if hospitalizations pertaining to the diagnosis of diabetes should be reported locally as serious adverse events.