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## 8. ADVERSE EVENT REPORTING

### 8.1 Definitions

An adverse event is defined as any medical problem experienced by a DPP participant that is not a benefit to the participant whether or not considered intervention-related by the clinical center staff. Serious adverse events have been defined to include any adverse experience occurring at any dose that results in any of the following outcomes:

- Death
- A life-threatening adverse experience
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity; or
- A congenital anomaly/birth defect
- Important medical events that may not result in death, be life-threatening or require hospitalization if, based on appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent a serious adverse event.

Non-serious adverse events are all adverse events which do not meet the above criteria for “serious”.

A treatment-emergent adverse event is defined as any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments. A baseline-emergent adverse event is defined as any event which occurs or worsens during the staged screening process (after informed consent) including the randomization visit.

### 8.2 Eliciting and Recording Adverse Events

Reporting of adverse events will be accomplished by collecting information on adverse experiences during the staged screening process and at Standard (Form F01), Major (Form F02) and Interim (Form F03) follow-up visits. In order to avoid bias in eliciting adverse events, participants will be asked, “Have you had any new symptoms, injuries, illness or side effects or worsening of pre-existing conditions?” All adverse events (serious and non-serious; treatment-emergent and baseline-emergent; pharmacological treatment groups and intensive lifestyle intervention group) must be recorded on the DPP Adverse Event Report (Form E01).

#### 8.2.1 Expedited Reports

For participants assigned to the pharmacological treatment groups, the NIDDK-NIH must provide a written report of all serious and unexpected adverse events to the Food and Drug Administration (FDA) within fifteen calendar days. If the event is a death or life-threatening and unexpected, the FDA must be notified by phone or fax within seven calendar days, followed by the written report within fifteen days.

In order to facilitate timely reporting of serious adverse events to the FDA by the NIDDK-NIH, the clinical center staff must contact the Coordinating Center (CoC) at the George Washington University Biostatistics Center immediately (301-881-9260) and fax (301-881-8752) the completed Adverse Event Report (Form E01) and the “initial” Serious Adverse Event Report (Form E02) prior to the close of the following business day. The serious adverse events will be monitored by the CoC’s medical consultant. It is important to note that all serious and unexpected adverse events must be reported to the CoC, regardless of the intervention-related assessment. For example, a patient struck by lightning requires a report, even though this is not likely to be an intervention-related event.

The clinical center staff will not unmask the pharmacological treatment assignments. If, however, there is a serious adverse event which is thought by the clinical center staff to be possibly or probably related to the coded medication, the clinical center staff, when necessary for the safety of the participant, will contact the drug distribution center for pharmacological treatment assignment unmasking upon conferring with the clinical center’s principal investigator. In this event, the clinical center staff must promptly contact the CoC with an explanation of the need for unmasking the pharmacological treatment assignment. A detailed written report must also be submitted to the CoC within three working days of the initial CoC contact.