

CHAPTER 3

ADVERSE EXPERIENCES REPORTING

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3.1 DEFINITION OF ADVERSE EXPERIENCE

An adverse experience is some unplanned, unwanted event which occurs to a person and which is possibly related to the use of protocol therapy. While some events may not appear to be associated with the use of the study treatment, a relationship may not become apparent until a number of reports accumulate from various Transplant Centers.

It is the COBLT Study policy that adverse experience reports shall be submitted even if the investigator is unsure whether a relationship exists between the adverse experience and the use of the study treatment.

Serious Adverse Experience. A serious adverse experience, as defined by the FDA as any experience that suggests a significant hazard, contradiction, side effect, or precaution. With respect to human clinical experience, a serious adverse experience includes any experience that is fatal or life-threatening or permanently disabling or requires in-patient hospitalization (or prolonged hospitalization) or, in a pregnant woman, results in a congenital anomaly, or a cancer or an overdose. (An overdose is defined as an inadvertent or deliberate administration of a treatment at a dose higher than specified in the protocol or higher than known therapeutic doses. It must be reported, regardless of outcome, even if toxic effects were not observed).

Expected Adverse Experiences. Expected adverse experiences are those adverse experiences which are listed in the Informed Consent, product inserts, or study protocol materials.

Unexpected Adverse Experiences. Unexpected adverse experiences are those which are NOT listed in the study protocol or Informed Consent.

Adverse Experiences - Association With Use of Study Treatment. A determination is made by the investigator as to what relationship, if any, the study medication has to the adverse experience.

Category Definition

Definite: Clear-cut temporal association with a positive rechallenge test or laboratory confirmation

Probable: Clear-cut temporal association not reasonably explained by the subject's known clinical state

Possible: Less clear temporal association; other etiologies are also possible

Remote: Less clear temporal association; other etiologies are probable

CORD BLOOD TRANSPLANTATION STUDY MOP

None: No temporal association; related to other etiologies such as concomitant medications/conditions or subject's known clinical state

The assessment may change based on information which develops later in the study.

3.2 ADVERSE EXPERIENCE REPORTING AND MANAGEMENT

Because all participants in the COBLT Study will be receiving toxic preparative therapy, significant regimen-related toxicity is anticipated for patients on all study arms. The study forms will capture information on these adverse experiences. Likewise, substantial mortality is anticipated and will be captured via filing of the Death Form.

All centers should report Adverse Experiences to the Medical Coordinating Center (MCC) as described below.

<u>Adverse Experiences</u>	<u>Reporting Requirement</u>
Unexpected and fatal or life-threatening adverse experiences	Call MCC and/or fax Adverse Experience Form within 24 hours Telephone: (301) 251-1161 Fax: (301) 251-1355
Other unexpected and serious adverse experiences	Call MCC and/or fax Adverse Experience Form within three days Telephone: (301) 251-1161 Fax: (301) 251-1355

All serious adverse events must be reported for the duration of the study. All other events will be reported via data forms submission requirements.

3.2.1 Medical Coordinating Center Reporting

All unexpected fatal or life-threatening adverse experiences will be reported to the FDA by telephone within three working days after receipt of the information following FDA guidelines (21 CFR 312.32). All other unexpected serious adverse experiences should be reported to the FDA within ten days of receipt of the information. All expected adverse experiences (i.e., those listed in the informed consent, product inserts, or study materials) not covered under the above requirements need not be reported. Although death and graft failures are not considered unexpected experiences, they will be reported to the FDA via annual reports submitted to address FDA guidelines (21 CFR 312.33).

A physician trained in Cord Blood transplantation will serve as Medical Monitor for the MCC. The Medical Monitor will review all adverse experience reports. The Monitor will also be responsible for reporting to the FDA and DSMB as required.