

Attn: DAIDS Networks and DAIDS Staff

From: Richard Hafner, M.D.
Director
DAIDS, Office for Policy in Clinical Research Operations (OPCRO)

Date: August 25, 2009

Re: "DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS, VERSION 1; DECEMBER, 2004, CLARIFICATION AUGUST, 2009"

DAIDS has developed clarifications for the "DAIDS AE Grading Table" in order to address questions and comments received from site investigators, Operations Offices, Statistical and Data Management Centers, and Medical Officers within the Division. The subsequent clarifications have been outlined in the Table cover information or incorporated directly into the body of the Table for convenience.

Please be advised that the version number 1.0 for the DAIDS AE Grading Table remains the same as well as the publication date, December 2004. Therefore, while this clarified Table may be used for protocols in development, there is no requirement to change any references to the Table (i.e., title, version, date) in approved protocols. The clarified Table is attached to this message and is now posted on the RCC web page (http://rcc.tech-res.com/tox_tables.htm).

This message also is an official notice from DAIDS that deaths should be reported as grade 5 events.

The clarifications include new language in the Table cover information addressing grading of deaths as grade 5, not grading lab values below grade 1, grading lab values that "fall between" grades, information concerning Addenda 1-3 to be used for AE grading in microbicide trials, and grading when local laboratory normal values overlap with Grade 1 ranges in the Table.

In addition, the following specific parameters have been clarified and also appear directly in the clarified Table in bold and blue:

- Hypertension, Adult > 17 years, Page 6:
Correction: Blood Pressures in Grade 2 to 160-159 from > 160-179 (systolic) and to 100 – 109 from > 100-109 (diastolic) and in Grade 3 to \geq 180 from > 180 (systolic) and to \geq 110 from > 110 (diastolic).
- Anorexia, Page 7:
Comment: Please note that, while the grading scale provided for Unintentional Weight Loss may be used as a guideline when grading anorexia, this is not a requirement and should not be used as a substitute for clinical judgment.
- Absolute lymphocyte count, Adult and Pediatric > 13 years, Page 16:
Comment: Values in children \leq 13 years are not given for the two parameters above because the absolute counts are variable.

- Absolute neutrophil count, Infant, 1 day, Page 16:
Correction: Parameter changed from “Infant, 1 day” to “Infant, \leq 1 day.”
- Hemoglobin, Adult and Pediatric \geq 57 days, Page 17:
Comment 1: The Hgb values in mmol/L have changed because the conversion factor used to convert g/dL to mmol/L has been changed from 0.155 to 0.6206 (the most commonly used conversion factor). For grading Hgb results obtained by an analytic method with a conversion factor other than 0.6206, the result must be converted to g/dL using the appropriate conversion factor for that lab method.

Comment 2: The decrease is a decrease from baseline.
- Laboratory, Hemoglobin, Infant $<$ 21 days, Page 17:
Correction: Parameter changed from “Infant $<$ 21 days” to “Infant \leq 21 days”
- Bicarbonate, serum, low, Page 18:
Comment: Some laboratories will report this value as Bicarbonate (HCO_3) and others as Total Carbon Dioxide (CO_2). These are the same tests; values should be graded according to the ranges for Bicarbonate as listed above.
- Calcium, serum, high and low, Page 18:
Comment: Do not adjust Calcium, serum, low or Calcium, serum, high for albumin.
- Lactate, Page 19:
Comment: Added ULN to Grade 1 parameter

The Division is grateful to site physicians and staff, Network Leadership, Operations Offices SDMC personnel, DAIDS MOs, and particularly the members of the DAIDS SAEC Working Group for their thoughtful contributions to these clarifications.