UPDATED: Manual for Expedited Reporting of Adverse Events to DAIDS

What are the major changes?
How does this affect VOICE?
<table>
<thead>
<tr>
<th>Old</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td><strong>All SAE</strong> – VOICE will be using this reporting category</td>
</tr>
<tr>
<td>Intensive</td>
<td></td>
</tr>
<tr>
<td>Targeted</td>
<td>SUSAR</td>
</tr>
</tbody>
</table>
New: All SAE Reporting Category

Does the AE, following study agent exposure, meet any of the following criteria?
1. Results in death
2. Is life-threatening
3. Requires inpatient hospitalization or prolongation of hospitalization
4. Results in persistent or significant disability/incapacity
5. Is a congenital anomaly/birth defect
6. Is an important medical event (may jeopardize the patient or may require intervention to prevent one of the other outcomes above)

YES

NO

Do NOT Report to DAIDS

Report to DAIDS within three (3) reporting days:
- A Reporting day starts at 12:00 AM (Midnight) and ends at 11:59 PM Monday through Friday local time. (For more information consult the EAE Manual)
- Any holiday (U.S. or in country/local) that falls on a Monday through Friday count as reporting days.

Contact Information for the DAIDS Safety Office:
Website: http://rcc.tech-res.com • E-mail: RCCSafetyOffice@tech-res.com
Office Phone: 1-800-537-9979 (U.S. only) or +1-301-897-1709 • Fax: 1-800-275-7619 (U.S. only) or +1-301-897-1710
(Office Phone and Fax are accessible 24 hours per day)
Mailing Address: DAIDS Safety Office 6500 Rock Spring Drive, Suite 650, Bethesda, MD 20817
<table>
<thead>
<tr>
<th>Old</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely Related</td>
<td>Related - There is a reasonable possibility that the AE may be related to the study agent(s)</td>
</tr>
<tr>
<td>Probably Related</td>
<td>Not Related - There is not a reasonable possibility that the AE may be related to the study agent(s)</td>
</tr>
<tr>
<td>Possibly Related</td>
<td>NA</td>
</tr>
<tr>
<td>Probably Not Related</td>
<td>Not Related</td>
</tr>
<tr>
<td>Not Related</td>
<td>Pending</td>
</tr>
<tr>
<td>Old</td>
<td>New</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>No guidance was given in the manual</td>
<td>Submit an updated report to DAIDS for each AE when significant additional information is available</td>
</tr>
</tbody>
</table>
Updating EAE Reports

- **When to update an EAE report:**
  - AE is stable or has resolved,
  - Change in the severity,
  - Change in the relationship between the AE and the study agent,
  - Additional significant information on a previously reported AE

- **NOTE:** Change in the severity of an AE will still require a new AE Log form to be completed and datafaxed to SCHARP per the VOICE SSP Manual
## Old vs. New: Timeframe for reporting

<table>
<thead>
<tr>
<th>Old</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 business days</td>
<td>3 reporting days</td>
</tr>
<tr>
<td>Business day – Monday through Friday, not including holidays or weekends</td>
<td>Reporting day – Monday through Friday, <strong>including holidays</strong>, not including weekends</td>
</tr>
</tbody>
</table>

*NOTE: Reporting day ends at 11:59 pm local time*
New: Site Investigator Assessment and Signature

- The IoR must designate at least one other physician at the site who can perform AE assessments and sign the appropriate forms.

- VOICE sites must have the second physician who can perform AE assessments listed as sub-investigator on 1572.
 Clarification: Life-Threatening

- “Life-threatening” refers to an event in which the patient was at risk of death at the time of the event.

  It does NOT refer to an event that might have caused death if it were more severe.

- A grade 4 severity does not automatically qualify as “life-threatening”.
Hospitalization is NOT an adverse event (AE), but is an outcome of the event.

Do not report:

- Admissions unrelated to an AE;
- Admission for diagnosis or therapy of a condition that existed before receipt of study agent(s) and has not increased in severity or frequency as judged by the clinical investigator.
Clinically insignificant physical findings at births including those regarded as normal variants should NOT be reported.

When a clinically significant anomaly is reported, all findings (including those of no individual significance) should be included in the same report.
Questions?