GENERAL INSTRUCTIONS – IND SAFETY REPORTS

WHAT TYPE OF SAFETY INFORMATION MUST I REPORT TO THE FDA?

IND regulations require that a narrative or tabular summary of the most frequent and most serious adverse events be reported to the FDA in the annual report. However, serious and unexpected adverse events must be reported quickly in the form of an IND Safety Report. For your convenience the reporting time tables for the FDA and the Duke IRB are listed below.

You must also submit findings from laboratory animal studies that suggest a significant risk for human subjects (this is most relevant to commercial companies developing drugs).

<table>
<thead>
<tr>
<th>Type of SAE</th>
<th>FDA Timeline</th>
<th>Duke IRB Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal or life-threatening adverse drug experience</td>
<td>7 calendar days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Serious and unexpected adverse drug experience</td>
<td>15 calendar days</td>
<td>5 business days</td>
</tr>
<tr>
<td>New animal findings that suggest significant risk to human subjects</td>
<td>15 calendar days</td>
<td>5 business days</td>
</tr>
<tr>
<td>Follow-up reports</td>
<td>As relevant information is available</td>
<td>As relevant information is available</td>
</tr>
</tbody>
</table>

WHERE DO I SEND MY IND SAFETY REPORT? (To your IND as an Amendment)

For a Drug:
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltville, MD 20705-1266
ATTN: [Insert Appropriate Name]

For a Therapeutic Biological Product:
Food and Drug Administration
Center for Drug Evaluation and Research
Therapeutic Biological Products Document Room
5901-B Ammendale Road
Beltville, MD 20705-1266
ATTN: [Insert Appropriate Name]

For a Biologic:
Food and Drug Administration
Center for Biologics Evaluation and Research
HFM-99, 200N
1401 Rockville Pike
Rockville, MD 20852-1448
ATTN: [Insert Appropriate Name]
WHOM DO I ADDRESS IN THE SUBMISSION?

All IND Amendments, including IND Safety Reports are sent to the attention of the person identified by the FDA in your initial notification letter.

IS THERE A FORMAT I SHOULD FOLLOW?

You may use FDA Form 3500A or you may submit in narrative form. We recommend using Form 3500A as it will ensure you provide all the required information. For Foreign events, the 3500A or CIOMS I form may be used. For animal studies, a narrative format is used.

WHAT DEFINITIONS SHOULD I UNDERSTAND?

**Serious adverse drug experience:** Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug 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 may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

**Unexpected adverse drug experience:** Any adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. "Unexpected," as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

**Life-threatening adverse drug experience:** Any adverse drug experience that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.
WHERE CAN I GET MORE INFORMATION?

- See instructions provided with FDA Form 3500A


- 21 CFR 312, Investigational New Drug Application