INTRODUCTION/PURPOSE

The goal of this study is to determine the efficacy of anti-CD20 monoclonal antibody therapy (alone), oral insulin (alone), or the combination of anti-CD20 plus oral insulin to reverse hyperglycemia in NOD mice with recent onset autoimmune diabetes.

The purpose of this Standard Operating Procedure is to describe the endpoints of this study.

DEFINITIONS

**Diabetes:** Blood glucose $\geq 250$ mg/dl (14 mmol/L)

**New onset diabetic:** Blood glucose readings of $\geq 250$ mg/dl (14 mmol/L) on two consecutive days.

**Therapy failure:** For purposes of removing animals from the study for euthanasia. Maximum weight loss as permitted by each site's IACUC (or 20% weight loss if IACUC does not have a weight loss restriction) or 3 consecutive maximum blood glucose measurements as permitted by each site's IACUC (or 3 consecutive blood glucose measurements of $\geq 500$ mg/dl (28 mmol/L) if IACUC does not have a guideline for blood glucose measurements).

**Therapy success:** Two consecutive blood glucose measurements of $< 250$ mg/dl or 14 mmol/L after 120 days post-onset of diabetes.

PROCEDURES

Animals will be removed from the study and euthanized according to IACUC protocol once their weight drops below that permitted by each site's IACUC (or 20% weight loss if IACUC does not have a weight loss restriction) or 3 consecutive maximum blood glucose measurements as permitted by each site's IACUC (or 3 consecutive blood glucose measurements of $\geq 500$ mg/dl (28 mmol/L) if IACUC does not have a guideline for blood glucose measurements).

DOCUMENTATION TO BE MAINTAINED

None

REFERENCES TO OTHER APPLICABLE SOPS

None

REFERENCES
None

FORMS/ATTACHMENTS

None

REVISION HISTORY

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Revision</th>
<th>Author</th>
<th>Description of Changes</th>
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<tbody>
<tr>
<td>August 5, 2011</td>
<td>.01</td>
<td>T Kupfer</td>
<td>Corrected characters that did not import properly.</td>
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<tr>
<td>September 1, 2011</td>
<td>.02</td>
<td>T Kupfer</td>
<td>Changed definition of therapy failure for purposes of humane euthanasia to maximum weight loss per IACUC or 20% or 3 consecutive maximum blood glucose measurements per IACUC or &gt;= 500 mg/dl.</td>
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