CIT-02

STUDY-SPECIFIC MANUAL OF PROCEDURES

VERSION 6.0

SEPTEMBER 14, 2010

CONFIDENTIAL

Table of Contents:

1. CIT-02 Protocol Communication Plan

TOPIC/RELATED QUESTIONS	STUDY ROLE AND CONTACT INFORMATION
• Serious Safety Concerns • Publications • Statistical Questions • Endpoint Questions • Major Protocol Deviations • Clinical Care Questions/Concerns • SAE Review and Reporting • Grantee Budgets	**Thomas L. Eggerman MD, PhD** **Medical Monitor** Director Islet Transplantation Program DDEMD/NIDDK/NIH 6707 Democracy Blvd. Room 697 Bethesda, MD 20892 Phone: 301-594-8813 Fax: 301-480-3503 eggermant@extra.niddk.nih.gov
• Day to Day Site Activities • Informed Consent • Protocol Deviations • Amendments to Protocol • Enrollment/Screening • Investigator Meetings/Teleconferences • Site Visit Concerns • Clinical Protocol Issues • Protocol Development / Finalization • Protocol Compliance • Data Compliance	**Neal Green** **NIDDK Project Manager** Clinical Islet Transplantation Consortium DDEMD/NIDDK/NIH 6707 Democracy Blvd. Room 686A Bethesda, MD 20892 Phone: 301-594-8815 Fax: 301-480-3503 greene@niddk.nih.gov
• eCRF / Data Entry Questions • Data Management / Query Resolution • CIT Web-site Questions and Postings • Study Material Supplies (binders, QOLs, source documents etc.) • General MOP questions	**Traci Schwieger, MA, CCRA** **CIT02 Protocol Coordinator** Clinical Trial Statistical Data Management Center University of Iowa 2400 UCC Iowa City, IA 52242 Phone : 319-384-4180 Fax : 319-353-3960 traci-schwieger@uiowa.edu **Holly Riss, BA, CCRC** **Protocol Coordinator** Clinical Trials Statistical Data Management Center University of Iowa 2400 UCC Iowa City, IA 52242 Phone: 319-353-4267 Fax: 319-353-3960 holly-riss@uiowa.edu

TOPIC/RELATED QUESTIONS	STUDY ROLE AND CONTACT INFORMATION
• Statistical Questions in Parallel with NIH Medical Monitors	**Kathryn Chaloner, PhD** **DCC Statistician** University of Iowa Department of Biostatistics C22-1-GH Iowa City, IA 52242 Phone: 319-384-5029 Fax: 319-335-6535 kathryn-chaloner@uiwoa.edu **Bill Clarke, PhD** **DCC Statistician** University of Iowa Department of Biostatistics 2400 UCC Iowa City, IA 52242 Phone: 319-384-5027 Fax: 319-335-6535 william-clarke@uiowa.edu
• SAE/AE notification	**Larry Hunsicker, MD** **DCC Clinical Trial Physician** Department of Internal Medicine T304 GH University of Iowa Hospitals and Clinics Iowa City, IA 52242 Phone: 319-356-4763 Fax: 319-353-4231 Lawrence-hunsicker@uiowa.edu
• Manufacturing • Out of Specs (OOS) for Manufacturing • Regulatory • cGCP/cGMP • Drug Accountability/Reconciliation • Drug Stability Issues • Shipping of Drugs and Islets	**Julia Goldstein, MD** **Senior Regulatory Affairs Officer** DAIT/NIAID/NIH 6610 Rockledge Drive Room 3044 Bethesda, MD 20892 Phone: 301-451-3112 Fax: 301-480-1537 goldsteinj@niaid.nih.gov **Christine W. Czarniecki, PhD** **Chief, Regulatory and Industry Affairs** DAIT/NIAID/NIH 6610 Rockledge Drive Room 3059 Bethesda, MD 20892 Tel: 301-451-4407 Fax: 301-402-2571 cczarniecki@niaid.nih.gov
• Collection of Regulatory Documents	**Deb Feddersen, R.N., ARNP** **Lead DCC Regulatory Coordinator** Clinical Trials Statistical Data Management Center University of Iowa 2400 UCC Iowa City, IA 52242 Phone: 319-353-4240 Fax: 319-353-3960 deb-feddersen@uiowa.edu

TOPIC/RELATED QUESTIONS	STUDY ROLE AND CONTACT INFORMATION	
• General Laboratory Manual Questions	**Cynthia Diltz, RN, BSN, CCRC** **Protocol Coordinator** Clinical Trials Statistical Data Management Center University of Iowa 2400 UCC Iowa City, IA 52242 Phone : 319-353-4982 Fax : 319-353-3960 cynthia-diltz@uiowa.edu	
• Scheduling of Site Monitoring Visits	**Betty Cosen** **Monitoring CRA** PPD **929 North Front Street** **Wilmington, NC 28401** **Phone: 910-558-7217** **Fax: 919-65409431** **betty.cosen@wilm.ppdi.com**	**Mary Hale** **Lead CRA** PPD 12 Elbow Lane Sicklerville, NJ 08081 Phone: 856 740-0073 Fax: 919 654-8866 Mary.Hale@columbia.ppdi.com

2. Exenatide Tracking and Destruction

Please be sure to inform all patients that you provide the drug to that there will be two protocol numbers on some items and only one on others. Of particular note is the cartridge where there will only be the Amylin protocol number.

As a reminder, patients should also be instructed to return all used drug supplies, except for the needles, to the site. At the conclusion of the trial, after drug reconciliation has been completed, drug supplies provided by Amylin per the NIH CTA must be returned to the site and then sent back to Amylin for destruction. Drug supplies purchased commercially by the site must be destroyed on-site with appropriate documentation, using drug destruction procedures described in the site SOP's.

Proper accounting and reconciliation is also needed for drug used during the manufacturing process. If the drug was provided per the NIH CTA, it should also be returned to Amylin. The manufacturing group must return all used drug to the study coordinator, who will return to Amylin with the used patient drug supply. If the drug was purchased commercially by the site, it must be destroyed on-site with appropriate documentation, using drug destruction procedures described in the site SOPs.

When the site has enough materials to ship to Amylin, please request a pre-paid return box from:

Jennifer Tomer
Associate, Medical Affairs
Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
San Diego, CA 92121 USA
Tel: 858-458-8668
Fax: 858-824-7692
www.amylin.com

AMYLIN™

9360 Towne Centre Drive
San Diego, CA 92121

Manifest #_____

Drug Tracking and Reconciliation Form

FedEx Tracking # _____

Investigator Name:	Amylin Protocol No.:	Investigational Product Description:
Study Title: _____		

Dispensing Inventory Log

Units Received			Units Dispensed			Units Returned			Comments
Package # or kit #	Quantity Received	Received By/Date	Subject initials/Screen #	Quantity Dispensed	Dispensed by/date	Quantity Returned	Quantity Not Returned	Recorded by/date	
Total			Total						

Accountability and Reconciliation

Disposition of returned/remaining investigation product (check one): ( ) Destroyed at site ( ) Returned to Amylin/Xerimis: Date returned _____

Signature: _____ Print Name: _____

PLEASE FAX FORM BACK TO: (858) 334-1100 Investigational Supplies

Page ____ of ____
Version 5
August 29, 2007

Instructions for Completing Drug Tracking and Reconciliation Form

"DTRF"

Amylin Medical Affairs completes the following fields: Investigator Name, Amylin Protocol #, Investigational Product Description, Study Title.

Site completes the form as follows:

A) UNITS RECEIVED:

1. In the first column, **"Package #/Kit #"**, list the kit numbers (i.e. L12345) received in the shipment. Enter only ONE kit number per line. If reconciling loose vials or pens, list vial # or pen #.

2. In the second column, "**Quantity Received**", list the number of cartridges/vials/etc. received in the shipment.

3. In the third column, "**Received By/Date**", enter the recipient's initials and the date when the drug is received.

B) UNITS DISPENSED:

4. In the fourth column, "**Subject Initials/Screen #**, enter the corresponding subject's initials and screening number.

5. In the fifth column, "**Quantity Dispensed"**, enter the number of cartridges/vials/etc. dispensed to the subject.

6. In the sixth column, **"Dispensed by/Date"**, enter the initials of the dispenser and the date when the drug is dispensed to the subject.

C) UNITS RETURNED:

7. In the seventh column, **"Quantity Returned"**, enter the number of cartridges/vials/etc. returned by the subject.

8. In the eighth column, **"Quantity Not Returned"**, enter the number of cartridges/vials/etc. **not** returned by the subject.

9. In the ninth column, **"Recorded by/Date"**, enter the returned drug recipient's (staff) initials and the date when the drug is returned.

D) COMMENTS:

10. In the tenth column, **"Comments"**, document any discrepancies or provide clarification on returns. Examples:

    a. Document discrepancies between what was dispensed to the patient and what is being returned. Examples:

        i. Cartridge lost by patient.
        ii. Cartridge broken at site.
        iii. Entire kit missing. The package # of the kit must be entered in the first column. If the kit was dispensed to the subject, enter the subject initials on the 3rd column.

    b. To clarify entries. Examples:

        i. The tamper seal of the kit was broken and was not dispensed. (Note: A kit with a broken tamper evident seal is considered "Used".)
        ii. Kit was not dispensed because it was damaged.

11. Complete the Accountability and Reconciliation section on the bottom of the DTRF. Check either "destroyed at site" or "returned to Amylin/Xerimis" and write the date the items were destroyed or returned respectively.

12. Sign the bottom of the DTRF and print your name.

13. Complete the bottom of the DTRF with the appropriate page number(s).

14. Retain a copy of the signed DTRF for site files, fax a copy to **Amylin Investigational Supplies** at **(858) 334-1100** and mail the original DTRF to Amylin Investigational Supplies in the self addressed stamped envelop provided.

15. If study drug is to be returned to Xerimis for destruction, place a copy of the DTRF in an envelope on the outside of the return box. Tape the envelope securely to the box with the tamper-evident tape.

16. If study drug is to be destroyed at the site, a destruction certificate must be faxed or mailed to Amylin Investigation Supplies with a copy of the corresponding DTRF. A manifest number should be noted on both the destruction certificate and DTRF.

Amylin Drug/Device Return Process Packing Instructions

NOTE: *The shipment box and/or any other boxes at the site may be used for returns*
More Return packets are available upon request

Contents of the Shipment Return Packet should include the following:

a. One shipping container (box)
b. Packing peanuts in 1 or 2 plastic bags (enough for 3 boxes of returns)
c. One Amylin Clinical Supplies Return Authorization Form (CSRAF)
d. 4 Plastic bags for the pens and or kits (pack separately)
e. 3 zip lock bags for loose pens or vials
f. 7 Tamper-Evident Labels for sealing the plastic bags and zip lock bags
g. Tamper-Evident tape for sealing the shipping box(es)
h. 3 FedEx Air bills with Xerimis return address/3rd party billing number
i. Instructions for completing CSRAF
j. Instructions for packing (Amylin Drug/Device Return Process Packing Instructions)

How to Package a Return Shipment: Please check box (☐) as each step is completed.

☐ Complete Amylin's CSRAF, include a copy with the shipment and keep a copy in your study file

- Material from different protocols must be listed on separate CSRAF and returned in separate shipping boxes
- Any box maybe used for returns. Additional Return packets are available upon request.
- **REMOVE All NEEDLES FROM PENS! DO NOT RETURN NEEDLES AND SYRINGES!**

☐ Pen and Drug kits, including loose drug and pens not in a kit, must be bagged SEPARATELY (by type)

☐ LARGE Plastic Bags – Place Pen and Drug kits so the labels are visible through the plastic bag. Seal the bags with the tamper-evident labels supplied in the Return packet

☐ SMALLER zip lock Bags – place loose vials or pens into smaller zip lock bags and seal with the tamper-evident labels supplied in the return packet.

- Do not place the smaller zip lock bags in the larger bags with the kits or pens

☐ Place all bags with the tamper-evident seal and the **original CSARF(s)** into a box(es) for return.

- If reusing a box, deface all existing shipping information
- Do not pack kits from several protocols in one box

☐ Seal the entire box(es) with the adhesive tamper-evident tape provided in the return packet. Please make sure the adhesive tamper-evident tape goes **all** the way around the box

☐ Attach one (1) FedEx Air bill shipping label that was provided on the top of each box

☐ Keep a copy of air bill for your records

☐ Sign this form, date it and fax it to Investigational Supplies (858-334-1100)

Signature: _____ Date: _____

Version 8 dated 16-Mar-07
Amylin Pharmaceuticals, Inc.