Title: Apheresis Collection and Logistics for DeltEx DRI Manufacturing	
Document Number: INB-400 Apheresis Manual	**Version:** 04
Effective Date: 2024JUN18	**Page:** 1 of 21

Apheresis Manual:

Title	**Apheresis Collection and Logistics for DeltEx DRI Manufacturing**		
Version	**04**	**Effective Date**	**2024JUN18**
Manual Document ID	**INB-400 Apheresis Manual**	**Last Updated Date**	**2024JUN17**

Referencing Clinical Trial Study Protocol:

Title	**A PHASE 1B / 2 OPEN-LABEL STUDY TO INVESTIGATE THE SAFETY, TOLERANCE AND EFFICACY OF DRUG RESISTANT IMMUNOTHERAPY WITH ACTIVATED, GENE MODIFIED ALLOGENEIC OR AUTOLOGOUS γδ T CELLS (DELTEX) IN COMBINATION WITH MAINTENANCE TEMOZOLOMIDE IN SUBJECTS WITH RECURRENT OR NEWLY DIAGNOSED GLIOBLASTOMA**		
Protocol Document ID	**INB-400 Protocol**	**Sponsor**	**IN8bio**

Title: Apheresis Collection and Logistics for DeltEx DRI Manufacturing	
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IN8bio Approvals:

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1. PURPOSE

1.1 The purpose of this document is to describe the procedures and guidelines for the apheresis (leukapheresis) product collection, testing, chain of identity, labeling, specification, packaging, and transportation from the clinical trial site's collection facility to IN8bio's contracted manufacturing facility to support the product manufacturing for the INB-400 clinical trial sponsored by IN8bio.

2. SCOPE

2.1 This document applies to apheresis products collected to be manufactured into the DeltEx DRI product, in clinical trial INB-400, IND#28676, sponsored by IN8bio.

2.2 The target audience of this document is primarily the collection facilities / apheresis unit's staff, shipping personnel, couriers, CROs, and applicable coordinating personnel at IN8bio.

2.3 Note: the receipt, handling and dose preparation for administration of the manufactured DeltEx DRI product at the administering facility will be described in the Pharmacy Manual.

3. STUDY TEAM & RESPONSIBILITY

Study team members, contact information, and responsibilities in the execution or oversight of apheresis collection and management:

Institution, Role	Responsibility	Name, Address, Phone Number, Email
Trial Site Primary Investigator or designee	Ensure trial site personnel are properly trained for this procedure. Ensure that all patient apheresis products and related specimens are obtained according to the current clinical protocol as scheduled	Please refer to site contact master list
Syneos Health	Responsible for oversight of sample collection and logistics communication with vendor (e.g., CryoPort) and IN8bio	DL_IN8Bio_Logistics@syneoshealth.com jennifer.grimes@syneoshealth.com Jenn Grimes Phone: +1 804 694 6936

Institution, Role	Responsibility	Name, Address, Phone Number, Email
Apheresis Unit Personnel	Perform activities related to apheresis product collection, testing, labelling, and packing for shipping, according to this manual.	Please refer to site contact master list
IN8bio, Clinical Operations	Ensure the apheresis manual is timely and accurately revised to reflect the current study protocol; Coordinate the apheresis product collection activities with Operations.	Stacey Bilinski 350 5th Ave, Suite 5330 New York, NY 10118 O: 917-813-1450 sabilinski@IN8bio.com
IN8bio, Chief Scientific Officer	Edit this manual as needed.	Lawrence Lamb, 2901 Second Ave South, Suite 230, Birmingham, AL 35233, O: 205-855-5002, larry@in8bio.com
IN8bio, Chief Operating Officer	Edit this manual as needed; Coordinate manufacturing schedules with manufacturing and clinical sites.	Kate Rochlin, 350 5th Ave, Suite 5330, New York, NY 10118 O: 646-933-5605, kmrochlin@in8bio.com
IN8bio, Sr. Director, Quality Operations	Provide Quality and Laboratory Operation related revision suggestions to this Manual to facilitate safe, user-friendly, streamlined and standardized execution of this manual.	Guoling Chen, 2901 Second Ave South, Suite 230, Birmingham, AL 35233, O: 205-855-5009, gchen@in8bio.com
IN8bio, Operations Director	Responsible for review of applicable sections of this manual; schedule, communicate or work with vendor (e.g., Syneos) to communicate with trial sites, manufacturing site, regarding apheresis product logistics activities or related concerns.	Marsia Silletti, 350 5th Ave, Suite 5330, New York, NY 10118 O: 917-813-1452 msilletti@IN8bio.com
CryoPort, Director of Program Management-Consulting Services	Responsible for providing shipping containers, detailed SOPs, and couriers services in order to enable apheresis product and manufactured product transportation between sites	Gwendolyn Erskine, 112 Westwood Place Suite 350 Brentwood, TN 37027 O: 610-810-7094 gerskine@cryoport.com

4. DEFINITIONS AND BACKGROUNDS

4.1 DeltEx DRI: Gamma Delta T cell (γδ T cell) Drug Resistant Immunotherapy.

4.2 **MNC-A**: Peripheral blood mononuclear cell (MNC) collection by apheresis.

4.3 **ACD-A** (Anticoagulant citrate dextrose solution A): A chemical substance added to blood that inhibits clotting by binding ionized calcium; for Formula A, each 10mL of solution contains 2.2g sodium citrate hydrous, 730 mg citric acid anhydrous and 2.45g dextrose hydrous; also known as sodium citrate. **ACD-A is the only anticoagulant approved for this procedure.**

4.4 **Manufacturing:** Manufacturing in this manual refers to the processing, modification, expansion, culture, manipulation of the apheresis product for the production of cell therapy products.

4.5 **Manufacturing Facility**: IN8bio's contract manufacturing facility to manufacture the INB-400 DeltEx DRI drug product.

4.6 **CRO**: Clinical research organizations. Such as Syneos Health.

4.7 **CryoPort**: Courier services used in this trial. Managed by Syneos Health.

4.8 **ISBT 128:** Is the global standard for the terminology, identification, coding and labeling of medical products of human origin (including blood, cell, tissue, milk, and organ products).

4.9 **DIN:** Donation Identification Number. A unique product-specific number associated to the subject's blood product from the time of the MNC collection through DeltEx DRI product injection.

4.10 **Subject ID:** Assigned by IN8bio, a unique identifier. Clinical trial specific numbering scheme with elements of the clinical protocol, clinical site ID and sequential subject numbering. For INB-400, the subject ID format is: INB400-XXX-YYY. Where "XXX" is a numeric ID of the site, "YYY" is a numeric ID of the subject.

4.11 **Lot number:** manufacturing lot, a unique identifier. For INB-400, the format is yymmdd-400-XXX-YYY. "yymmdd" is the actual collection date, "XXX-YYY" are the same as the last digits of the Subject ID.

4.12 **Spectra Optia Apheresis System:** Automatic blood component separator manufactured by Terumo BCT that uses centrifugation and optical detection (automated interface management system) to perform apheresis procedures. The Spectra Optia Apheresis System is FDA-approved to perform MNC collections.

4.13 Room Temperature: 15 to 25°C.

4.14 Chain of Identity (**COI**): The process that links a subject's peripheral blood apheresis product to their final product throughout the MNC collection, shipping, manufacturing, clinical site receipt and product infusion. In addition, this process should link a subject product to a subject when subjects are enrolled in the allogeneic arms.

4.15 Collection End Time: The clock time at the completion of the mononuclear cell collection at the end of rinse-back/ reinfusion. This date and time represent the start of the clock for expiration of the MNC product.

4.16 Mononuclear Cell Collection Bag*:* The bag attached to the MNC procedure tubing kit where collected MNCs are stored. Specific instrument terms used for this volume are as follows:

4.16.1 Spectra Optia Apheresis System- Collection bag.

4.17 Local Patient Identifiers: Personal identifying information (e.g., name and date of birth) by which an individual can be recognized, to be used within the collection facility. All HIPPA/PHI information should be redacted before sending the associated documents to the manufacturing facility and /or IN8bio. Only study Subject ID should be utilized on labeling of materials.

4.18 Subject Identity Verification The act of confirming subject identity. Site should follow their institutional guidelines for confirming identification, such as: by ensuring the subject's identifiers, subject number, and product identifier on the MNC bag label exactly matches the Pre-screening Slot Assignment Form. E.g.,upon patient arrival, this activity can be performed by either visually confirming the subject's identifiers on the MNC bag label exactly matches their identification (e.g., driver's license or medical institution identification). If the subject does not have ID and verbal confirmation is required, the subject must initial the label.

4.19 Whole Blood Processed Volume (WBPV): The amount of subject whole blood that travels over the collection inlet pump during the collection procedure. Specific instrument terms used for this volume are as follows:

4.19.1 *Spectra Optia Apheresis System*- this volume does not include anticoagulant.

4.20 Coordinated Universal Time (UTC): the primary time standard globally used to regulate clocks and time. It establishes a reference for the current time, forming the basis for civil time and time zones.

4.21 Total Product Volume (to enter on the apheresis product label)**:** volume from the apheresis device. The volume containing the ACD-A in the product.

5. EQUIPMENT & MATERIALS

5.1 Apheresis Equipment approved by IN8bio for this study

NOTE: IN8bio will provide written notification if other instruments are approved.

Equipment Name	Manufacturer	Model
Spectra Optia Apheresis System	TERUMO BCT	Spectra Optia

5.2 Reagents

Only reagents for Apheresis are included within this manual

Reagent Name, specifications	Manufacturer	Cat#
ACD-A, USP	As provided by collection facility	As provided by collection facility

5.3 Supplies

Supply Name, specifications	Manufacturer	Cat#
Spectra Optia Disposable Set	TERUMO BCT	#12120 CC-MNC protocol (standard filler) #12310 CC-CMNC protocol (IDL filler) (or as provided by collection facility)
Biohazard zip-lock bags with absorbent Material	Provided by CryoPort	Safepak®XL Barrier Control Bag (integrated absorbent material used for secondary containment of infectious substances" and "developed to be used in the safe transport of IATA rated Category B infectious substances")
Bubble Wrap	Provided by CryoPort	½ inch bubble size, perforated
Shipping box	Provided by CryoPort	C3™ Controlled Room Temperature (CRT) Shipper (15 to 25°C)

Supply Name, specifications	Manufacturer	Cat#
Temperature logger, Room Temperature	Provided by CryoPort	Smartpak II LTE data logger

6. PRE-APHERESIS COLLECTION PATIENT READINESS CONFIRMATION

6.1 Health Assessment

6.1.1 Subject should have completed a basic health assessment to confirm their eligibility to undergo apheresis as part of the study protocol. All subject testing, including infectious workup should be complete prior to the initiation of apheresis.

6.2 Timing to stop other Medication and / or Therapeutic Procedures before the Apheresis Date:

6.2.1 Subject should hold blood pressure medications morning of the apheresis and resume after the collection.

6.2.2 If medically reasonable, the patient should not be on steroids for at least 2 (preferably 3) weeks prior to apheresis

6.3 Other concerns on active infections, vaccination, etc.

6.3.1 Subject should have completed all infectious workup as indicated for screening. There should not be signs of an active infection at the time of donation.

7. APHERESIS COLLECTION PROCEDURE

7.1 Collection goal:

7.1.1 Process 2-4 blood volumes to collect approximately 175 to 200mL of apheresis product (the volume from the apheresis machine is acceptable for determining the mL).

7.1.2 Record the collection volume on INB-400 Apheresis Manual **App1_IN8bio INB-400 Apheresis Collection Summary Form**. Select if collection goal was met.

7.1.3 Use **only ONE** of the sample bulbs on the collection bag and take 0.5-1mL sample to perform the following cell counts. This additional testing to be performed at the Collection Site prior to shipping:

7.1.3.1 **Required:** Automated CBC with automated differential (manual differential is acceptable if automated cannot be done)

7.1.3.1.1 WBC concentration requested for information purposes only to assist with Manufacturing process.

7.1.3.2 **Optional:** Viability

7.1.3.3 Record the results from any additional testing performed on INB-400 Apheresis Manual **App1_IN8bio INB-400 Apheresis Collection Summary Form**.

7.1.3.4 If selecting "results to follow" please send the results to **DL_IN8bio_logistics@syneoshealth.com** by the end-of-day on the day of collection.

7.1.4 Collected apheresis products with a volume below the minimum requested volume may not yield sufficient DeltEx DRI product for patient dosing. The apheresis product may still be processed and manufactured at IN8bio's discretion, in consultation with the clinical site PI, if needed.

7.2 The apheresis systems, reagents, and supplies must be also approved for MNC-A collection by the collection facility's local health authorities. Do not use research-grade reagents.

7.3 Considerations during the collection procedure when using the Spectra Optia Apheresis System:

7.3.1 Inlet to AC ratio range: 6-12:1

7.3.1.1 Begin the procedure at an Inlet to AC ratio of 12:1

7.3.1.2 Monitor the product and device every 15 min for at least the first hour of collection and assess if there is any clumping observed in the centrifuge or collect line. After the first hour please follow institutional SOPs for monitoring.

7.3.1.3 If clumping is observed in the centrifuge or collect line, decrease the Inlet to AC ratio to 8:1. Process at least 100 mL of inlet volume then reassess for clumping.

7.3.1.4 If clumping has not resolved, leave the Inlet to AC ratio at 8:1 until clumping is resolved.

7.3.1.5 Once clumping is resolved, increase the Inlet: AC ratio to 10:1 for at least 500 – 1000 mL of inlet volume processed.

7.3.1.6 Some study subjects may need a lower Inlet to AC ratio to maintain good anticoagulation in the circuit.

7.3.2 Collection Preference (CP) Setting:

7.3.2.1 Before adjusting the CP, ensure the interface is established. When the interface is established, a message will appear on the Spectra Optia stating:

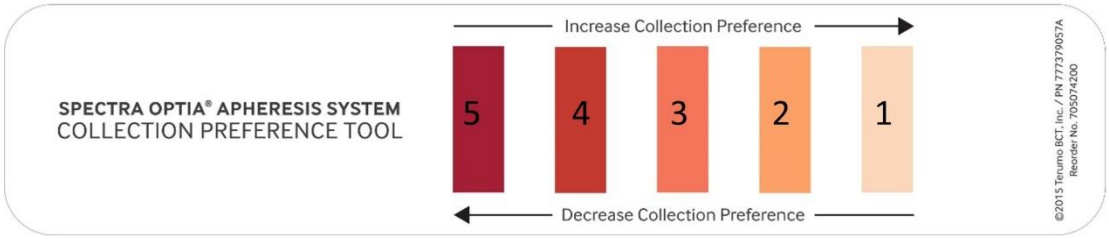
7.3.2.1.1 For MNC: "Filling the chamber"

7.3.2.1.2 For CMNC: "Collecting MNC"

7.3.2.2 Observe the position of the green diamonds on the Collection Status screen and ensure they are tracking to the black line.

7.3.2.3 Once the interface is established, adjustments can be made to the CP number to target the desired color on the CP Tool.

7.3.2.4 For collections on the Spectra Optia, target between colors #2-3 on the CP Tool. (see below)



7.3.3 Troubleshooting alarms on the Spectra Optia

7.3.3.1 The most common alarms will be related to access (inlet or return lines). When an alarm occurs, onscreen instructions will be available on the Spectra Optia. Read the onscreen instructions and follow Spectra Optia troubleshooting suggestions.

7.3.3.2 Common causes of access issues are:

7.3.3.2.1 Occluded or kinked lines: remove the occlusion or flush the line.

7.3.3.2.2 Access is too small for flow rate: reduce the inlet flow rate.

7.3.3.3 Troubleshooting assistance or uncommon alarms, contact Terumo BCT at 877-339-4228.

7.4 MNC Bag handling:

7.4.1 Do not access the spike-ports on the collection bag. Please utilize only one sample bulb to obtain the sample required for testing and cell count.

7.4.1.1 Refer to the manufacturer's operator manual on how to use the sample bulbs, if needed.

7.4.2 When disconnecting the collection bag, **please do not strip the collection line**.

7.4.3 At a minimum, leave 5 inches of tubing once the collection line is sealed.

7.4.4 Place 3 hermetic seals on the collection bag line leaving a 5" piece of tubing on the bag. Disconnect the bag at the middle seal, leaving 2 seals towards the collected product bag. Do not use knots to tie the collection line.

7.5 Whole blood processed during collection should be a minimum of 2 to 4 total blood volumes unless otherwise instructed by IN8bio. It is acceptable to process greater or less than due to clinical or technical issues; complete as much of the collection as is safe for subject. **NOTE: ~175 to 200mL collection volume is recommended to ensure sufficient volume for** manufacturing.

7.6 Label the product according to "ISBT 128 Labeling" below.

7.7 Ensure sample testing has been performed per step 7.1.3 and results are recorded or noted as results to follow in the collection form. If results to follow, they must be sent by end-of-day on the day of collection.

7.8 Follow institutional policy for the following practices: Personal protection, Aseptic technique, Venipuncture or central venous access, Biospecimen handling, Biohazard waste disposal.

8. ISBT 128 labeling

8.1 ISBT 128 label and any additional institutional labels must be affixed to the MNC product. ISBT-128 labels are generated by the collection facility. It should include:

8.1.1 Donation Identification Number (DIN) number assigned by the collection facility

8.1.2 Collection Facility Name and Address

8.1.3 Collection End Date, Time, Time zone

8.1.3.1 NOTE: IF the Date/Time is hand-written, please enter it in the format shown in the example labels below, AND ensure "UTC" time is also entered in the second line of the date/time field (see example label next page), to allow the MFG site to convert to local time zone (if needed) and still match the UTC time.

8.1.4 "Do Not Irradiate", "Do not Use Leukoreduction Filters"

8.1.5 Product code, Product Name and Description: S2967, "MNC, APHERESIS, For Further Processing", (or other equivalent codes that states these product name and description)

8.1.6 Total Product Volume

8.1.7 ACD-A Volume in product

8.1.8 "Store at Room Temperature"

8.1.9 ABO/Rh (on the label or in the accompanying document)

8.1.10 Applicable statement based on donation type and eligibility determination

8.1.10.1 Statement for Autologous product "For Autologous Use Only", OR "Biohazard For Autologous Use Only"

8.1.11 "Process as soon as possible"

8.1.11.1 If using the label template as shown in the left image below, this is **Selected** in the "expiration date" field;

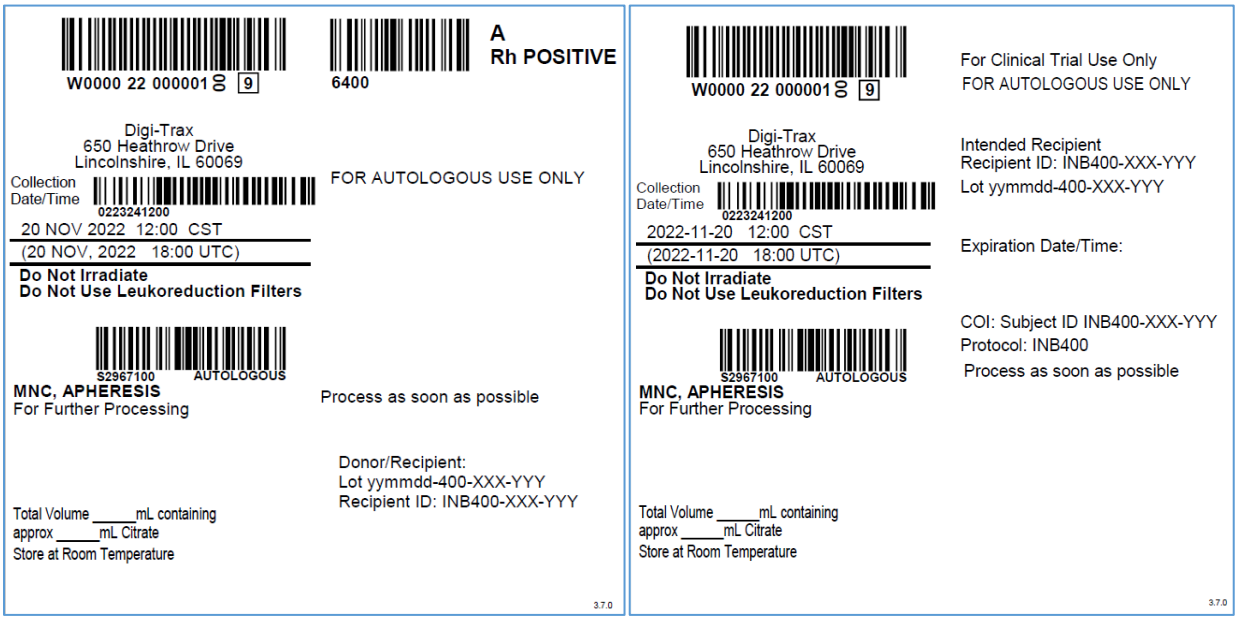
8.1.11.2 If using the label template as shown in the right image below, this is **Entered** in the "Facilities" tab, the MFG free text field.

8.1.12 Subject/Recipient (Subject)'s Unique Subject ID (assigned by IN8bio), entered in the "Recipient ID" field, in the format of "**INB400-XXX-YYY"**.

8.1.13 Unique Lot number entered in the Subject/Recipient's Name field, in the format of "**Lot yymmdd-400-XXX-YYY**"
NOTE: do not add ":" or "#" behind the word "Lot".

8.1.14 In the "**COI**" field, enter in the format of "Subject ID INB400-XXX-YYY". NOTE: **the word "Subject ID" must be included**.

8.1.15 See example label formats below and select the one that is best for use at the collection facility. **Either the "Full Face" (left) or the "HemaTrax MFG" (right) format is acceptable**:



8.1.16 Follow other general applicable institutional ISBT 128 labeling requirements.

8.1.17 **Redact PHI**, e.g. the patient's name, date of birth, MRN (if used) on the product label AND accompanying documents, before sending them to the manufacturing site. If relabeling is needed, make sure to use the same DIN, Lot number, and the subject ID from original collection label to maintain COI.

8.1.18 Biohazard and / or warning labels, if applicable, should be attached (by tie tag or equivalent). As applicable:

8.1.18.1 Statement "NOT EVALUATED FOR INFECTIOUS SUBSTANCES"

8.1.18.2 Statement "WARNING: Advise Patient of Communicable Disease Risks"

8.1.18.3 Statement "WARNING: Reactive Test Results for [name of disease agent or disease]"

8.2 Accompanying Documents.

8.2.1 **Each page** of all accompanying documents must have the **Subject ID** and **DIN**. If the Subject ID and DIN are hand-written, the person who added this information must also initial and date beside the manual entries.

8.2.2 IDM (Infectious Disease Marker) results and interpretation, performed within 30 days prior to apheresis collection, and statement that such tests were performed by a CLIA Clinical Laboratory Improvement Amendments) Laboratory, or equivalent as determined by CMMS (Centers for Medicare and Medicaid Services).

8.2.3 "Chain of Custody Form for INB-400" **(Appendix 2)**.

8.2.3.1 NOTE: In the event the Manufacturing Facility and the Collection Facility are located at the same institution, and/ or when the Manufacturing facility and the Administering facility (clinical site) are in the same institution, the corresponding fields referring to physical shipments conducted by Cryoport are to be completed using "N/A". Please attach the institutional shipping/transfer/chain of custody form or equivalent, for the corresponding section(s) of the chain of custody.

8.2.4 "Apheresis Product Packaging Checklist for INB-400" (**Appendix 3).**

8.2.5 Apheresis product CBC with differential report.

8.2.6 Optional: viability report.

8.2.7 "Apheresis Collection Summary Form" **(Appendix 1).** Particularly, fill out WBC density, unless noted as "results to follow". The "Volume" should match that on the apheresis bag label.

8.2.8 Other applicable documents required by FACT-JACIE standards, applicable local laws, regulations and SOPs.

8.2.9 Optional For Autologous: Subject Eligibility Determination (Institutional form; the actual name of the document may vary).

8.2.9.1 The form should include Summary of records used to make the subject eligibility determination, Name and address of the site that made the subject eligibility determination.

8.2.9.2 Note: For AUTOLOGOUS, a subject eligibility determination is not required by the FDA. However, if any subject screening or testing is performed and risk factors or reactive test results are identified, accompanying documentation shall be provided [per FACT-JACIE standards].

8.2.10 NOTE: While some of the above information might have been sent electronically, we request that the collection facility provide them in hard copies accompanying the products, if possible, to ensure the most current copies are readily available to the manufacturing site's personnel, and to comply with FACT-JACIE standards. **If it will delay shipping, the results of the CBC w/ Diff may be sent electronically before the end-of-day on the collection day.**

8.2.11 NOTE: ALL IN8bio forms MUST BE COMPLETELY FILLED OUT. N/A FIELDS THAT ARE NOT APPLICABLE. DO NOT LEAVE BLANKS.

8.2.12 NOTE: All reports and documents must be complete. For data integrity and good documentation practice, please ensure reports are not partially scanned and /or cut-off.

9. Collected Product Temporary Storage (Optional, ONLY needed if Courier does not pick up the apheresis product immediately after collection)

9.1 The apheresis bag is to be stored in the shipping packaging at room temperature, **15 to 25°C** until pick up by the courier. **DO NOT REFRIDGERATE THE APHERESIS PRODUCT**.

9.2 The product should be received at the manufacturing facility **within 36 hours** of collection end time. It is the Collection site, CryoPort, and the Manufacturing Site's responsibilities to ensure the collected apheresis product is stored and transported in the proper conditions when the product is in their custody.

10. Apheresis Product Packaging and Transportation by CryoPort

10.1 The apheresis product and accompanying documentation should be transported to IN8bio as soon as possible. Shipping arrangements and apheresis collection dates will be scheduled and confirmed by Syneos following patient enrollment and manufacturing slot scheduling.

10.2 The documentation described above will accompany the apheresis product.

10.3 CryoPort will receive from Syneos the key clinical site personnel contact information and the pickup address / preferences. Following the coordination and confirmation of the shipping dates, the pre-conditioned (15 to 25°C) validated room temperature shipper listed above will be delivered to the collection facility the morning of the collection. Instructions on how to load the sample and prepare the shipper for pickup by Cryoport can be found in **Appendix 3**.

10.4 Syneos will coordinate the pickup with Cryoport, and will notify IN8bio and the manufacturing facility about the shipment and tracking information.

11. Communications between trial site, Syneos and IN8bio

11.1 Manufacturing Request (**Appendix 4 of this manual**):

11.1.1 Following apheresis scheduling **AND** the final patient pre-screening**, IN8bio Operations fills out the key information** in section 0 of this form, including but not limited to: Subject ID, involved sites/facilities, intended collection date.

11.1.1.1 NOTE: refer to the clinical site's "INB-400 Dose Prep Equipment and Material Checklist", to select whether Dose Prep ISBT 128 labels should be made by IN8bio or the Dose Prep Site. Such **Labels should be requested to be pre-printed by IN8bio, ONLY IF the clinical site specifically noted in this assessment that they do not have the capability to print the required ISBT 128 labels**. All other clinical sites should print their own Dose Prep labels.

11.1.1.2 IN8bio Operations will then circulate this form to the relevant institutions / departments for electronic signatures, and complete it **no less than 5 business days** before the intended collection date.

11.1.1.3 This form is only to be completed upon the final patient pre-screening prior to apheresis and NOT at the time of initial identification and pre-screening activities, **no more than 10 business days** prior to scheduled apheresis.

11.1.2 **Clinical Site Requesting Physician / PI signs to confirm the request.** If there is any incorrect information, it should be resolved with Syneos before signing.

11.1.3 The form is routed to the following facilities/units simultaneously. Each unit's representative shall sign to acknowledge the responsibilities listed on the manufacturing request for the patient.

11.1.3.1 Collection Site's Apheresis Unit

11.1.3.2 Collection Site's Responsible Release Unit

11.1.3.3 Manufacturing Facility

11.1.3.4 IN8bio

11.1.4 IN8bio Operations must ensure a completed copy is sent to all parties AND IN8bio Logistics team (DL_IN8bio_logistics@syneoshealth.com).

11.2 Collection site must confirm collection date and patient scheduling with the study team by email via the logistics distribution list **DL_IN8bio_logistics@syneoshealth.com** at least **5 business days prior** to the collection. If a change in the collection schedule occurs, the collection site must notify the study team as soon as possible to allow the sponsor to attempt to shift the manufacturing dates, which may not be possible.

11.3 If a collection schedule is changed due to unforeseen circumstances, trial site staff must also notify IN8bio by the above method as soon as possible. Please note that **IF** the manufacturing facility is unable to accommodate the change in schedule, the patient may not be able to continue on the trial. It is critical that IN8bio Operations has as much lead time as possible to attempt to find a date that can be accommodated.

12. APPENDICES RELATED FORMS

Please see appendices in the appendices pages (after the "Revision History" section).

13. REVISION HISTORY

Version #	Last Revised by/Date	Approval by/ Date	Effective Date	Summary of Revision/ Review Activity
01	Guoling Chen, Marsia Silletti, Stacey Bilinski/ 2023JAN23	Kate Rochlin, Trishna Goswami/ 2023 JAN 23	2023 JAN 23	New manual with 3 appendices.
02	Guoling Chen, Marsia Silletti, Stacey Bilinski, Kate Rochlin / 2023 OCT 10	Trishna Goswami, Jessie Ann Flaim-Spetsas / 2023 OCT 10	2023 OCT 11	Updated section 7 to clarity the collection goal, the cell count is for "MNC" and the upper limit of the apheresis product is 200mL instead of 150mL, also updated Appendix 1 accordingly. Updated section 8 (ISBT 128 labelling), to added the HemaTrax MFG label option based on site feedback. Updated Appendix 2 & 3 to allow courier drive signing on the air waybill instead of the Chain of Custody form, based on Shipping Lane Validation feedback. Added Appendix 4, Manufacturing Request Form, added instructions around it in the manual accordingly.
03	Marisa Silletti, Kate Rochlin, Guoling Chen/ 2023 DEC 21	Stacey Bilinski, Trishna Goswami, Jessie Ann Flaim-Spetsas / 2023 DEC 21	2023 DEC 22	Updated the "collection goal" section: Added "corresponds to 2 to 4 blood volume" to reflect current practice; deleted "minimum 25 to 50x10^6 MNC cells/mL" to avoid excess testing and to maintain un-accessed sample port for MFG process. Added clarity regarding saving the sampling ports and clearing the tubing of the apheresis bag at the collection site. Section 8.2.3, added instructions to "N/A" fields in Appendix 2 related with CryoPort, IF the apheresis collection, MFG, and Administering are at the same institution, and the use of institutional forms. In section 11.1.1.1, added clarity regarding how the clinical site can request/ communicate the Dose Prep ISBT 128 labels to be pre-printed by MFG Site. Removed "Circular of Information booklet" from the minimum accompanying documents list, in Appendix 3 and in the Apheresis Manual, based on lane validation feedback from sites and CryoPort.

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Version #	Last Revised by/Date	Approval by/ Date	Effective Date	Summary of Revision/ Review Activity
(see previous page)	(see previous page)	(see previous page)	(see previous page)	In Appendix 1: Removed the MNC density goal to align with manual revision. Removed "subject ID" field avoid confusions during this autologous arm of the trial. In Appendix 2 (Chain of Custody): deleted "Subject ID" field. In Appendix 3 (Packaging Checklist): Deleted the "Subject ID" field; deleted the generic CryoPort packaging image, added detailed instructions instead; in the "ship to MFG Facility" field, deleted the "UAB" "UofL DCTC" checkboxes, added text "enter Facility name and Ship-To address as it appears on the Shipper Order Details email from Cryoport", based on logistic team feedback.
04	Marisa Silletti, Kate Rochlin, Guoling Chen/ 2024 JUN 17	Stacey Bilinski, Trishna Goswami, Jessie Ann Flaim-Spetsas / 2024 JUN 17	2024 JUN 18	Removed "Fenwal Amicus Separator" from the Apheresis machine list, and the associate sections and language around it, because "Terumo Spectra Optia" is the only apheresis device used in all current enrolled sites, and the technical instructions provided in this manual is for Spectra Optia. Added section 7.3 to cover specific recommendations for troubleshooting, alarm management, clumping, AC ratio and CP settings, updated proper collection set catalogue number, per consultation with Terumo BCT. Clarified subject Identity verification should follow institutional procedures. Added the definition of "Lot number" and its format, and that it is required on the apheresis label, to align with the current label format. Added the definition of "UTC" and "Total Product Volume" for clarity. Clarified the definition of collection end time. Clarified apheresis product labelling instruction: Added the collection date/time format, and the entry of "UTC" time. Clarified the word "Subject ID" is required in the "COI" field on the label. Section 7.4: added clarity on MNC bag's sample bulbs and tubing handling. Section 7.1 & 7.5: updated collection goal: Removed "should not exceed 200mL", changed to "~175 to 200mL collection volume is recommended", based on sites feedback. Emphasized Good Documentation practices and data integrity, all IN8bio forms must be completed filled out

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(see previous page)	(see previous page)	(see previous page)	(see previous page)	and leaving no blanks, and that documents should not be partially scanned or cut-off. Updated Appendix 1, "Flow Speed" changed to "Flow Rate" to align with Spectra Optia's terminology. Added Lot number field. Removed MNC density field to align with manual edit, based on site feedback and observations. Added instruction to add "apheresis product", DIN, subject ID to all reports pages. Clarified date format to be yyyyMMMdd. Updated Appendix 3: added "Lot" field. Reduced initials needed, changed to check boxes. Simplified form layout, separated required and Optional accompanying documents. Revised Appendix 4 (MFG Request) to reflect that Operations Director circulates this form and not Syneos, and clarified that IN8bio makes Dose Prep labels, not MFG Site. Other edits for conciseness and clarity.

Title: IN8bio INB-400 Apheresis Collection Summary Form	
Document Number: INB-400 Apheresis Manual Appendix 1	**Version:** 04
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IN8bio INB-400 Apheresis Collection Summary Form

NOTE: If an institutional form is in use, please complete this form as well, and please **ONLY** send **THIS** form with the apheresis product to the manufacturing site.
Please N/A sections if not applicable. Do not leave blanks. All Date Format is yyyyMMMdd.

Apheresis Date (yyyymmdd)	_ _ _ _ / _ _ _ / _ _	**Lot number** (Used on the ISBT 128 Label)	_ _ _ _ _ _- 400 -_ _ _ - _ _ _
DIN		**Recipient Subject ID**	INB400 -_ _ _ - _ _ _

Apheresis Device and Collection Information	**Manufacturer**	**Model**	**SN**	**PM due date** (yyyyMMMdd)
				_ _ _ _ / _ _ _ / _ _
	Total Blood Volume Processed (L)	_ _ . _	Flow Rate (mL/ min)	_ _
	Collection **Begin** Time (24hr), Time Zone	_ _ : _ _, _____	Collection **End** Time (24hr), Time Zone	_ _ : _ _, _____
	Post Collection Apheresis Product Volume		_ _ _ _ mL (Goal: ~175 to 200mL)	
	Was the collection goal met?		☐ YES ☐NO, Explain: _____	
	Performed by	**Print**	**Sign**	**Date** (yyyyMMMdd)
				_ _ _ _ / _ _ _ / _ _

Critical Reagents	**Manufacturer**	**Catalogue #**	**Lot #**	**Exp date** (yyyyMMMdd)
ACD-A				_ _ _ _ / _ _ _ / _ _
Other:_____ (Please N/A row if none)				_ _ _ _ / _ _ _ / _ _

Additional Apheresis Product Sample Testing
(Please add "Apheresis Product", Subject ID, DIN, on EACH report page.)
(*Please send results **DL_IN8bio_logistics@syneoshealth.com** when available.)

	Sample Taken? (circle one)	**Test Result**	
CBC with Diff (Required)	Y / N	WBC ____ ×10^6/mL	☐ Results to follow*
Viability	Y / N	_____%;	☐ Results to follow*
Other: _____(Please N/A row if none)	Y / N	_____;	☐ Results to follow*

NOTE: Please verify that the product label is complete and accurate, applicable tie tags are present.

Recorded by	**Print**	**Sign**	**Date** (yyyyMMMdd)
			_ _ _ _ / _ _ _ / _ _

TG	GC	KR	MS	SB	MF
6/17/2024	6/17/2024	6/17/2024	6/17/2024	6/17/2024	6/17/2024

IN8bio **Confidential and Proprietary** **Apheresis Manual Appendix - Form**

Title: Chain of Custody Form for INB-400	
Document Number: INB-400 Apheresis Manual Appendix 2	**Version:** 04
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Recipient Subject ID	INB400- _ _ _ - _ _ _	**DIN** (use sticker if available)	

NOTE: IF MFG is not occurring at the clinical site, the entire form must be completed.
IF Apheresis collection, MFG, Administration occur at the same institute, N/A (1), (2), (3) (4); record on **institutional shipping / transfer/ chain of custody form** or equivalent, and **attach to this form.**

Status		Facility	Activity	Room #	Print	Sign	Date	Time (24hr) Time zone	# of bags	# of vials
Fresh	End of Collection	Collection Site: ___	For Hand-off between Apheresis Unit and institution Cell Lab (if applicable), refer to collection site's internal records.							
	(1) Picked up by Cryoport		Packed for Release to Cryoport by collection site: (✓ one) ☐ Cell Lab ☐ Apheresis Unit				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		
			Collection Site: Please file Cryoport air waybill with Cryoport pick-up hand-off signatures, date, time. Also retain a photocopy of this form until receiving the completed copy back from the MFG site, and receiving the Cryoport record from IN8bio. **Cryoport order#** _____							
	Received at MFG Site	Manufacturing (MFG) Facility: ___	Received and verified by MFG				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		
			(2) MFG site: File Cryoport record with Cryoport delivery hand-off signatures, date, time.							
Cryopreserved	**End of MFG** (LN2 Storage Begins)		Stored in MFG site LN2 by				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		Product: ___
			MFG site LN2 Storage Verifier				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		QC: ___
	(3) Release to Trial Site		Released to Cryoport by MFG				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		Product: ___
			MFG site: Please file Cryoport air waybill with Cryoport pick-up hand-off signatures, date, time. Also retain a photocopy of this form until receiving the completed copy back from the Trial Site, and receiving the Cryoport record from IN8bio. **Cryoport order#** _____							
	(4) Receipt and storage at Trial Site	Trial Site: ___	Received by Trial Site				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		Product: ___
			Inspected & stored in Trial Site LN2 by				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		
			Trial Site LN2 Storage Verifier				_ _ _ _/ _ _ _/ _ _	_ _:_ _, _____		
			Trial site: Please file Cryoport air waybill with Cryoport delivery hand-off signatures, date, time.							
Thawed	**Administration**		For hand-off at bedside for injection, refer to Trial Site's internal documentation and dose prep records.							

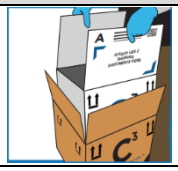
TG	GC	KR	MS	SB	MF
6/17/2024	6/17/2024	6/17/2024	6/17/2024	6/17/2024	6/17/2024

Apheresis Manual Appendix - Form

Title: Apheresis Product Packaging Checklist for INB-400	
Document Number: INB-400 Apheresis Manual Appendix 3	**Version:** 04
Effective Date: 2024JUN 18	**Page:** 1 of 2

Human Cells for Further Processing. Handle with Care. Desired Transport Temperature: Room Temp (15 to 25°C)					
Subject ID	**INB400 - __ __ __ - __ __ __**	**DIN**		**# of bags**	
Lot	**_ _ _ _ _ _ - 400 - _ _ _ - _ _ _**				

Ship from Collection Facility		**Ship to Manufacturing Facility** (Enter Facility name and Ship-To address as it appears on the Shipper Order Details email from Cryoport)	

#	Steps (Packaging by Collection Facility personnel)	Performed: (Initials) _____	Verified: (Initials) _____
P1	Confirm there is no damage to the outer brown shipping box received. Remove the inner white box from the outer brown box by pulling up on the 2 flaps. Discard the outer brown box. 	☐	☐
P2	Open the white box and confirm it has not sustained any damage. Set aside the documents and accessories that are inside, including (1) a custom label with the IN8bio logo, (2) Exempt Human Specimen Label, (3) red tamper-resistant serialized tape. **NOTE the Serial Number of the included serialized tape here:_____**	☐	☐
P3	Verify the **completeness and accuracy** of the cell product label, tie tags and accompanying documents. **EVERY page** of accompanying documentation must have the **DIN and Subject ID**, and the writer's initials and date for any free text added. Please ensure **PHI is redacted**. **Required Accompanying documents:** (please ✓ or explain) ☐ IDM results with interpretation ☐ ABO/Rh ☐ Chain of Custody Form (emailed by Syneos) ☐ Apheresis Collection Summary Form ☐ Apheresis product CBC (please check if results to follow ☐) **Optional:** (✓ or N/A, do not leave blank) ☐ Viability ☐ Donor Eligibility Determination / Screening Summary	☐	☐
P4	Locate the Cryoport air waybill on Flap "A" of the white shipping box. Confirm it accurately shows the **name, address, contact person, and phone number** for both the "Ship-from" and "Ship-to" facilities listed at the top of this checklist.	☐	☐
P5	Confirm **integrity** of the apheresis bag and product (e.g., no clumps, no signs of contamination, no leaks to the bag and tubing).	☐	☐
P6	Log into **Cryoportal®** to access the **Live View** function by following the provided web link on the Shipper Order Details provided by Cryoport via email. The shipper's Internal Temperature should be within **15° to 25°C**.	☐	☐

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Title: Apheresis Product Packaging Checklist for INB-400	
Document Number: INB-400 Apheresis Manual Appendix 3	**Version:** 04
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Human Cells for Further Processing. Handle with Care. Desired Transport Temperature: Room Temp (15 to 25°C)

Subject ID	**INB400 - __ __ __ - __ __ __**	**DIN**		**# of bags**	
Lot	**_ _ _ _ _ _ - 400 - _ _ _ - _ _ _**				

#	Steps (Packaging by Collection Facility personnel)	Performed: (Initials) _____	Verified: (Initials) _____
P7	**Recommended, but not required:** Using an Infrared Thermometer or equivalent, measure the temperature of the apheresis product: _ _ . _°C OR ☐ N/A – this step was not performed.	☐	☐
P8	Remove the silver cooler lid. Be sure not to puncture the box. Remove the Phase Change Panel.	☐	☐
P9	Place the apheresis product into the provided Safepak® and ensure it is sealed.	☐	☐
P10	Place the Safepak® into the chamber of the shipper and surround it with the provided bubble wrap. Ensure the bottom the product itself makes contact with the thermoprobe at the bottom of the chamber. The bubble wrap should surround all sides of the product except for the bottom, so as to not interefere with temperature monitoring of the product. Replace the **Phase Change Panel** and the silver cooler lid.	☐	☐
P11	Adhere the custom label with the IN8bio logo and Exempt Human Specimen Label from Step P2 to the outside of the white shipping box.	☐	☐
P12	Complete the first row shaded in yellow of the ***Chain of Custody Form for INB-400***, along with the Collection Site name along the left, and the Cryoport order # below. Make a copy of all accompanying documents listed above, **including this checklist once completed**, and retain the copies at the collection site. Put the original copies of the **accompanying documents, including this completed checklist**, inside the prepackaged envelope provided on top of the silver cooler lid. Close the flaps of the box, MAKING SURE TO HAVE FLAP "A" SHOWING ON THE OUTSIDE OF THE BOX.	☐	☐
P13	Seal the box using the provided red tamper-resistant **serialized tape** that was documented in step P2.	☐	☐

	Print	Sign	**Date** (yyyyMMMdd)	**Time (24hr), time zone**
Packaged by			_ _ _ _ / _ _ _ / _ _	_ _ : _ _ , _____
Verified by			_ _ _ _ / _ _ _ / _ _	_ _ : _ _ , _____

IN8bio

Form

Title: DeltEx DRI Manufacturing Request for INB-400	
Document Number: INB-400 Apheresis Manual Appendix 4	**Version:** 02
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By signing this form, the signers acknowledge that the information in this form is correct.

Part 0: IN8bio Operations Director: circulate this form to obtain electronic signatures. Send the completed form to all parties AND IN8bio Logistics team (DL_IN8bio_logistics@syneoshealth.com). This form is circulated by:						
IN8bio (Title)		**Print**		**Sign**	**Date**	
Subject ID	**INB400 - __ __ __ - __ __ __**		**Intended Collection Date** (yyyyMMMdd)	_ _ _ _ / _ _ _ / _ _		
Collection Product Type	MNC-A		**Collection Site**			
Transportation condition from Collection to MFG	Room Temp (15 to 25°C)		**Manufacturing (MFG) Facility**			
Manufacturing Request	INB-400 Autologous DeltEx DRI Cryopreserved (≤-150°C)		**Clinical Site (Dose Prep)**			
Dose Prep ISBT 128 Labels to be made by (please choose one)	☐ Dose Prep Site	☐ IN8bio				
Part 1: **Clinical Site Requesting Physician / PI**						
Requested by (Title/Role)		**Print**		**Sign**	**Date**	
Part 2a: **Collection Site's Apheresis Unit** [responsible to collect the product, redact PHI on label/ Re-label.]						
Acknowledged by (Title)		**Print**		**Sign**	**Date**	
Part 2b: **Collection Site's Responsible Apheresis Product Release Unit** (Apheresis Unit or Cell Therapy Lab. Syneos to route it to appropriate personnel) [responsible to pick up apheresis product, package and release it to the courier for shipment to the MFG Facility.]						
Acknowledged by (Title)		**Print**		**Sign**	**Date**	
Part 2c: **MFG Facility** [responsible to receive the apheresis product, perform manufacturing, and release it to the courier for shipment to the Clinical Site.]						
Acknowledged by (Title)		**Print**		**Sign**	**Date**	
Part 2d: **IN8bio** (Chief Operating Officer or designee) [responsible to support product manufacturing, testing, and release.]						
Note to MFG Facility: Vector Lot ID to use						
Comments						
Acknowledged by (Title)		**Print**		**Sign**	**Date**	

DS TG	DS GC	DS KR	DS MS	DS SB	DS MF
6/17/2024	6/17/2024	6/17/2024	6/17/2024	6/17/2024	6/17/2024