Cellular Therapy Registry

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A research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin

Objective of CIBMTR Cellular Therapy Initiative

- To study therapies using cellular products for indications other than hematopoietic replacement or recovery.
- To provide an infrastructure to allow long-term follow-up of patients treated with cellular therapy products.

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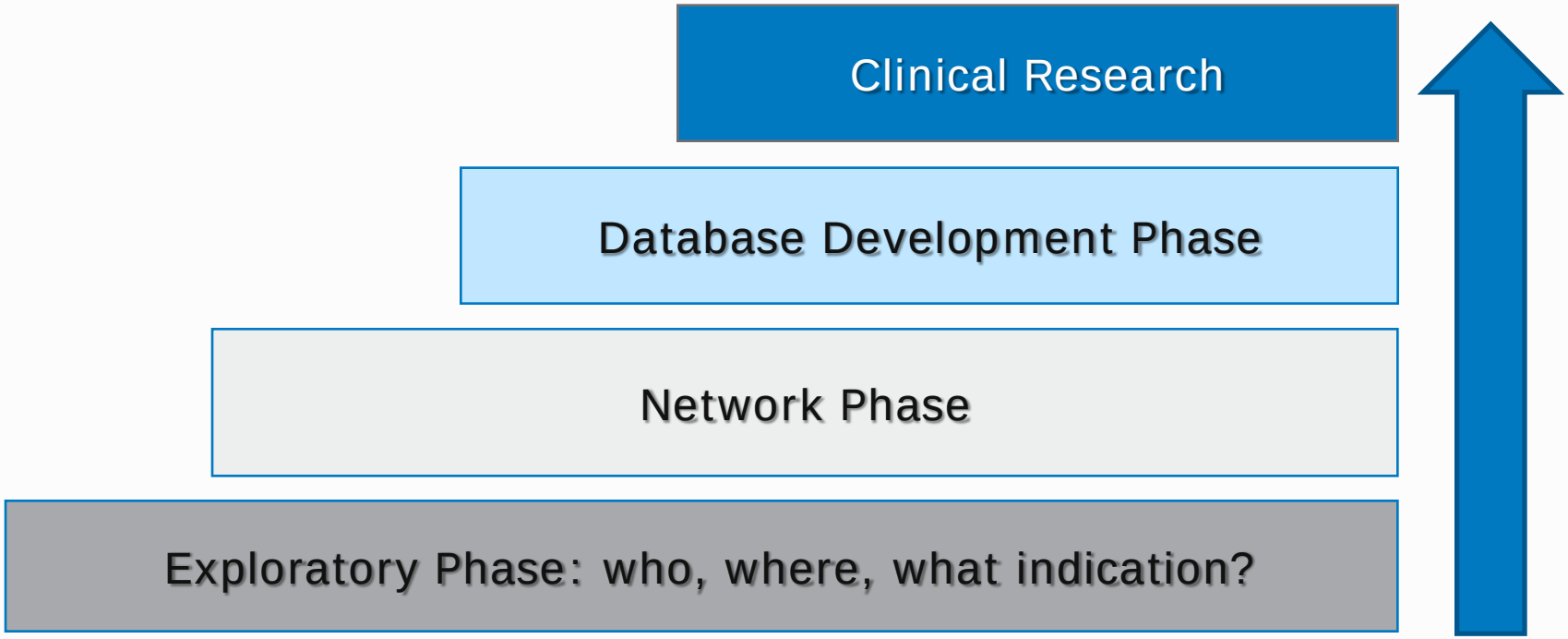
Cellular Therapy Registry Implementation: Phases



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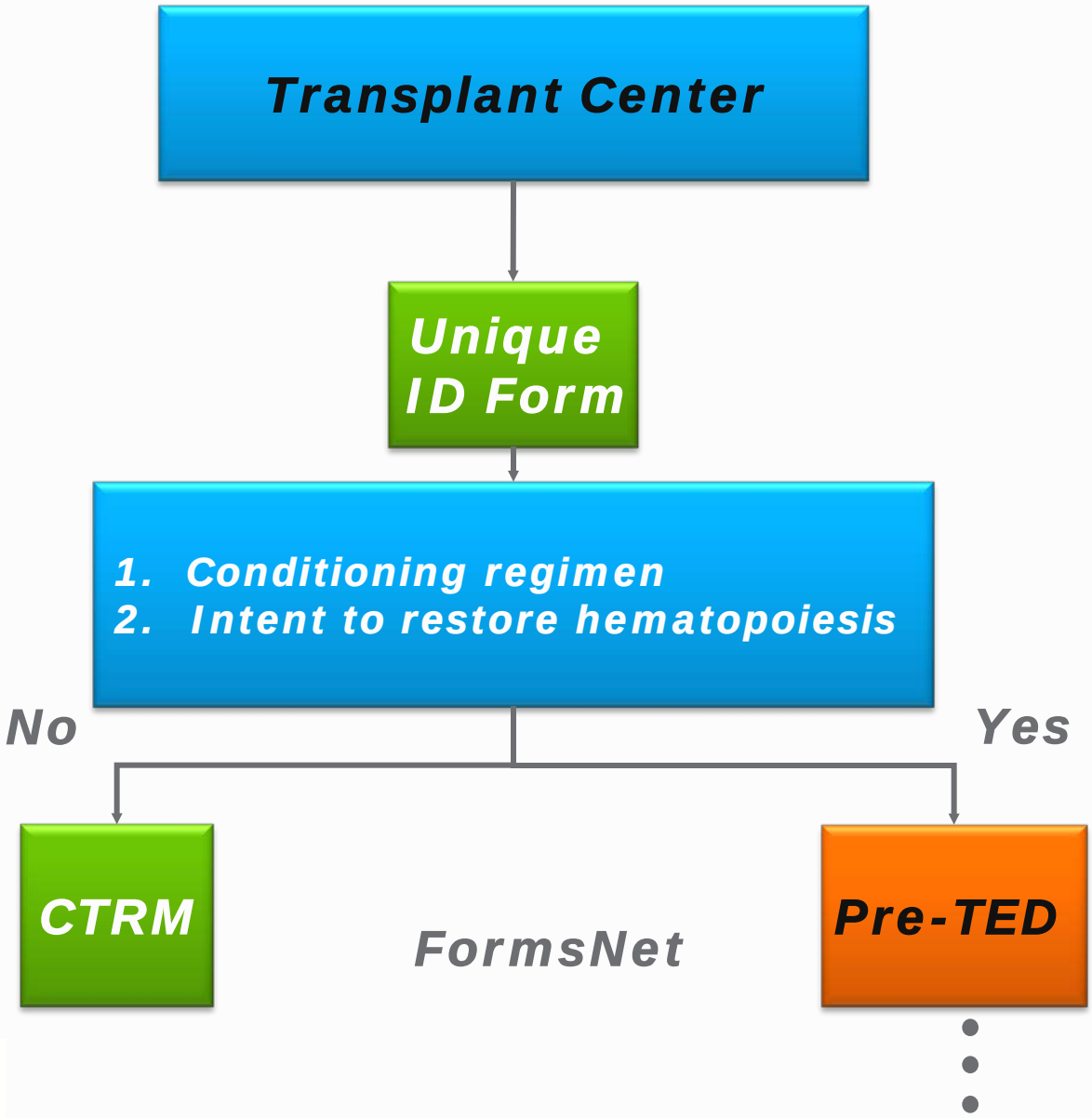

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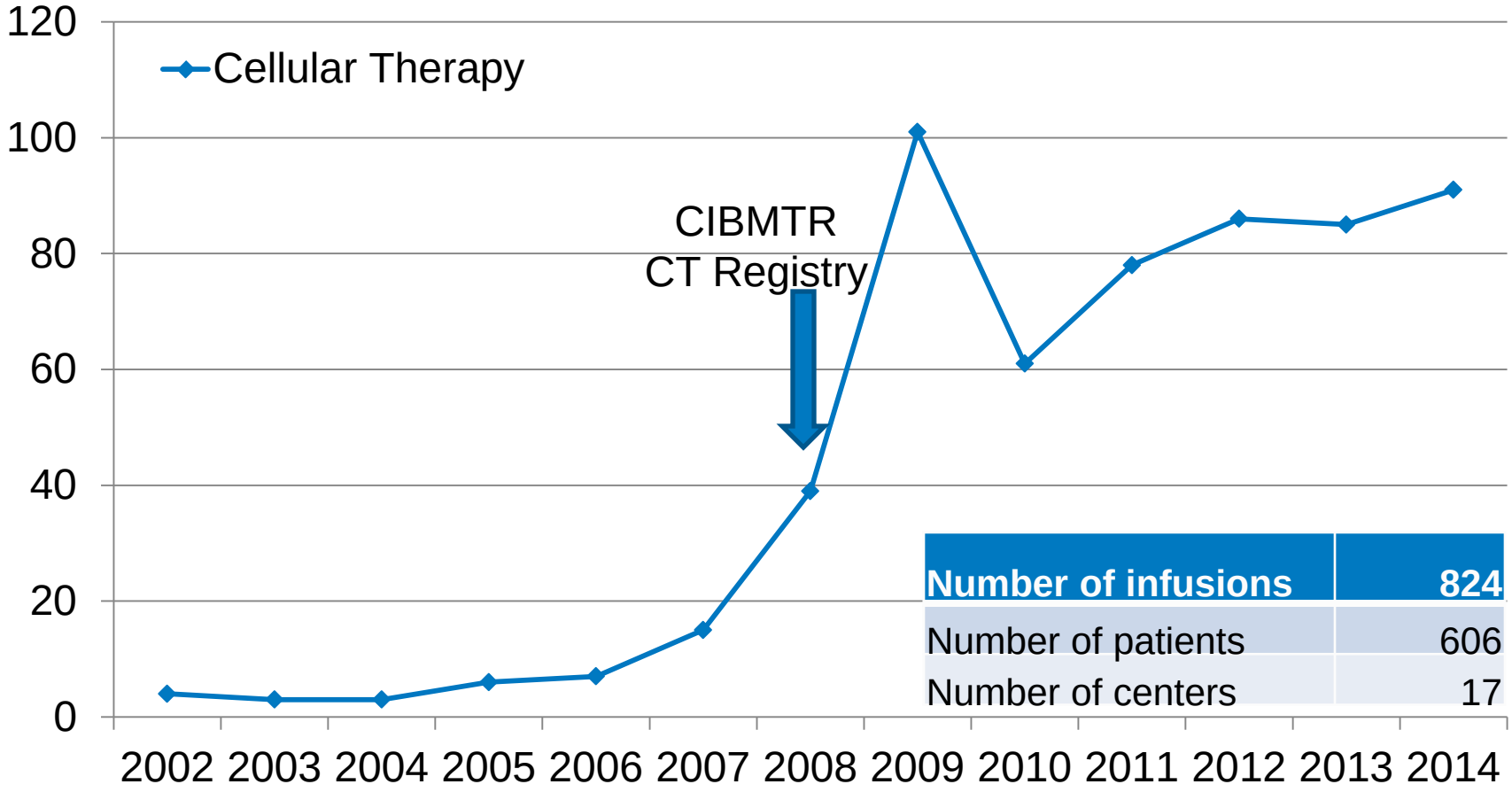
Cellular Therapies Registered with the CIBMTR – 2002 to 2014



Number of infusions	824
Number of patients	606
Number of centers	17

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Cellular Therapies for Registered with the CIBMTR

Characteristics	N (%)
Number of patients	606
Indication	
Neurologic	467 (77)
Cardio and peripheral vascular	85 (14)
Autoimmune disease	1 (<1)
Musculoskeletal disease	1 (<1)
Other	50 (8)
ALL (CAR-Tcells)	**30**
Tissue source	
Cord blood unit	467 (77)
Bone marrow	86 (14)
Peripheral blood	37 (6)
Adipose tissue	4 (<1)
Cardiac tissue	2 (<1)
Pancreatic tissue	1 (<1)
T-lymphocyte	7 (1)
Missing	2 (<1)

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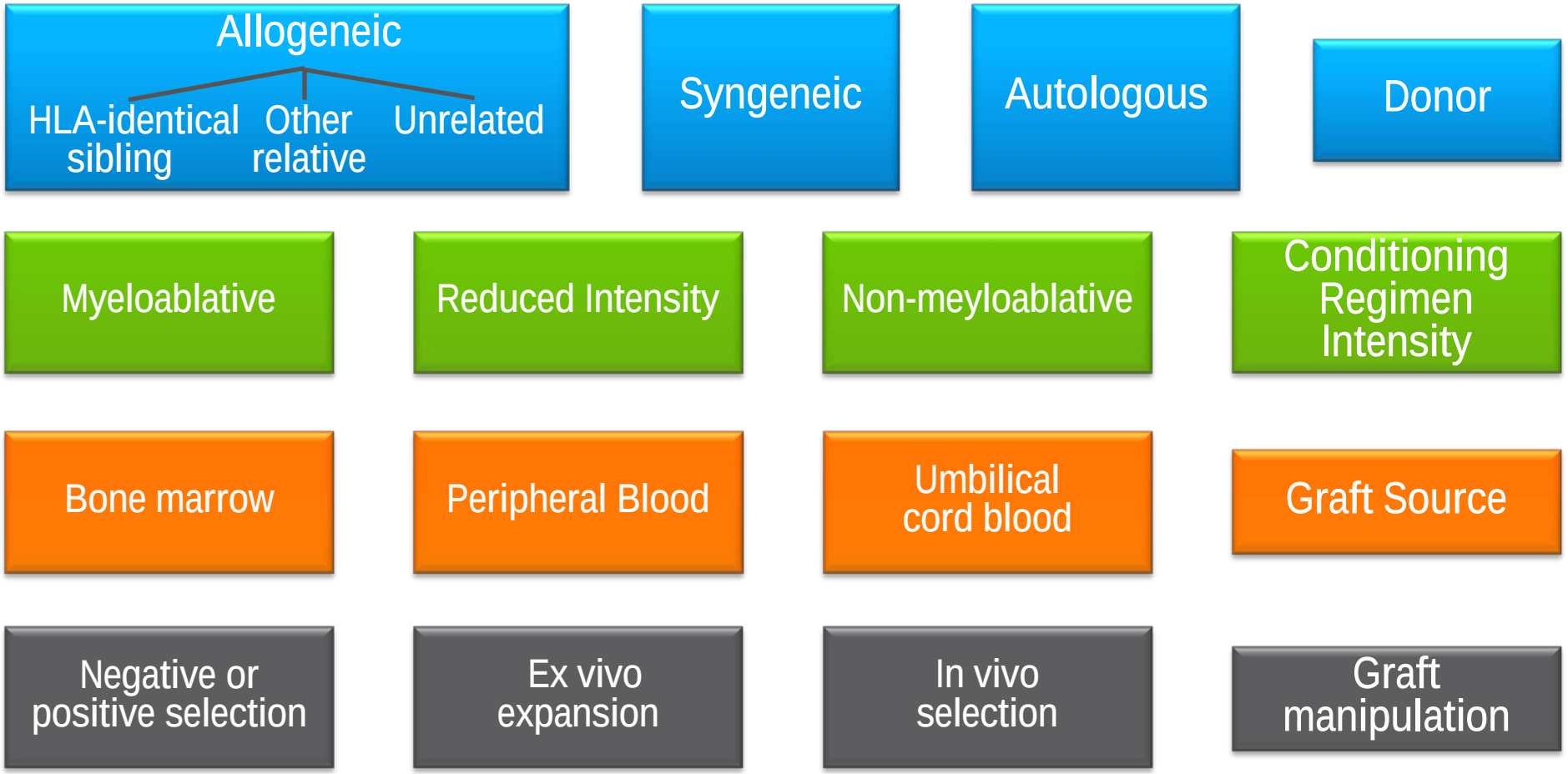
Hematopoietic Stem Cell Transplantation - Classification



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Cellular Therapies - Classification

Autologous Allogeneic Syngeneic	Single vs. Donor Pool	Live or cadaveric	Donor
Tissue Specific	Differentiated Stem cells Progenitor cells	Genetic Modified cells	Cell Type
Bone marrow Peripheral blood	Placenta Cord blood Amniotic Fluid	Cardiac, Skin Liver….	Graft Source
Unmanipulated Selected	Cells in solution	Genetically modified	Graft manipulation
Infusion route	HLA matching	Recipient preparation	Other Classifications

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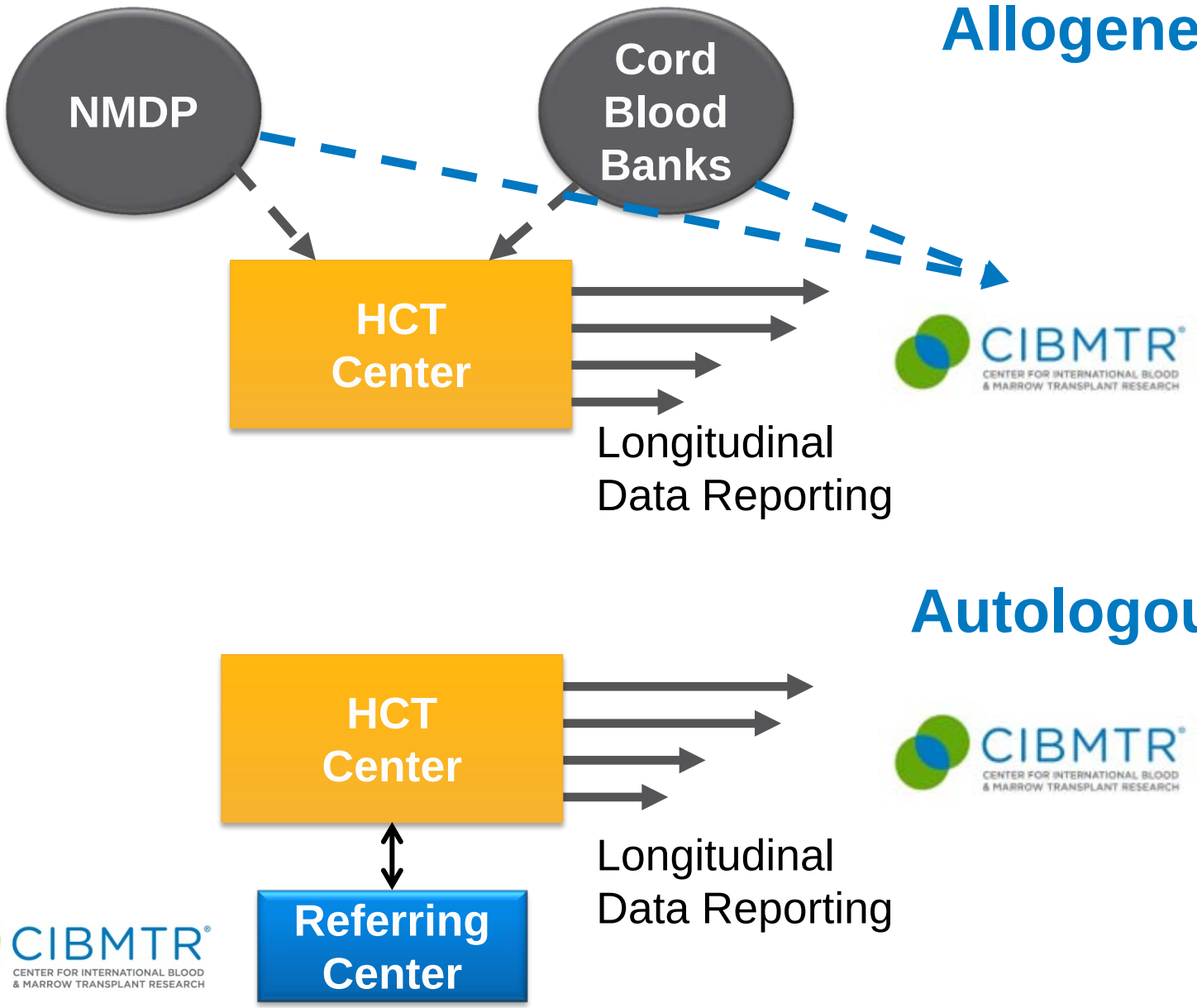
HCT Model


Allogeneic HCT
NMDP
Cord Blood Banks
HCT Center
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Longitudinal Data Reporting
Autologous HCT
HCT Center
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Longitudinal Data Reporting
Referring Center
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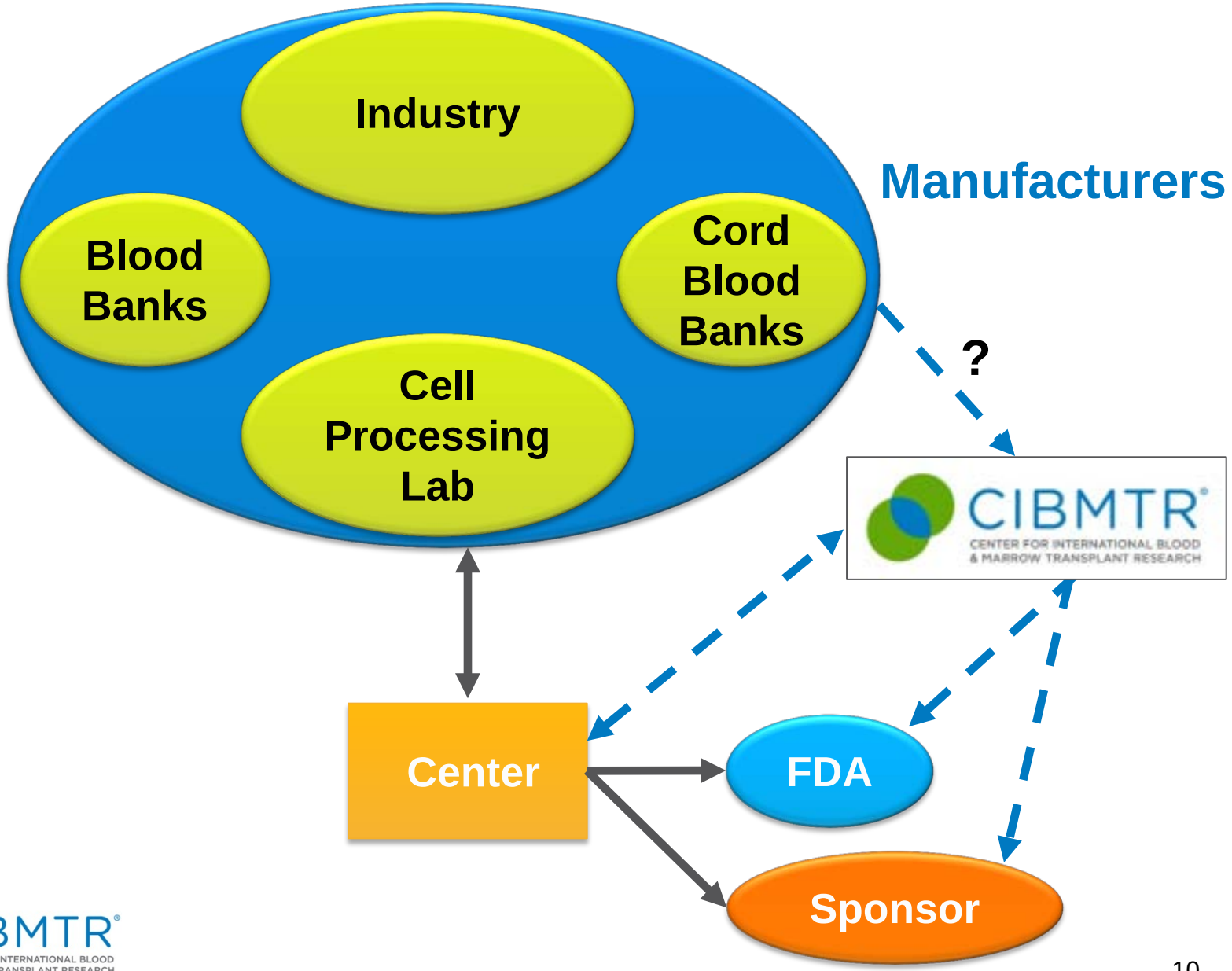
CT Model


Industry
Blood Banks
Cord Blood Banks
Cell Processing Lab
Manufacturers
?
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Center
FDA
Sponsor

Cellular Therapy Task Force - Objectives

- Build upon the existing infrastructure to develop a cellular therapy registry for research purposes
- Develop a cost-effective tool for long-term follow-up for cell therapy trials (centers, biotech, regulatory)
- Increase center participation in this initiative

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Outline of the Registry

- Change the existing form 4000 from CTRM to CTED ("Cellular Therapy Essential Data Form")
- Trigger the pre-CTED whenever a cellular therapy is done, regardless of HCT
- Establish a follow-up structure for submission of post-CTED appropriate to each cellular therapy indication
- Create CRF forms for certain indications
- Develop an infrastructure to support collection and analysis of these data

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CIBMTR Cellular Therapy Registry

- Prioritize certain indications for CRFs:
  - Malignancies (ALL, CLL and others)
  - Infections (Viral infections)
- Prioritize certain products for CRFs:
  - Genetically modified cells
    - Chimeric antigen receptors (CARs) for malignancy
  - Multi-virus-specific T-cells for infection
- But capture any cell therapy that is not a transplant
  - Including Donor Cellular Infusions (DCIs)

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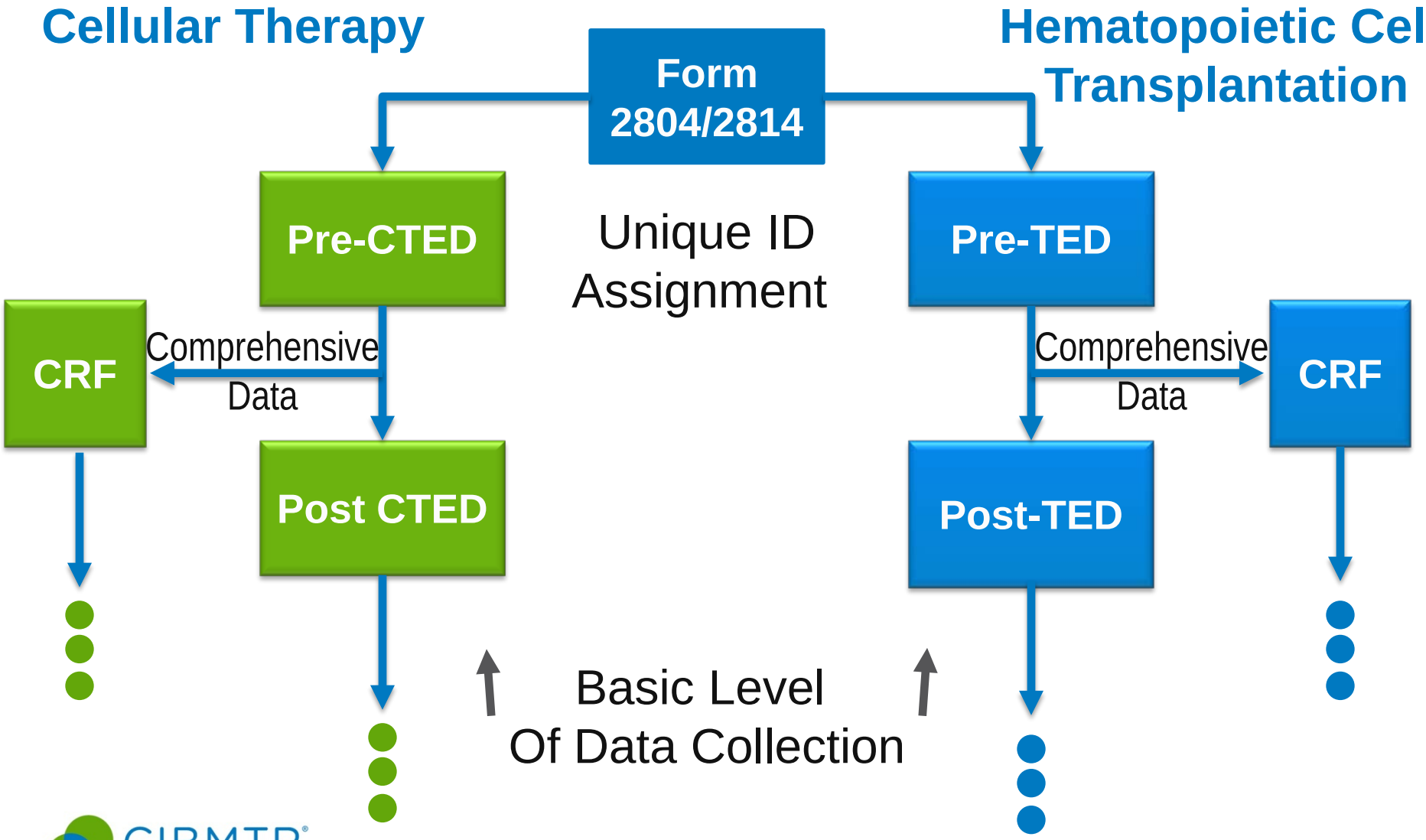
Model for the Cellular Therapy Registry



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CTED Level Data – Applies to all Cellular Therapies

- Pre-CTED: demographic, indications, disease status prior to CT (if applicable) and therapy prior to CT.
- Infusion form: description of the product, information on manufacturing, product analysis and infusion details.
- Post-CTED: follow-up infusions, recipient survival and disease status, cause of death, development of malignancies, persistence of the product, development of CRS.

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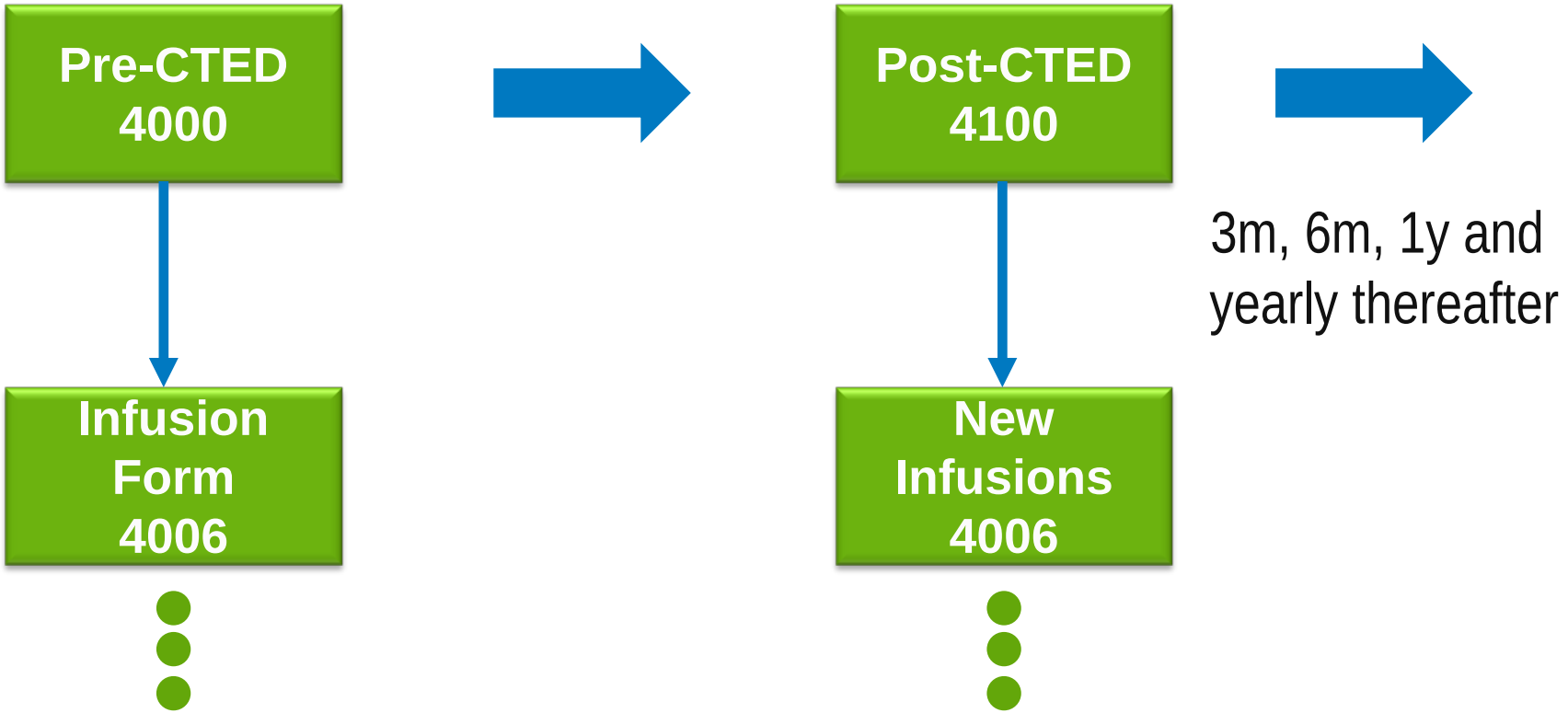
Basic Model for Collection of all Cellular Therapies



For All Planned Infusions

For All Infusions Given: *since the last form*

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CRF Level Data for Cellular Therapies

- Data collected:
  - Disease information and follow-up
  - Infection information and follow-up
  - HLA typing and matching (if applicable)
  - Make use of forms already in existence for HCT
- Case selection:
  - Based on the indication and the cell product utilized

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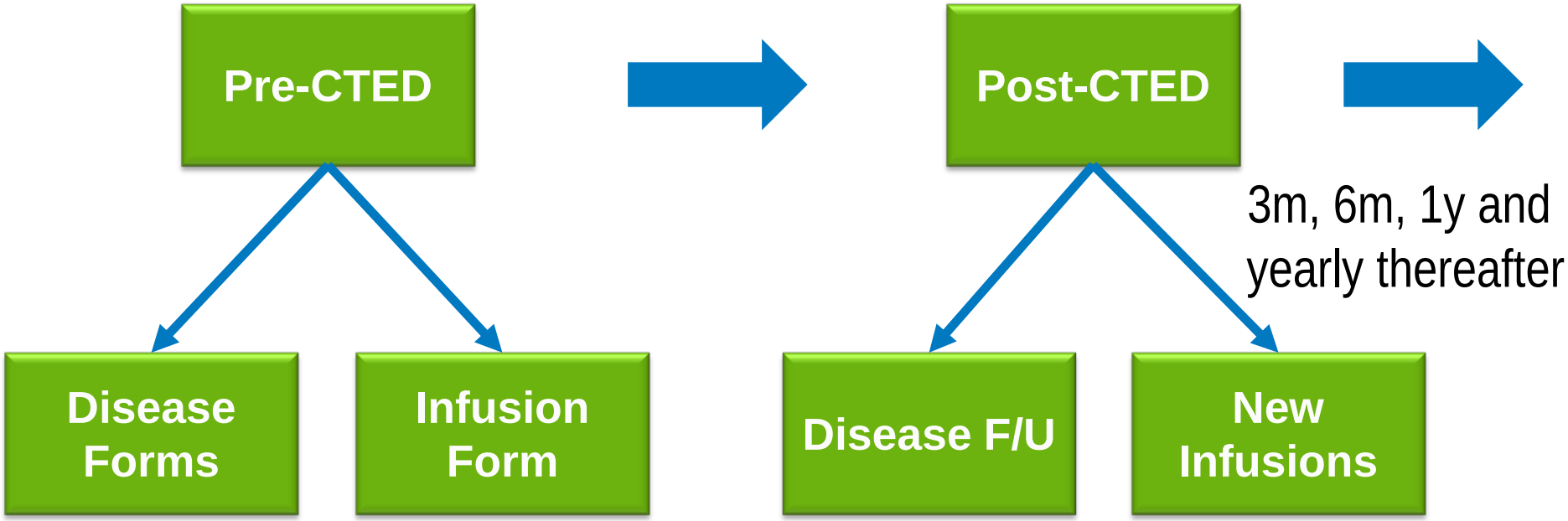
Model for Collection of Cellular Therapy for Hematologic Malignancies



For All Planned Infusions

For All Infusions Given: *since the last form*

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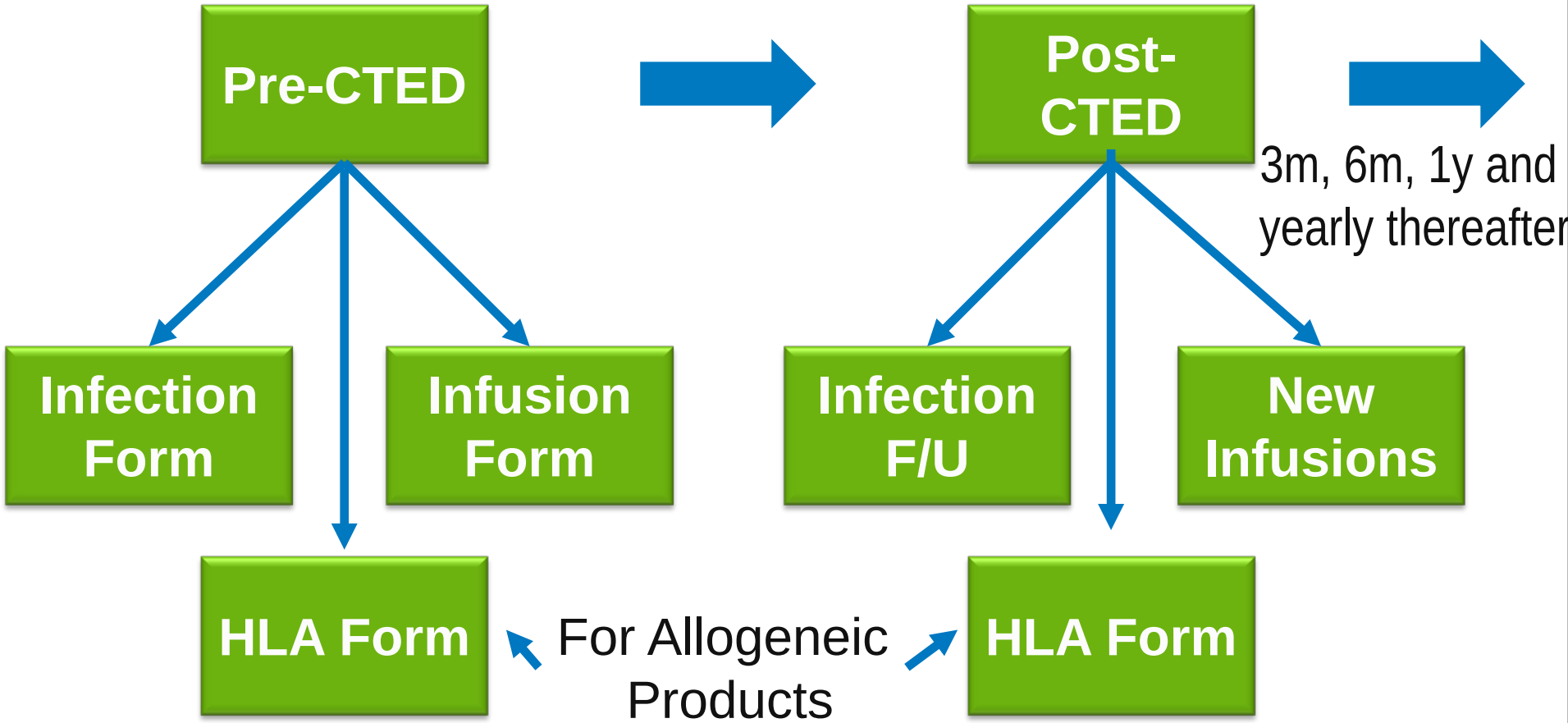
Model for Collection of Cellular Therapy for Infection



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Should all Follow-up be the Same?

- Follow-up will vary according to the type and indication of cellular therapy:
  - Genetically modified cells for any indication
  - Unmanipulated donor lymphocyte infusion after HCT for treatment of infection
  - MSC infusions for treatment of GVHD
  - Third party CTLs
- Example: FDA mandates 15-year follow-up after the infusion of genetic modified cells.

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How to Define a Cell Product? Example CD19-CAR

Donor — **Autologous**

Tissue Source — **Peripheral Blood**

Cell Type — **Lymphocytes: CD8+ cells**

Specific Commercially Available Product

Capture the name of the product

Product ID

Clinicaltrials.gov Number for the Protocol

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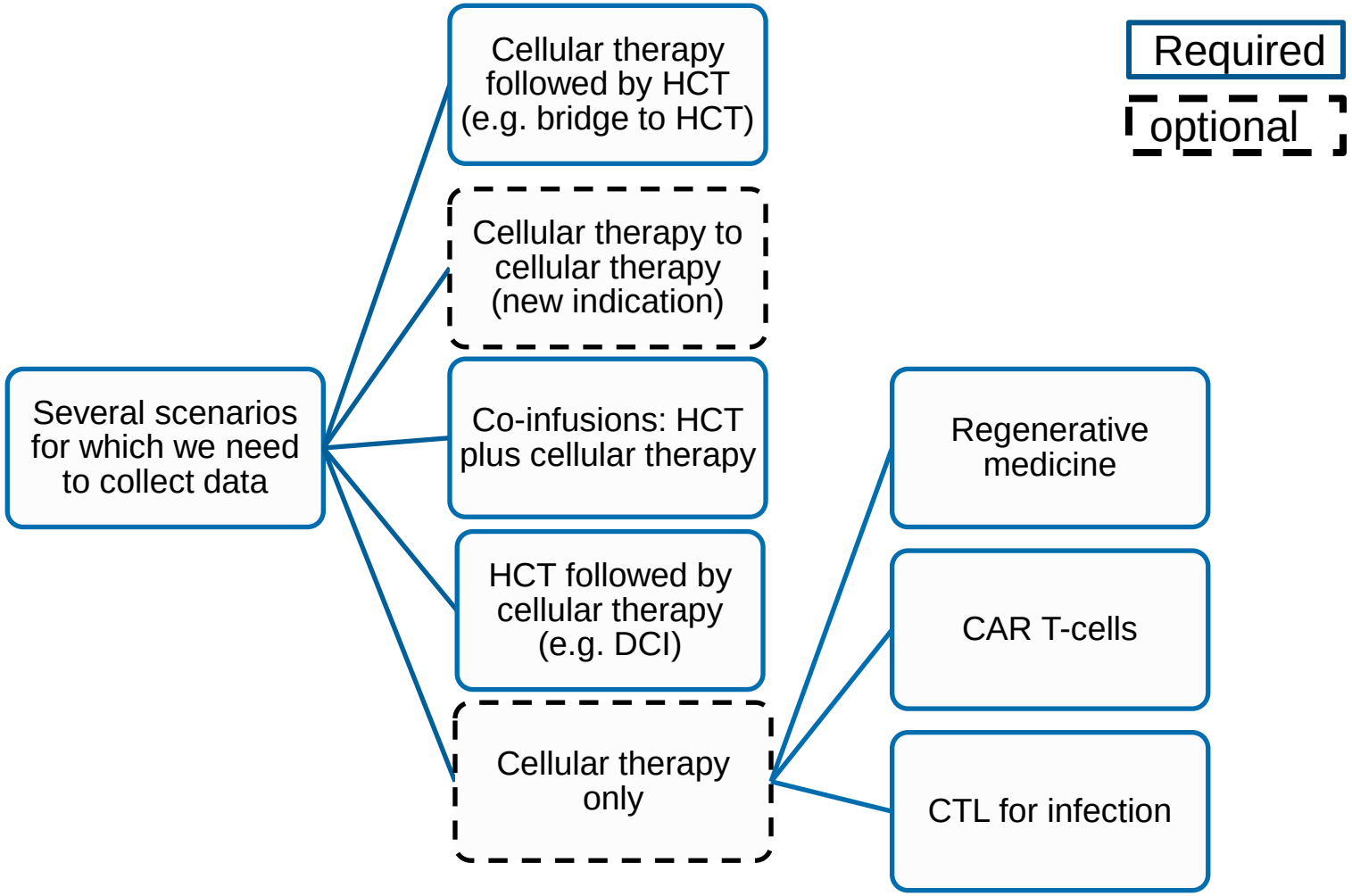
Cellular Therapy Scenarios

- Several scenarios for which we need to collect data
  - Cellular therapy only
    - Regenerative medicine
    - CAR T-cells for malignancy
    - CTL for infection
  - Co-infusions: HCT plus cellular therapy
  - Sequential cellular therapies for same/different indications
  - Cellular therapy followed by HCT (e.g. bridge to HCT)
  - HCT followed by cellular therapy (e.g. DCI)

Cellular Therapy Scenarios



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Data Collection Approach

- Reimbursement similar to HCT
- Pilot data collection at different centers in patients receiving diverse products for diverse indications
- Data collection at centers:
  - Important to include cell processing laboratory;
  - Multiple programs (including HCT program) at a single center
- Implement Data Back to Centers functionality for CT

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Important Issues to Address in Establishing a Mechanism for Long-term Follow-up of Cellular Therapy

- Ability to capture all patients of interest
- Ability to capture all variables of interest
- Ensuring data quality
- Maintaining long-term follow-up
- Ensuring confidentiality, security and regulatory compliance
- Making data rapidly available for multiple users / uses
- Cost-effectiveness

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Important Issues to Address in Establishing a Mechanism for Long-term Follow-up of Cellular Therapy

- Similar to the issues that have been tackled by the BMT community for the past 40+ years
- Effectively addressed by large multi-center, multi-national outcomes registries/research networks dealing with:
  - Similar patient population
  - Interventions with similar issues
- Data accumulated has been used effectively to advance the field
- Represents cost-effective approach since much of the infrastructure already exists

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Additional Issue to be Addressed for Cellular Therapy: Proprietary Data

- Projects under IND / IDE or pharmaceutical cell products
- Data collection will be the same
- Establish embargo plan that would control release of outcome data until agreed upon milestone
- These plans will be protocol or project specific

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Funding

- Infrastructure development, even though it takes advantage of existing systems, is expensive
- Submitting application for administrative supplement to U24
  - Will ask for additional funding in next competitive renewal
- Discussions with several companies
  - Novartis discussions most advanced

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Cellular Therapy Registry Status

- CTED level forms are completed are designed
- Release in FormsNet planned for Summer 2016
- CRF level forms under development
- Next steps:
  - Harmonization with EBMT
  - Develop a protocol for collection of long-term follow-up data for genetically modified cells

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