Labeling of Cellular Products with Unique Product and Patient Identifiers When Products Are Intended for Further Manufacture by a Contract Organization or Study Sponsor

Stakeholder Associations:
AABB
American Association Tissue Banks
American Society for Blood and Marrow Transplantation
Foundation for the Accreditation of Cellular Therapy
ICCBBA

CTLM Meeting
Bethesda, MD
10/19/2016

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CTLM Lead Designate, ISCT North America
Legal & Regulatory Affairs Committee

Agenda

- Why cellular products should not be treated as routine “Off the Shelf” drugs
- Current Labeling Practice for Cellular Products amongst accredited laboratories (AABB, FACT, CAP)
- Labeling workarounds developed for “off-site” manufacturing of novel cellular products
- Examples of near misses
- Request from clinical sites, accrediting agencies, and ICCBBA

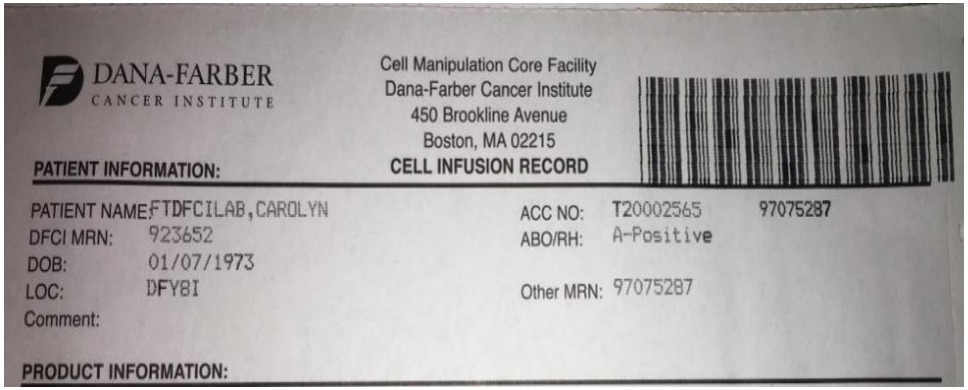
Sources of Cellular Products

- Patient-specific
  - Autologous donors
  - HLA-matched allogeneic donors (related or unrelated)
- Not patient-specific
  - Partially HLA-matched but not an actual “directed” collection, could be considered “Off the Shelf”
- Product identity testing
  - No real time serological or antigen testing to confirm identity of product to a specific patient
  - Serologic HLA testing / matching done weeks prior to collection
- Reliance on labeling and identifiers to confirm identity
  - Matching based on donor / patient identifiers linked to HLA testing results

Bar-coding of Cellular Products and Patient Information for Documentation and Confirmation

Patient Identifier:

Infusing institution's medical record number and patient name bar-coded onto the Cell Infusion Record


DANA-FARBER CANCER INSTITUTE

Cell Manipulation Core Facility
Dana-Farber Cancer Institute
450 Brookline Avenue
Boston, MA 02215
CELL INFUSION RECORD

PATIENT INFORMATION:

PATIENT NAME: FTDFCILAB, CAROLYN
DFCI MRN: 923652
DOB: 01/07/1973
LOC: DFY8I
Comment:

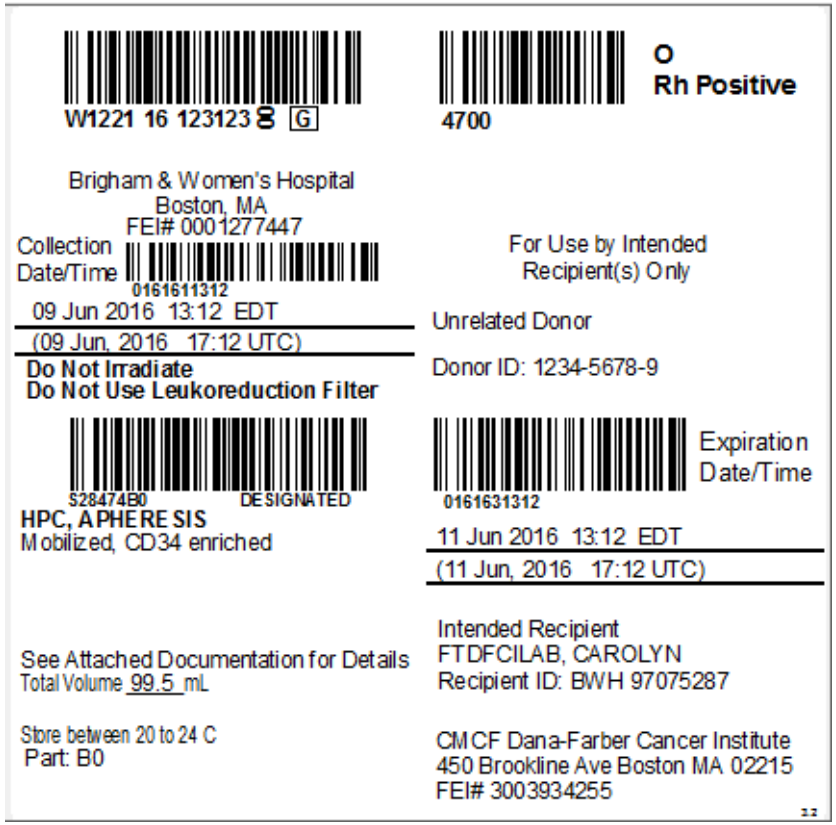
ACC NO: T20002565 97075287
ABO/RH: A-Positive
Other MRN: 97075287

PRODUCT INFORMATION:

- Unique Product number
  - **W1221 16 123123**
  - **Traceability from donor to patient and back in eMR**
- Standard Product Codes
  - **S28474BO**
  - Standard product types in eMR for data gathering, outcomes
- Bar-coding for easy scanning into eMR

Product Identifiers:

All products have:
Unique ISBT compliant product Identifiers ,
Bar-coding of Product Type and modifiers
Bar-coding of Expiration and ABO/Rh


W1221 16 123123 8 G

4700

O
Rh Positive

Brigham & Women's Hospital
Boston, MA
FEI# 0001277447

Collection Date/Time
0161611312
09 Jun 2016 13:12 EDT
(09 Jun, 2016 17:12 UTC)

Do Not Irradiate
Do Not Use Leukoreduction Filter

S28474B0 DESIGNATED
HPC, APHERESIS
Mobilized, CD34 enriched

See Attached Documentation for Details
Total Volume 99.5 mL

Store between 20 to 24 C
Part: B0

For Use by Intended Recipient(s) Only

Unrelated Donor

Donor ID: 1234-5678-9

Expiration Date/Time
0161631312
11 Jun 2016 13:12 EDT
(11 Jun, 2016 17:12 UTC)

Intended Recipient
FTDFCILAB, CAROLYN
Recipient ID: BWH 97075287

CMCF Dana-Farber Cancer Institute
450 Brookline Ave Boston MA 02215
FEI# 3003934255

An Example where Sponsor and CMO will accept PHI
Institutional Labels with PHI can be applies, but PHI is not bar-coded

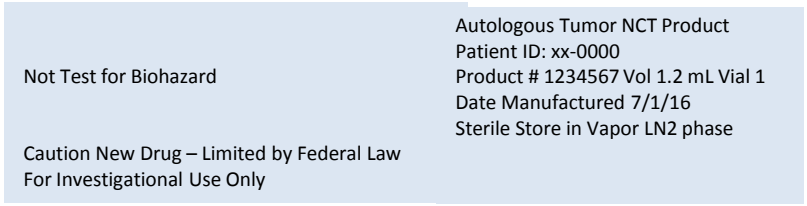
Leukapheresis Collection

PHI (protected health information)

Final Label at Receipt for Infusion

Use of Institutional label applied at collection

Various Labeling Formats and Practices for "Off-Site" / Commercially Prepared Cellular Products



- Label format varies with each company
  - Private manufacturers are not accredited and are not required to followed standard cellular product labeling standards such as ISBT-128
  - Autologous and directed HLA-matched cellular products are being labeled as drug products BUT should be handled as autologous and directed blood products following ISBT-128 format
- Many sponsors refuse to use patient identifiers making it impossible to use without relabeling of product at infusion
  - Unable to scan product into eMR for positive patient identification
  - Those manufacturing under IND often use study numbers that are not a unique number nor can the be found in the patient's eMR
- Products often need to be deidentified when shipped out and reidentified / labeled when received back
  - Increased risk of error in properly linking the product to the intended patient

The Re-Labeling Cycle

Patient Screened

Enrolled

Collection

Shipped to CMO

Product Manufactured

Returned to clinical site

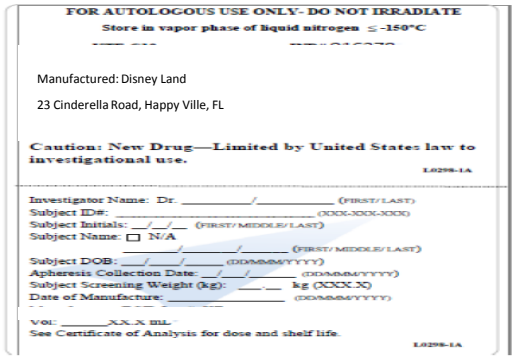
Patient treated / Product stored

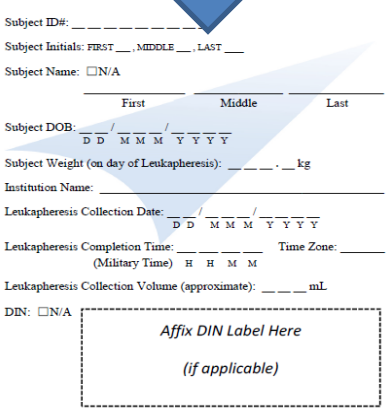
Product infused

Collection through Infusion

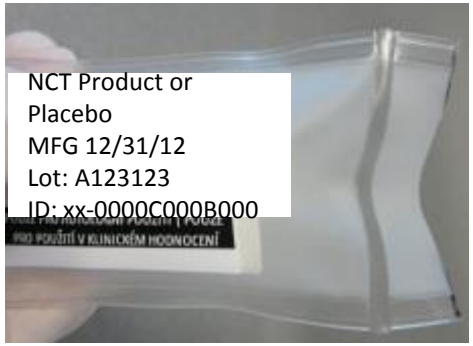
De identified

Re identified





Some Products Require Final Packaging and Relabeling



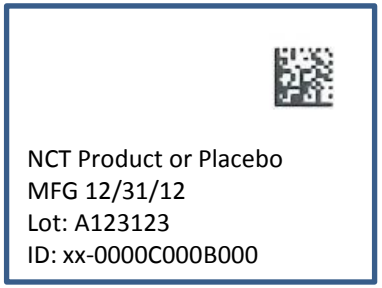


Figure 18: Secondary Label

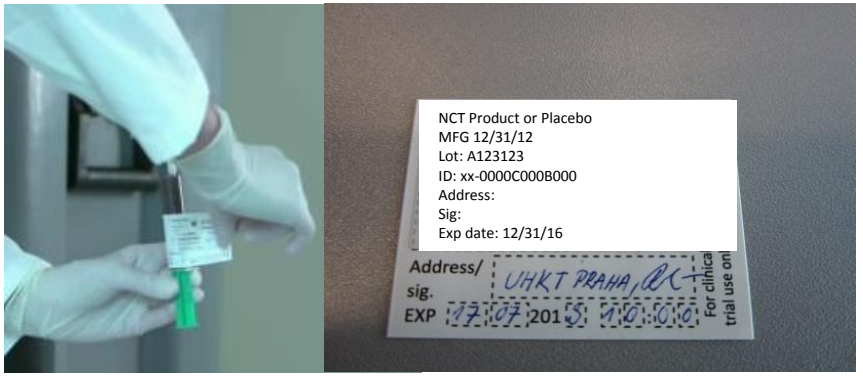
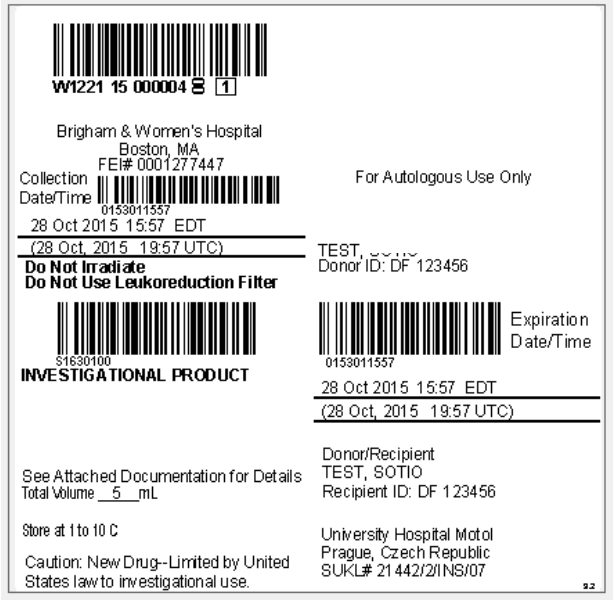


Figure 19: Primary Labels (x3)



Requirements for Infusion / Use

- Accreditation standards & clinical team require:
  - patient's name and
  - two unique identifiers also found in medical record
- To enhance patient safety, the move is to scan the following into the patients e-Medical Record along with the patient identifiers listed above:
  - Product unique identifier / lot
  - Product code and attributes
  - Unique aliquot, if applicable
  - Expiration date and time

Use of Patient Identifiers, HIPAA and Rationale Companies Use to avoid Using PHI

- "Not allowed to have access to PHI, under HIPAA"
  - Especially if product is under an IND
- Legal Statutes
  - Privacy Rule is to ensure that individuals' health information is properly protected while allowing the flow of health information needed to provide and promote high quality health care and to protect the public's health and well being.
  - Authorization of PHI access can be disclosed in consent
  - Language can be added to sponsor / CMO agreements & contracts for use of PHI
  - PHI can be used by third parties for research products if approved by IRB

Example 1 – Near Miss

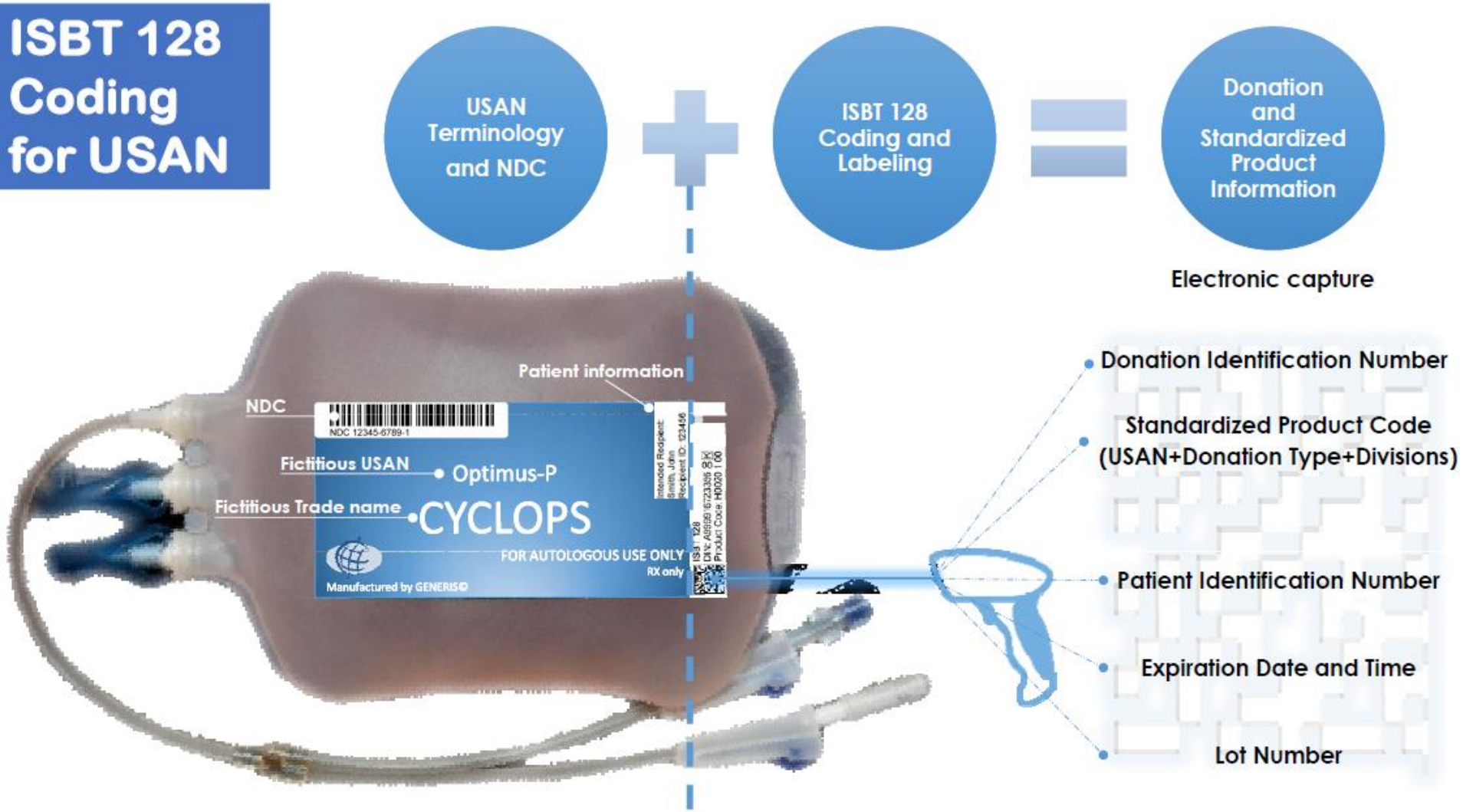
- Autologous MNC products from two patients on same trial from same institution are collected and de-identified post collection
- The following information represented the unique identifiers used (Pt initials – study #-enrollment # and DOB)
  - Product #1 MS – 16034-01 5/1/56
  - Product #2 MS – 16034-02 12/15/55
- CAR-T Products returned
  - MS – 16034-01 12/15/55
  - MS – 16034-02 5/1/56

- Reliant on labeling and identifiers to confirm identity
- No real time serological or antigen testing to confirm identity
- Products could not be used. Error reported to sponsor.

Example 2

- Require Sponsor & CMO to label products with:
  - Patient's name
  - Medical Record Number
  - DOB
- Without notification changed their policy and sent a product without identifiers
- Urgent situation created of not being able to use the product as delivered
- Finally CMO was able to provide documentation linking the product lot number back to the patient and unique identifiers

Marriage of both USAN / NDC and ISBT128



Desired Outcome of This Meeting

- To inform the agency about patient safety risks that is a current and growing concern amongst healthcare providers with advent of manufacturing by industry / commercial CMOs.
  - Unique and traceable product and patient identifiers are not being used.
- To recommend that we work towards using common healthcare standards (AABB, FACT, ISBT 128) regardless of the point of manufacturing for tracking and labeling of cellular product.
  - The use of common standards set forth by accreditation agencies will improve safety, standardize practice and reduce risk of product/patient misidentification.
- To develop working subgroups (the Agency, industry commercial CMO partners, software partners, and accrediting agencies) to educate why moving to common ISBT-128 labeling practices is a win for everyone.
  - Will benefit those developing electronic medical records and cellular manufacturing systems.
  - Will ultimately provide safer products by ensuring the right product gets to the correct patient.

References

- AABB Standards for Cellular Therapy Services, 7th edition
- FACT-JACIE International Standards for Hematopoietic Cellular Therapy, 6th edition
- FACT - STANDARDS FOR IMMUNE EFFECTOR CELL
- ADMINISTRATION, 1st edition - Draft
- ICCBBA – ISBT 128 Cellular Therapy Standard Labeling formats and nomenclature