IMPLEMENTATION GUIDE

Applying ISBT 128 Labels to Collection Products for Further Manufacture

Version 1.0.0

January 2021

Tracking Number ICCBBA IG-045

Published by:
ICCBBA
PO Box 11309, San Bernardino, CA 92423-1309 USA

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1 Introduction

1.1 Purpose

This document is intended to provide guidance to help users implementing standardized labeling of collection products for further manufacture in compliance with the *ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing* (ST-018). This guidance focuses on the labeling of apheresis collection products, but the same principles can be applied to collection products from other sources.

1.2 Scope

This guideline applies to collection products labeled by apheresis collection facilities for further manufacture. These products are intended for further processing, either as part of a clinical trial, or to prepare a manufactured licensed/approved product. Although not explicitly intended for labeling of collection products from other sources, the same principles apply and its use for these products is not prohibited.

The labeling described in this document is NOT suitable for labeling products for direct infusion.

This document is a supplement to the

- *ISBT 128 Standard Technical Specification* (ST-001),
- *ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing* (ST-018),
- *ISBT 128 Standard Labeling of Medical Products of Human Origin with INN and USAN Nonproprietary Names* (ST-016), and
- *ISBT 128 Standard Use of Clinical Trials Product Description Codes (PDCs)* (ST-022).

1.3 Intended Audience

The intended audience of this document is clinical trials' sponsors, manufacturers, staff at clinical trials facilities, apheresis collection centers, hospitals that receive clinical trials or manufactured products (managers, information technology, quality, validation, and laboratory), software developers, and label/software vendors.

1.4 Normative References

ISBT 128 Standard Technical Specification (ST-001)

ISBT 128 Standard Terminology for Medical Products of Human Origin (ST-002)

ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing (ST-018)

ISBT 128 Standard Labeling of Medical Products of Human Origin with INN and USAN Nonproprietary Names (ST-016)

ISBT 128 Standard Use of Clinical Trials Product Description Codes (PDCs) (ST-022)

1.5 Other References

ICCBBA website (www.iccbba.org)

Implementation Guide: Use of the Donation Identification Number [Data Structure 001] (IG-033)

Implementation Guide: Use of Flags in the Donation Identification Number for Process Control of Critical Points during Processing and Distribution (IG-010)

Implementation Guide: Product Coding [Data Structures 003 and 032] - Cellular Therapy (IG-022)

Implementation Guide: Use of Data Matrix Symbols with ISBT 128 (IG-014)

1.6 Overview

This document provides guidance on the use of the standardized hybrid ISBT 128/manufacturer label specified in ST-018. It includes information on:

1. Donation Identification Numbers and their assignment.
2. Selecting Product Description Codes.
3. Data Structures used on the label.
4. Guidance on text used on the label.
5. Traceability.

The guidance has been prepared in collaboration with industry stakeholders through the Standards Coordinating Body.

2 Donation Identification Numbers and their Assignment

2.1 Donation Identification Number (DIN)

The Donation Identification Number (DIN) uniquely identifies a collection event and provides an anonymous secure means of providing a single electronically readable identifier from the point of collection to infusion.

The DIN is thirteen characters long and it contains three elements:

- The first element is a five-character Facility Identification Number (FIN) that identifies the organization that assigned the DIN. The FIN is globally unique and is assigned to facilities registered with ICCBBA.

- The second element is a two-character year, and it supports uniqueness for a one-hundred-year period. This is a nominal year identifier and should not be used as an alternative to other data structures (such as collection date, expiration date, etc.).

- The third element is a six-character sequence number assigned by the facility. The facility is responsible for ensuring the sequence number is unique to each collection event for a given year and FIN.

2.2 Facility Identification Number (FIN)

All ISBT 128 DINs commence with a five-character Facility Identification Number (FIN). FINs are globally unique identifiers issued by ICCBBA to licensed facilities. In order to obtain a FIN a facility needs to register with ICCBBA and become licensed. Information on the registration process is available on the ICCBBA website (www.iccbba.org).

The FIN is an integral part of the Donation Identification Number (DIN) and identifies the organization that assigned the DIN.

The ISBT 128 Facility Identification Number Database is available to licensed users in the password-protected area of the ICCBBA website.

Facilities may request more than one FIN if it is not possible to manage the FIN allocation on a centralized basis.

2.3 When to Assign a DIN

The DIN should be assigned prior to, or at the time of collection. It must be affixed to the product at the time of collection and be transferred to all products prepared from the collection product through to the point of clinical application or product pooling.

When product pooling occurs, a new DIN is assigned by the facility performing the pooling to identify the product pool. The new DIN should carry the FIN of the pooling facility, and the name and location printed beneath the DIN bar code should be that of

the pooling facility. The facility responsible for issuing the pooled product DIN is responsible for maintaining traceability information to link the pooled product DIN to the DINs of the constituent products.

The DIN must be recorded in the patient record at the time of clinical application for traceability purposes.

The responsibility for assigning the DIN may vary depending on the sponsor/manufacturer procedures. Guidance is provided for the following situations:

- **Assignment by the Apheresis Collection Facility**

  The collection facility must be registered with ICCBBA and will have a Facility Identification Number (FIN). They are likely to already be using DINs on their collection products. Depending on the number management strategy at the facility, DINs may be allocated sequentially as used, or the facility may "reserve" a specific range of sequence numbers (e.g., A9992 21 000700 to A9992 21 000800) for use on apheresis collection products for further manufacture. In either case, the collection facility retains the responsibility for ensuring uniqueness of each DIN assigned using its FIN.

- **Assignment by the Sponsor/Manufacturer**

  The sponsor/manufacturer must be registered with ICCBBA and will have a Facility Identification Number.

  The sponsor/manufacturer can provide a range of DINs commencing with their FIN to the collection facility for use on products collected specifically for that sponsor/manufacturer.

  The sponsor/manufacturer is responsible for managing the allocation of DINs carrying their FIN and for ensuring uniqueness is maintained across all collection facilities. They are also responsible for retaining information to link the DIN to the collection facility.

3 Selecting Product Description Codes

3.1 International Product Description Codes

Each International Product Description Code (PDC) is described using internationally standardized terminology that is developed by technical expert advisory groups such as the Cellular Therapy Coding and Labeling Advisory Group (CTCLAG).

The advisory groups utilize a system of Classes that are broad product descriptions (e.g., T CELLS, APHERESIS) and Attributes that provide the means to define the product in detail (e.g., CD34 enriched).

Each product is described minimally with a Class and may also have one or more Attributes. For example: T CELLS, APHERESIS|Citrate/XX/rt|Thawed.

The level of detail that is supported by standardized codes is determined by the technical expert advisory groups and is based on what is thought to be needed for communication of key characteristics to end users, traceability, biovigilance, routine inventory management, and other factors.

Most collection products for further manufacture should be able to use one of these codes:

Product Description Codes are assigned by ICCBBA and can be found in the ISBT 128 Product Description Code Database located at https://www.iccbba.org/tech-library/iccbba-documents/databases--reference-tables

or

ISBT 128 Product Lookup Program located at https://www.iccbba.org/lookup-tools/find-product-information.

If a Product Description Code has not already been assigned to the product, facilities can request a new code using the ISBT 128 Product Lookup Program located at https://www.iccbba.org/lookup-tools/find-product-information.

3.2 Other Types of PDC

Other types of PDC are available for products in clinical trials, or licensed/approved for manufacture, but these are most likely to be applicable to final product labeling.

If the clinical trials product has a nonproprietary name, INN and/or USAN, processing facilities should use the Product Description Code (PDC) corresponding to the INN/USAN. The organization that has acquired the INN/USAN should request the codes from ICCBBA.

Local or national codes might be used for clinical trials products without an existing PDC or a nonproprietary name.

ICCBBA has developed a new category of PDCs specifically for clinical trials products. These Clinical Trials PDCs are standardized global identifiers allocated by ICCBBA. Internationally standardized terminology is not associated with Clinical Trials PDCs. Facilities using Clinical Trials PDCs need to assign a Product Description to these PDCs and need to specify the eye-readable text to appear on the product label. When a product is approved/licensed for manufacture it is anticipated that a PDC corresponding to the INN/USAN or an international standard PDC would be used.

4 Data Structures Used on the Label

Data structures are the means by which information about medical products of human origin (MPHO) can be electronically encoded and interpreted by computers.

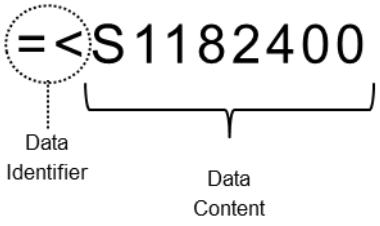
Data structures define the technical characteristics necessary for the interpretation of the information. They specify the context and structure and provide the links to the appropriate reference tables for conversion of codes to meaningful information.

Data structures comprise two elements:

- Data identifier: a two- or three-character code that identifies the type of data structure (e.g., product code, expiration date)
- Data content: the data characters that provide the information to be conveyed (e.g., coded information that indicates a product contains T-cells)

Figure 1 illustrates the two elements of a data structure.

Figure 1 Example of Data Structure



The technical specifications for the use of data structures are found in the *ISBT 128 Standard Technical Specification* (ST-001).

4.1 Required and Optional Data Structures

There are numerous ISBT 128 data structures but not all are required on the label of collection products for further manufacture. Data structures that are required for traceability of these products and must appear on the label include:

- Donation Identification Number [Data Structure 001]
- Product Code [Data Structure 003]

Where an expiration date is present, an additional data structure is required:

- Expiration Date and Time [Data Structure 005]

The collection date and time may be encoded using:

- Collection Date and Time [Data Structure 007]

In order to support the use of two-dimensional (2-D) symbols (Data Matrix), an additional data structure is required:

- Compound Message [Data Structure 023]

Note: Work is underway to develop a standardized format for a globally unique Chain of Identify Identifier. When this is complete, a new data structure will be developed to accommodate this identifier, and this will become a required data structure to be included in the 2-D symbol.

4.2 Donation Identification Number [Data Structure 001]

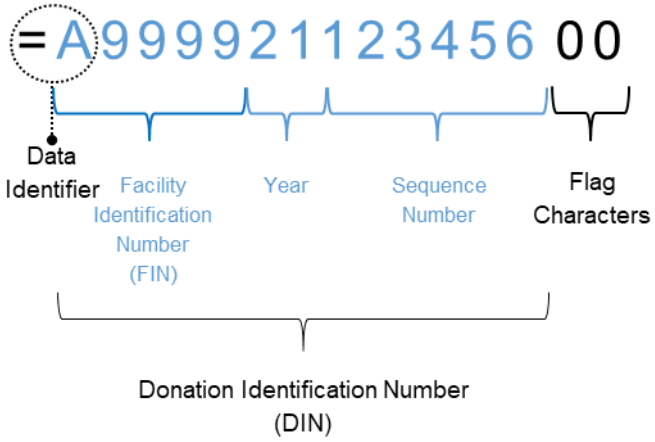
The DIN is carried in the Donation Identification Number [Data Structure 001]. This data structure also carries the optional flag characters.

The flag characters are optional and, when not used, the value of the flags shall be set to the default value of 00 (zero, zero).

Systems receiving ISBT 128 labeled products should be able to accept any valid product flag characters.

Figure 2 shows the Donation Identification Number Data Structure [001].

Figure 2 Donation Identification Number [Data Structure 001]



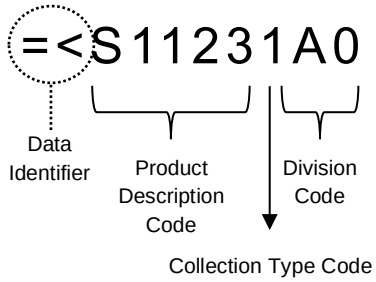
For further information on the use of Data Structure 001 and its elements, refer to:

- *Implementation Guide: Use of the Donation Identification Number [Data Structure 001]* (IG-033) and
- *Implementation Guide: Use of Flags in the Donation Identification Number for Process Control of Critical Points during Processing and Distribution* (IG-010).

4.3 Product Code [Data Structure 003]

Data Structure 003 encodes the information that uniquely defines a product intended for human use. The elements of this data structure vary among product categories. Figure 3 illustrates the elements of this data structure when used for cellular therapy products.

Figure 3 Product Code [Data Structure 003] - Cellular Therapy Products



As shown in the figure above, this data structure contains:

- A two-character data identifier.
- A five-character Product Description Code (PDC).
- A one-character Collection Type Code. The type of collection shall be encoded and interpreted according to reference table RT008 in the *ISBT 128 Standard Technical Specification* (ST-001). Biohazard collections (e.g., autologous biohazard, directed biohazard) are assigned specific codes.
- A two-character Division Code (DIV). This code specifies whether or not the product has been divided.

For further information on the use of Data Structure 003, refer to *Implementation Guide: Product Coding [Data Structures 003 and 032] - Cellular Therapy* (IG-022).

4.3.1 Division Code (DIV)

In order to support traceability, every product carrying the same Donation Identification Number (DIN) and Product Description Code (PDC) shall be differentiated using the DIV. Divisions need not be equal.

If the product has not been divided, and the Product Divisions [Data Structure 032] is not being used, DIV shall be set to the default value of 00 (zero, zero).

If the product has been divided:

- The first of the two characters in the DIV may encode first level divisions (up to 26) by using capital letters followed by a zero, that is, “A0,” “B0,” “C0,” “D0,” “E0,” “F0,” etc.

- Second level divisions (up to 26) may be encoded using the letter of the first level division followed by a lowercase letter indicating the subdivision. For example: “A0” would be subdivided as “Aa,” “Ab,” “Ac,” etc., “B0” would be subdivided as “Ba,” “Bb,” “Bc,” etc.

- The two characters in the DIV may also be used to uniquely identify divisions without regard to hierarchical level. Facilities utilizing this option shall ensure that each product is uniquely identified (i.e., multiple products with the same DIN and PDC shall have a unique DIV).

4.4 Expiration Date and Time [Data Structure 005]

Purpose: Data Structure 005 shall indicate the date and time when the product expires.

Structure: &>cyyjjjhhmm

Element	Length	Type
&	1	data identifier, first character
>	1	data identifier, second character
c	1	numeric {0–9}
yy	2	numeric {0–9}
jjj	3	numeric {0–9}
hh	2	numeric {0–9}
mm	2	numeric {0–9}

The ten (10)-character data content string, **cyyjjjhhmm**, shall be encoded and interpreted as follows:

c shall specify the century of the year in which the product expires

yy shall specify the year within the century in which the product expires

jjj shall specify the ordinal number within the calendar year (Julian date) on which the product expires

hh shall specify the hour at which the product expires (00 to 23)

mm shall specify the minute at which the product expires (00 to 59)

A day shall be defined as beginning at midnight (00:00) and ending at 23:59. When a time is not specified, the default of 2359 shall be encoded in the data structure.

4.5 Collection Date and Time [Data Structure 007]

Purpose: Data Structure 007 shall indicate the date and time of collection or recovery of the product.

Structure: &*cyyjjjhhmm

Element	Length	Type
&	1	data identifier, first character
*	1	data identifier, second character
c	1	numeric {0–9}
yy	2	numeric {0–9}
jjj	3	numeric {0–9}
hh	2	numeric {0–9}
mm	2	numeric {0–9}

The ten (10)-character data content string, **cyyjjjhhmm**, shall be encoded and interpreted as follows:

c shall specify the century of the year in which the product was collected or recovered

yy shall specify the year within the century in which the product was collected or recovered

jjj shall specify the ordinal number within the calendar year (Julian date) on which the product was collected or recovered

hh shall specify the hour at which the product was collected or recovered (00 to 23)

mm shall specify the minute at which the product was collected or recovered (00 to 59)

A day shall be defined as beginning at midnight (00:00) and ending at 23:59. When a time is not specified, the default of 2359 shall be encoded in the data structure.

4.6 Compound Message [Data Structure 023]

The Compound Message Data Structure allows multiple data structures to be combined into a single data string to be used in 2-D symbols and other newer technology delivery systems.

Structure: =+aabbb

Element	Length	Type
=	1	data identifier, first character
+	1	data identifier, second character
aa	2	numeric {0–9}
bbb	3	numeric {0–9}

The five (5)-character data content string, **aabbb**, shall be encoded and interpreted as follows:

aa shall specify the number of ISBT 128 data structures that follow;

bbb shall be either

- all zeroes – indicating this is an undefined message (i.e., only the number of data structures is identified, but not what each one is or the order in which they occur).

  OR

- a three-digit number referencing an entry in an ICCBBA maintained table that defines the sequence of the data structures within a compound message. See Table W2, [RT017] ICCBBA-Specified Compound Messages described in the *ISBT 128 Standard Technical Specification* (ST-001). The reference table is found on the ICCBBA website.

Note: Because of the complexity created by multiple product categories and the many codes that would result from permutations of order of data structures, ICCBBA now encourages the use of undefined messages.

Rules for constructing compound messages:

1. A compound message shall comprise a string of ISBT 128 data structures (excluding nationally defined structures), beginning with the Compound Message [Data Structure 023].

2. Data structures shall be combined with no intervening characters. Each data structure shall begin with its data identifier characters.

3. The string shall only contain ISBT 128 data structures.

4. The number of data structures following the Compound Message Data Structure shall be indicated in element **aa** of the Compound Message Data Structure.

5. If the sequence of the message is unspecified, the Compound Message Data Structure shall have element **bbb** set to zeroes and element **aa** shall be set as specified in Rule 4.

6. If a specified sequence is used, the reference number of the selected message from Table RT017 shall be included in element **bbb** of the Compound Message Data Structure. The order of the data structures shall be that shown in Table RT017 for the reference number selected.

ICCBBA-specified compound messages are defined in Table W2, [RT017] ICCBBA-Specified Compound Messages. While ICCBBA now encourages the use of undefined messages, requests for additional entries may be submitted to the ICCBBA office (tech.manager@iccbba.org).

Reading software should be able to interpret both undefined sequence and ICCBBA-specified sequence compound messages. The software should always verify the integrity of the data string, including checking that the correct number of data structures appears and, when specified sequence messages are used, that the sequence of data structures is correct. Data should only be interpreted if the integrity of the relevant data structures has been confirmed.

For more information, refer to *Implementation Guide: Use of Data Matrix Symbols with ISBT 128* (IG-014).

5 Guidance on Text Used on the Label

The *ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing* (ST-018) indicates the text elements that are required, and those that are optional. This guidance expands on the Standard statements and provides some further explanation.

Collection date and time is optional but recommended. The collection date/time shall be the date/time that the collection was completed. If labels are printed prior to the collection, it may only be possible to print the date – the completion time being unknown at the time of printing. The collection time can be added into accompanying documentation or hand-written alongside the printed collection date.

The intended recipient name and date of birth is optional, but if printed the full name and date of birth is required. The practice of using abbreviated information, such as intended recipient initials or year of birth is regarded as unsafe, as the potential for incorrect identification using this information is significant. Where regulation prevents the use of the full information being printed on the product label, intended recipient identification should be performed using other identifiers, such as the Intended Recipient Identification Number and/or the Chain of Identity Identifier.

Expiration date/time is required for all labile products, as it is important that the sponsor/manufacturer can identify if a product has been delayed in transit and thus rendered unsuitable for use. Shelf-life information should be provided by the sponsor/manufacturer and used by the collection facility to calculate the expiration date.

Expiration times are only required when the product shelf life is short and exact timing is important. If expiration time is not required, it can be omitted from the printed text.

If the product is to be shipped across time zones, the identifier for the time zone of origin is required by AABB and FACT-JACIE Standards. In addition, the ISBT 128 Standard requires that the expiration date/time be indicated using Coordinated Universal Time (UTC) - see Section 4.3 of the *ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing* (ST-018) for details.

The decision to require that dates be printed in ISO 8601-2004 numeric extended format was made to ensure consistent interpretation of dates internationally. Alternative representations using either all numeric dates, or a three-character month identifier, have potential for error. The order of numeric dates varies between counties, thus a date of 07-03-2020 is Mar 7 in Europe but July 3 in the USA. Three-character month identifiers differ depending on the language being used and can be misinterpreted.

6 Traceability

An individual collection event is uniquely identified by its DIN. Each product resulting from that collection event is uniquely identified by the DIN, PDC and DIV. The DIN, PDC and DIV should all be recorded at each point in the collection and processing pathway to ensure traceability.

Where a final product is prepared from a single collection event, the DIN of the collection event should be carried through to the final product labeling and recorded in the patient record. This provides the most direct and rapid form of traceability, as the DIN allows the facility that assigned the DIN to be identified.

For autologous products, a DIN can be affixed in the patient records at the time of collection of the starting material, and this identifier can be used to electronically verify a match with the DIN on the final product.

Where a final product is prepared from pooled material from multiple collection events, the facility performing the pooling should assign a DIN carrying their own FIN to the pooled product. The DIN on the final product should be carried through to the patient record. In this situation, traceability lookback uses the DIN to identify the facility that assigned the DIN (the pooling facility). That facility is responsible for maintaining the link between the collection product DINs and the pooled product DIN and therefore, can provide the information to track back to the original collection facility.

Sponsors/Manufacturers also allocate a “Chain of Identity” (CoI) identifier defined as “A unique code used to discern a cell or gene therapy and the intended therapy recipient.” As this identifier is associated with an individual therapy, it will be applied to all the collection products used to prepare that therapy. Thus, in the pooled example above, each individual collection would be identified by a different DIN, but because they are all intended for use in the same therapy, would carry the same CoI identifier. At the current time, this CoI identifier is manufacturer dependent, varies in format between manufacturers, and may not be unique across different manufacturers. An initiative is underway to develop a globally unique standardized CoI that can be incorporated into the bar coded information on the product label.

