ISBT 128
For Cellular Therapy

An Introduction

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1 Preface

A great deal of important information is presented on the label of a cellular therapy product. The information varies from country to country according to licensing regulations, language differences, and local practice but, in all cases, it is essential that it is recorded accurately, transferred correctly, and that critical items such as the blood groups, expiration date, and product description are clearly understood by medical personnel transfusing or transplanting the product. In addition, robust audit trails must be in place to allow tracing between donor and recipient.

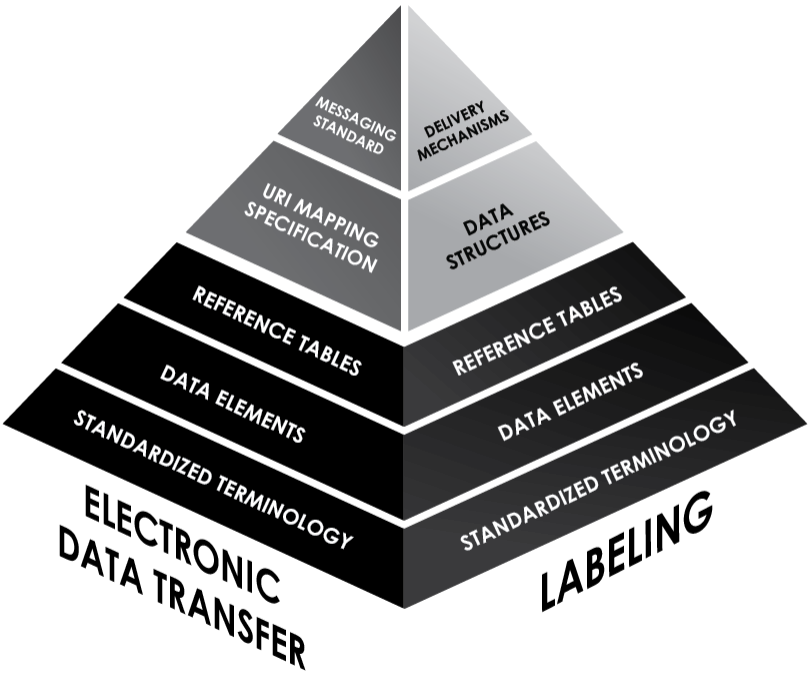
The field of Cellular Therapy (CT) is very much a global one and CT products are regularly transferred across national boundaries. There is a clearly identified need for international agreement on product descriptions and a means of ensuring the unique identification of each donation throughout the world. These fundamental requirements are essential for effective traceability on a global scale.

Increasingly, facilities dealing with the collection, processing, and administration of CT products operate sophisticated computer systems to enhance safety and efficiency. Transfer of information between such facilities by electronic means ensures accuracy, but can only be effectively achieved in a global context by use of internationally agreed standards to define the information environment.

2 What is the Information Environment?

The information environment model describes how ISBT 128 organizes information to achieve standardization for both labeling and electronic messaging for medical products of human origin.

The foundation of the information environment contains standardized terminology, data elements, and reference tables. These layers support the structures, mechanisms, specifications, and standards necessary to print labels and create electronic messages. These layers are illustrated and described below.



Standardized Terminology

At the base lies the standardized terminology, ISBT 128 Standard Terminology for Medical Products of Human Origin (ST-002), that will ensure a common understanding of terms. ISBT 128 Standard Terminology is the foundation used for both labeling and electronic messaging. Without clarity at this level any further attempt at standardization is lost. Obtaining agreement on standardized terminology at the necessary level of detail involves careful analysis and robust consensus.

ICCBBA ensures that an internationally agreed upon standardized terminology is defined at the required level of granularity. This provides confidence in the consistency of both the information being transferred and the quality of the product described. The standardized terminology is accessible to all users of the Standard and ISBT 128 stakeholders.

There are terms regularly used in certain categories of MPHO that require an appropriate level of granularity to clearly convey the characteristics of the product. For cellular therapy products, DMSO is used during the cryopreservation process. However, different concentrations may be used, and hydroxyethyl starch may be added. To accommodate these variations, a range of standardized terminology and associated values are required.

Data Elements

Product information and characteristics such as the Donation Identification Number, ABO RhD, and Product Description Code each constitute a data element. Data elements can be encoded within data structures suitable for use in bar codes applied to product labels, and they can also be identified by a unique resource identifier (URI) in the form of a uniform resource locator (URL) for use in electronic messaging. Data elements provide a mechanism to unambiguously define pieces of information. The data elements are used to build data structures, and in some instances, more than one data element is needed to encode a data structure.

Example:
The product code data structure contains up to 3 data elements: the Product Description Code, the Collection Type, and the Division Identifier.

Reference Tables

Reference tables are built to code/decode a single or multiple data elements to provide data compression for use in a data structure. Such tables can be large and complex, and it is essential that they are managed to ensure that they can be modified to meet changes within clinical practices in a manner that maintains their integrity and avoids ambiguity or redundancy.

Reference tables combine a tightly defined structure while allowing the flexibility to accommodate expansion and change in ways that cannot be anticipated.

Successful management of standardized terminology, data elements, and reference tables requires input from both clinical experts in the field and information specialists. The tables are published in a manner that allows all users of the Standard to access the most up-to-date versions in a timely manner.

Together, the standardized terminology, data elements, and reference tables provide the basis for accurately relaying information about medical products of human origin, whether on the label or via electronic data transfer.

Electronic Data Transfer

URI Mapping Specification for use in Electronic Messaging

To support the transmission of ISBT 128 information via electronic messaging, ICCBBA has developed a dictionary of data elements, ISBT 128 Dictionary of Standard Data Elements (ST-027). The information carried in these elements maps to the same information carried in data structures to ensure that information from either source is consistent. Each data element is identified by a unique resource identifier (URI) in the form of a uniform resource locator (URL).

To view an example of a Product Description Code, go to https://www.isbt128.org/uri/ProductDescriptionCode.

Messaging Standard for use in Electronic Messaging

ISBT 128 provides specifications ISBT 128 Standard for XML (ST-020) for use in electronic messages to convey information regarding MPHO in a consistent and standardized format.

The MPHO Unique Identifier is a single unique instance identifier developed to provide the basic elements of traceability. The MPHO Unique Identifier was developed to store traceability information on any MPHO and provides a single identifier for use in electronic messaging and electronic health records and should be used as the identifier element for the HL7 FHIR BiologicallyDerivedProduct resource.

This identifier can be created from a standard ISBT 128 label and clearly identifies the specific product being referenced in an electronic message. Specifications for the MPHO Unique Identifier are detailed in ISBT 128 Standard for the Medical Products of Human Origin (MPHO) Unique Identifier (ST-026).

Electronic Messages

The development of a standardized approach to incorporate ISBT 128 Data Elements into electronic messages is an important step in improving the communication between healthcare organizations involved in the production and clinical application of MPHO. By adopting this Standard, organizations will be able to benefit from the MPHO-specific standardized terminology and standard reference tables of ISBT 128 in a wide range of contexts and securely transfer more information about MPHO products with far greater flexibility.

Labeling

Data Structures for use in Labeling

Having built reference tables which convert the clearly defined information into codes suitable for use in bar codes applied to product labels, it is necessary to define data structures in which to embed the data. 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 must be clear and unambiguous and consider any constraints imposed by the anticipated delivery mechanisms. For example, data structures that will be used in linear bar codes are limited in the number of characters they can contain.

Data identifiers indicate the type of information being conveyed within data structures. It is imperative that the appropriate data identifiers are used for each data structure to ensure the correct interpretation of the encoded information.

Delivery Mechanisms for use in Labeling

The delivery mechanism is the means of delivering the electronic information encoded within data structures. The most well-known delivery mechanism is the linear bar code that has been used in blood transfusion practice for many years.

Higher capacity delivery systems are available using Data Matrix two-dimensional (2-D) or reduced space symbology bar codes. These codes can carry much more information in each symbol. More recently the use of radio frequency identification (RFID) chips that can carry encoded information is being developed for medical products of human origin.

It is important to recognize that a range of delivery systems can sit at this level of the hierarchy. The standardized terminology, reference tables, and data structures of the information Standard can be delivered as easily in a linear bar code as they can in an RFID tag. The Standards themselves must be adaptable to make the best use of new delivery mechanisms, such as Bluetooth Low Energy tags, as they are developed.

Information Environment Summary

Every ISBT 128-labeled product carries a standardized label where product information is encoded in bar codes or electronic tags. Although there will be other labeling requirements that fall outside the coding system, an effective coding system should consider the physical association between the information and the product. Whether incorporated into a bar code or an electronic tag, there needs to be a mechanism that will ensure the correct physical assignment of information to the product, and confidence in the association between electronically stored information and eye-readable printed information.

This latter requirement must not be overlooked in the enthusiasm to embrace remotely rewritable tags.

While highly effective and secure, labeling does have some limitations. In particular, the amount of information that can be encoded on the label depends on the amount of label space available to accommodate bar codes. Thus, as noted in previous sections, ISBT 128 has evolved to allow ISBT 128 information to be transmitted in electronic messages used in healthcare applications in a manner that is compatible with its existing labeling standards, giving the Standard the ability to overcome the limitations of bar codes.

The information environment works together to ensure that accurate ISBT 128 information is encoded within an electronic message or label to accurately identify MPHO products. For such a system to be, and to remain effective, it must be carefully designed and managed. There must be an ongoing dialogue between clinical users, information specialists, and equipment and software vendors to ensure that the Standard continues to support rapidly developing clinical practices, ensures traceability, improves biovigilance, and increases patient safety.

3 The ISBT 128 Standard

The ISBT 128 Standard provides the specification for many of the elements of the information environment required in transfusion and transplantation. It defines the lower three levels of the model: the standardized terminology, reference tables, and data structures. Minimum requirements are also defined for delivery mechanisms and labeling. By complying with ISBT 128, collection and processing facilities can provide electronically readable information that can be read by any other compliant system.

ISBT 128 specifies:

- a donation numbering system that ensures globally unique identification over a 100-year period;
- the information to be transferred, using internationally agreed reference tables;
- an international product reference database;
- the data structures in which this information is placed;
- a bar coding system for transfer of the information on the product label;
- a standard layout for the product label;
- a standard reference for use in electronic messaging.

The Standard, originally designed for use in blood transfusion, has been expanded and developed over time to accommodate the adapting needs of various MPHO industries. This inherent elasticity of the Standard has led to its international acceptance and widespread use for labeling of MPHO products, with more than 40 million MPHO products labeled using ISBT 128 each year.

Following meetings between FACT, JACIE, and ICCBBA, an agreement was reached to support the use of ISBT 128 for coding and labeling CT products, and this decision has been endorsed by the boards of major cellular therapy professional organizations. Third Consensus Statement of Terminology, Coding and Labeling of Cellular Therapy Products (JP-005).

A plan for full implementation of ISBT 128 is also required by AABB. The most current version of the standard terminology is maintained on the ICCBBA website at www.isbt128.org.

4 Unique Donation Identification Number (DIN)

ISBT 128 provides for unique identification of any donation worldwide. It does this by using a 13-character DIN built up from three elements: the first identifying the facility that assigned the DIN (e.g., the collection facility, registry, etc.), the second the year in which the DIN was assigned, and the third a sequence number controlled and maintained by the facility that assigned the DIN.

For example:

S0020 23 001021 10 **F**

Where:

S0020 identifies the collection facility (in this case Karolinska University Hospital, Stockholm, Sweden);

23 identifies the collection year as 2023;

001021 is the sequence number of the collection assigned by the collection facility.

The two digits printed vertically allow individual bar codes in a number set to be discretely identified, hence providing an option to add process control.

An additional character is enclosed in a box at the end of the identifier. This is a checksum character used when a number is entered into a computer system through the keyboard to verify the accuracy of the keyboard entry.

Facility codes are assigned by ICCBBA, who maintain a database of all registered facilities that can be found on their website (www.isbt128.org). A lookup program allows the look up of individual facility codes. ICCBBA licensed facilities and vendors are able to download a full listing of all registered facilities.

5 Product Descriptions

ISBT 128 provides a comprehensive and highly flexible system for describing products and assigning Product Description Codes. The foundation of this system is a standard terminology which is constructed by international consensus to ensure global consistency in use and understanding. The standard terminology is maintained on the ICCBBA website and is publicly available. Cellular therapy terminology and coding is managed by ICCBBA and the international Cellular Therapy Coding and Labeling Advisory Group (CTCLAG). Following the standardization of cellular therapy product labeling using ISBT 128, it has been recognized that there is a need to uniquely identify Clinical Trials products using the Standard. To accommodate this need, rather than assigning a wide range of terminology to describe these products, the CTCLAG approved a new category of PDCs specifically for clinical trials. These clinical trials PDCs are allocated by ICCBBA and maintained within the Clinical Trials PDC database separately from globally standardized PDCs. ISBT 128 Standard Use of Clinical Trials Product Description Codes (ST-022).

New products are defined by combining pieces of information from the standardized terminology in a way that unambiguously describes the product. This process is made easier by the use of the concepts of component class, core conditions, and attributes.

Each unique product description is assigned a Product Description Code that becomes incorporated into the ISBT 128 Product Description Code Database, ensuring that the product will be accurately identified in any country in the world that is using ISBT 128.

New entries into the Product Description Code Database can be readily accommodated allowing the system to expand to meet a growing range of products without losing the overall structure of the coding system.

The following example is taken from the database:

Component Class:	HPC, CORD BLOOD
Core Conditions:	NS (anticoagulant not specified)
	XX (variable volume)
	<=-150C (storage condition)
Attributes:	10% DMSO
	Other Additives:Yes
	Cryopreserved

Product Description Code: S1150

While the description of a product in the Product Description Code Database is standardized, the text that appears on the actual label of a product is under national control. This allows for differences in languages and regulatory requirements.

6 Other Data Structures

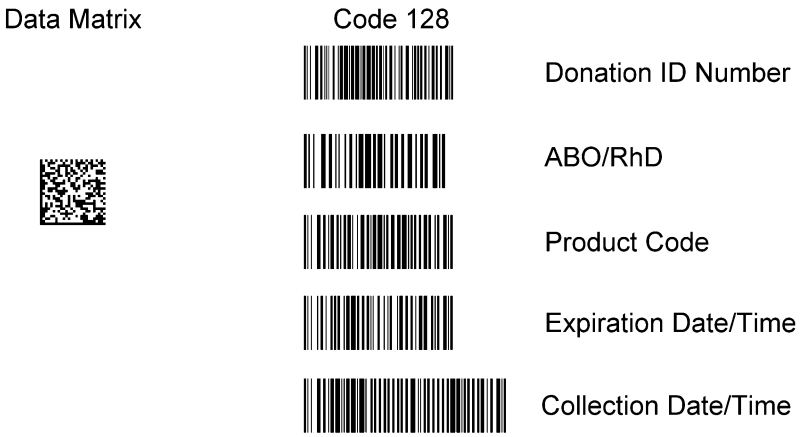
In addition to the donation identifier and product codes, many other pieces of important information need to be provided with a CT donation. Through its wide range of data structures, ISBT 128 provides significant information including, but not limited to:

- ABO and RhD Blood Groups;
- Collection Date and Time;
- Expiration Date and Time;
- Collection Container Catalog and Lot Number;
- Donor Identification Number;
- Patient Date of Birth;
- Patient Identification Number;
- Flexible Date and Time (supporting encoding of local time, or UTC)

7 Delivery Mechanisms

The delivery mechanism is the means by which the information is represented in a machine-readable manner. The most common such mechanism is the linear bar code. ISBT 128 has traditionally been based on the linear bar code using Code 128 symbology. However, a two-dimensional Data Matrix symbol can be used on cellular therapy labels and is preferable to maximize space on a partial label. A single Data Matrix symbol can carry the same information as encoded in multiple linear bar codes. With very small containers, label size is severely restricted and, in these situations, a more efficient two-dimensional Data Matrix symbol can be used.

Comparative Size of Code 128 and Data Matrix Symbols



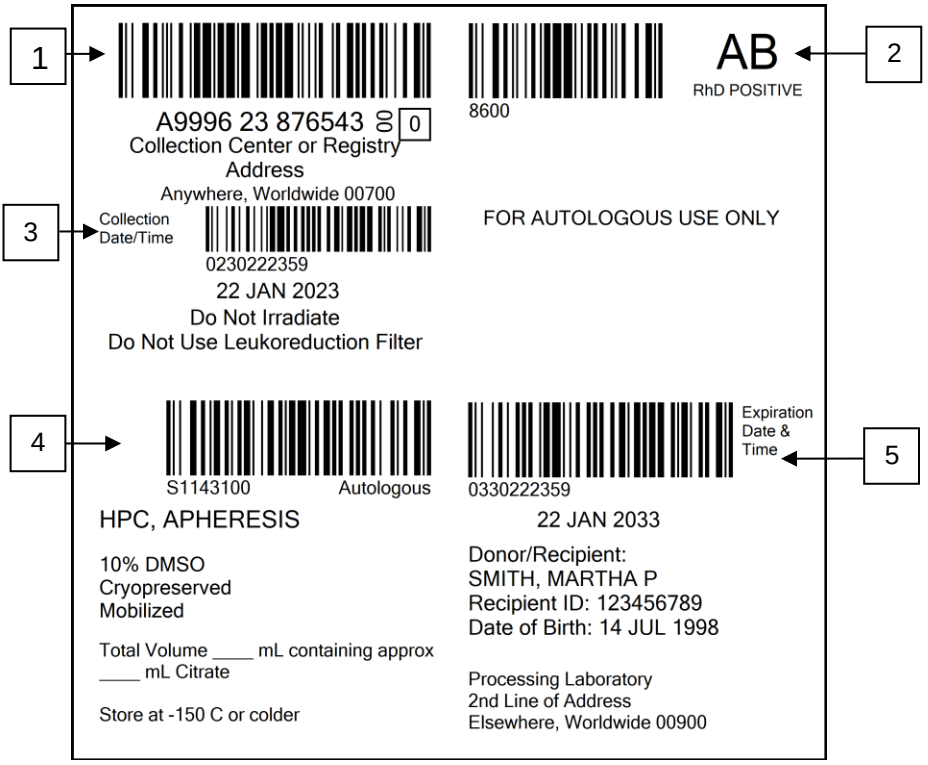
The Data Matrix symbol on the left contains all of the information held in the five Code 128 symbols on the right.

There is much interest in the use of RFID tags. This technology is still developing but may provide significant benefits in some situations. ISBT 128 Compound Messages are compatible with RFID.

8 Product Labeling

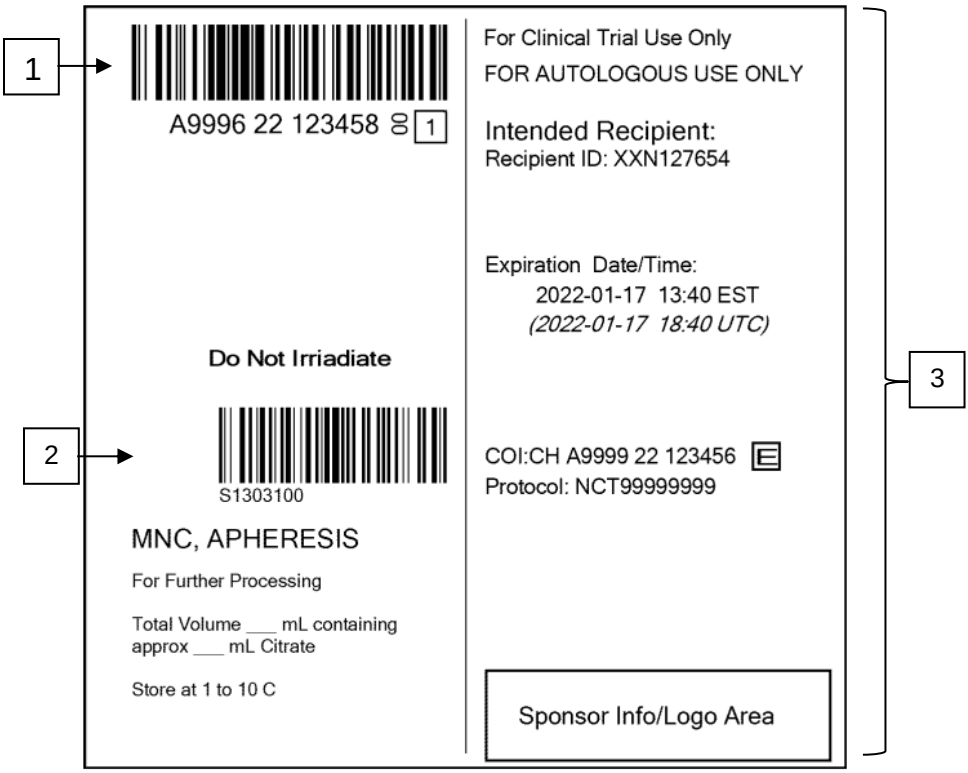
In addition to specifying the requirements for the electronic coding of information, ISBT 128 provides a standard labeling format that ensures a consistent layout of the bar codes on product labels. Critical eye-readable information such as blood groups, product description, and expiration date also appears in fixed positions on the label. This reduces the risk of confusion when products from multiple sources are being used.

The ISBT 128-specified label is illustrated below. Additional label examples and further information may be found in the ISBT 128 Standard Labeling of Cellular Therapy Products (ST-004).



1 Donation Identification Number
2 ABO/RhD
3 Collection Date/Time
4 Product Code
5 Expiration Date/Time

Products collected with the intent for further manufacture follow a labeling format similar to the ISBT 128 labeled products intended for transfusion and is illustrated below. This labeling format provides ISBT 128 traceability information on the left side of the label and manufacturer supplied information on the right side of the label. This hybrid-label format is detailed within the ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing (ST-018). Specifications for the structure of the ISBT 128 CoI can be found within the ISBT 128 Standard Chain of Identity (CoI) Identifier (ST-028).



1 Donation Identification Number
2 Product Code
3 Manufacturer Provided information

Labels have also been designed for smaller containers, such as cryopreservation container labels. The example shown below uses a Data Matrix 2-D bar code in the upper left corner to record the Donation Identification Number, Product Code, Expiration Date, Collection Date, Patient Identification Number (Patient ID), and Patient Date of Birth.

A9999 23 123456 DD 6
Product: S1142X00

HPC, APHERESIS

6% HES + 5% DMSO
Cryopreserved, Mobilized
____ mL containing ____ mL Citrate + ____ mL Heparin (____ units/mL)
Store at -150 C or Colder
Collection Center or Registry
Anywhere, Worldwide
Collection Date: 03 FEB 2023
Expiry Date: 03 FEB 2033 *Partial Label*

BIOHAZARD

FOR AUTOLOGOUS USE ONLY

Donor/Recipient:
PATIENT, JOHN Q
Recipient ID: 123456789
Date of Birth: 31 DEC 1984

Processing Facility
Anywhere, Worldwide

9 The Role of Technical Advisory Groups

ICCBBA involves international experts in various MPHO fields in the development and maintenance of the Standard. These experts are organized into Technical Advisory Groups (TAGs) that meet regularly (through conference calls, face-to-face meetings, and asynchronous discussion forums) to further develop and expand the Standard ensuring it continues to meet the needs of its users. The vital role of these groups cannot be overemphasized. It is only through the involvement of such expert panels that ICCBBA can be assured it has the knowledge base to anticipate the needs of its users in fields where change is constant. More than 300 experts participate in the ICCBBA TAGs.

For Cellular Therapy, the advisory group is the Cellular Therapy Coding and Labeling Advisory Group (CTCLAG). The group comprises representatives from the following professional organizations: AABB, Asia Pacific Blood and Marrow Transplant (APBMT), American Society for Blood and Marrow Transplantation (ASBMT), American Society for Apheresis (ASFA), European Group for Blood and Marrow Transplantation (EBMT), Foundation for the Accreditation of Cellular Therapy (FACT), ICCBBA, International Society of Blood Transfusion (ISBT), International Society for Cellular Therapy (ISCT), Joint Accreditation Committee of ISCT and EBMT (JACIE), Latin American Blood and Marrow Transplant Society (LABMT), National Marrow Donor Program (NMDP), and the World Marrow Donor Association (WMDA). In addition to these representatives, technical experts and regulatory liaisons also serve on the committee.

CTCLAG reviews requests for new terminology ensuring consistency and consensus in terminology, prepares educational materials, and assists ICCBBA with organization of workshops by providing expertise from the cellular therapy industry so that ICCBBA can better aid ISBT 128 users around the world.

10 The Role of ICCBBA

ICCBBA is the not-for-profit standards body responsible for the management, development, and distribution of the ISBT 128 Standard. It maintains a permanent office to manage the registration of facilities, update reference tables and databases, and develop additional functionality. It supports Technical Advisory Groups that include experts from both the transfusion/transplantation community and relevant manufacturers. Fees collected by ICCBBA from registered facilities are used to support these functions.

Through its activities ICCBBA provides the management support essential to sustain standard coding in the complex and rapidly changing field of cellular therapy. In particular it delivers:

1) Stability – users can be confident in the stability of the Standard to satisfy the long time periods over which information has to be retained (e.g. European Commission requirements for data to be stored and traceable for 30 years);
2) User focus – the user community are the experts in their field and ICCBBA, through its Technical Advisory Groups, ensures that the information standard meets, rather than dictates, user needs;
3) Flexibility – as clinical and scientific knowledge grows there is rapid development with changing information needs. ICCBBA ensures that the Standard is flexible enough to accommodate those needs;
4) Responsiveness – in these rapidly developing medical fields ICCBBA ensures that the Standard is able to respond to user needs in a timely manner;
5) Globalization – ISBT 128 is an international Standard with endorsement worldwide;
6) Compatibility – standards do not work in isolation but need to interface with equipment, software, and other standards. ICCBBA works with industry and other standards bodies to maximize compatibility.

MPHO collection and processing facilities, and manufacturers of equipment or software that uses ISBT 128, are required to register with ICCBBA and pay a registration and an annual licensing fee. Registered organizations obtain access to all ICCBBA documents and databases.

For further information on ISBT 128, visit the ICCBBA website at www.isbt128.org, email our help desk at support@isbt128.org or call us at +1 909 793 6516.

END OF PUBLICATION

FOR ICCBBA USE ONLY

These links are for internal document control and cannot be used externally:

ST-002 ISBT 128 Standard Terminology for Medical Products of Human Origin
ST-018 ISBT 128 Standard Labeling of Collection Products for Cellular Therapy Manufacturing
ST-020 ISBT 128 Standard for XML
ST-026 ISBT 128 Standard for the Medical Products of Human Origin (MPHO) Unique Identifier
ST-027 ISBT 128 Dictionary of Standard Data Elements
ST-028 ISBT 128 Standard Chain of Identity Identifier

